

SCIENTIFIC SECTION

A STUDY OF EPHEDRA NEVADENSIS.*

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CHAPTER I.

INTRODUCTION.

Purpose of the Study.—From time to time, specimens of *Ephedra nevadensis*, known as "Mexican Tea," have been submitted for analysis. A study of the available literature indicates that there is some question as to the active constituents of this drug. This research was undertaken to determine the constituents and the therapeutic properties of the plant *Ephedra nevadensis*, so that they might be more clearly understood and made available.

Botanical Classification of Ephedra.—The genus *Ephedra*, Family *Gnetaceæ*, may be divided into three geographical groups as follows:

1. *The Asiatic Group.*—This group consists of *Ephedra vulgaris* and its varieties, and *Ephedra distachya*.

2. *The European Plant.*—This is chiefly the variety *helvetica* of *Ephedra vulgaris*.

3. *The American Group.*—Some six species of *Ephedra* have been described as native of North America: five of these are mentioned as found in the California area (1). The six species are:

(a) *E. californica*, Watson ("Proc. Am. Acad.," 14, 300, (1879)). Localities, Mohave Desert (Lone Willow Spring) and in Panamint Valley, Whitewater (Riverside County), Campo and Jacumba Hot Springs, San Diego County, Tia Juana.

(b) *E. nevadensis*, Watson (*Ibid.*, 298). Localities, general in the Mohave Desert in the Juniper belt, near Acton, Jacumba Hot Springs.

(c) *E. trifurca*, Torrey in Emory ("Pas. R. R. Rep.," 152 (1848)). Localities, said to be abundant along the Mohave River around Daggett.

(d) *E. viridis*, Coville ("Centr. Nat. Herb.," 4, 220 (1893)). Localities, Mt. Pines, Sespe Creek, Bear Valley, Cushenberry Springs, San Bernardino Mts.

(e) *E. Torreyana*, Watson (*Ibid.*, 299). Probably not in California.

(f) *E. antisiphyletica*, found in Texas and New Mexico.

These three geographical groups of *Ephedra* are distinct in that their active constituents differ greatly.

1. *Asiatic.*—Nagai (2) studied the *Ephedra vulgaris* found in Japan, and from it extracted an alkaloid which he named Ephedrine. This substance was studied by Kinnessuke from the pharmacologic standpoint. It was found that in lower animals an acceleration of the pulse, elevation of the rectal temperature, and dilation of the pupils of the eyes resulted from the administration of the alkaloid. If given in large enough doses, convulsions and even death resulted from the arrest of the heart and the respiratory muscles. When administered to man, Scriba found that a mydriatic action resulted. The dilation was accomplished in from forty to sixty minutes, and was without irritation. The effects persisted over a period of from five to twenty hours.

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The therapeutics of this alkaloid have been studied recently by K. K. Chen and Carl F. Schmidt. A statement of their conclusions is as follows (3):

It appears from the pharmacodynamic studies that ephedrine is of considerable value as a circulatory stimulant in surgical shock, as a bronchial dilator in asthma, as a mydriatic, and as an apparently specific remedy in Addison's disease.

Chen and Schmidt also found that ephedrine was capable of being absorbed from the gastro-intestinal tract without change, and that the solutions of the salts were very stable. From this data, it would seem that the alkaloid might be of definite value in medicine. The other Asiatic species, *Ephedra distachya*, yields an alkaloid unlike ephedrine in that it is not mydriatic nor poisonous. This plant is used in the treatment of gout and syphilis, which require none of the vaso-effects prominent in the ephedrine. By some persons, this alkaloid is thought to be an isomeric form of ephedrine. For this reason it has been named pseudo-ephedrine.

2. *European*.—The plant *Ephedra vulgaris*, variety *helvetica*, has been naturalized in the Mediterranean Basin, and is found in certain localities in Central Europe. This plant yields an alkaloid which is isomeric with ephedrine, and has been named pseudo-ephedrine by Merck (4). Ephedrine, Merck, is an article of commerce and is listed in current price lists.

3. *American*.—Very little data are available through literature concerning the constituents of the five or six species of *Ephedra* common in the Southwestern part of the United States. The presence of the tannin seems to be the basis for the use of the drug, for "Loew thinks that their virtues reside in a peculiar tannin(2)." Rothrock states that the filtrate of the aqueous solution proved the presence of tannin and tartaric acid. Pectin was also shown to be in the filtrate, since a jelly-like precipitate appeared when the alcohol was added. The tannin belongs to the glucosidal group, furnishing sugar on treatment with acids and various other compounds, and upon distillation (dry) pyrogallic and carbonic acids. This tannin splits into sugar and a red amorphous powder. This powder Dr. Loew considers quite a distinct body which he names ephedrine: to this he attributes (probably correctly) the remedial properties of the plant.

CHAPTER II.

HISTORICAL REVIEW.

There is a wealth of reference to the genus *Ephedra* in literature, but most of these are from the botanist's viewpoint. Perhaps the earliest mention of the medicinal value of *Ephedra* was made by Dr. Harvard in 1885, when he described the plants as "Popular remedies among Mexicans and frontiersmen in the treatment of syphilis and gonorrhœa, especially the latter. The decoction or infusion of the stems has an acid reaction and an astringent taste resembling that of tannin (5)."

It is the extended use by the Mexican people of the drug which led to this study. The drug is known as Popotillo (popé-a-tella) among them, but also called various names such as Mexican Tea (6), Mormon Tea (7), Caynote (2), Canutilo (2), Teamster's Tea and Squaw Tea (7) by the early white settlers of the desert regions. While it has a very astringent taste, it is said that those who become accustomed to it prefer an infusion of this plant to the beverage made from the leaves of *Thea sinensis*. The teamsters are said to have carried bundles of the shrub hung under their wagons, hence the name of Teamster's Tea.

It has been said that the Indians of Arizona used the drug *Ephedra* as a kidney remedy. They used it in the form of an infusion in doses of from one-half to two ounces. The action is said to be of a diuretic nature, greatly increasing the flow of urine.

CHAPTER III.

THE PHARMACOGNOSY OF *EPHEDRA NEVADENSIS*.

Habitat Description.—The plant is a small, shrub erect in habit, approximately

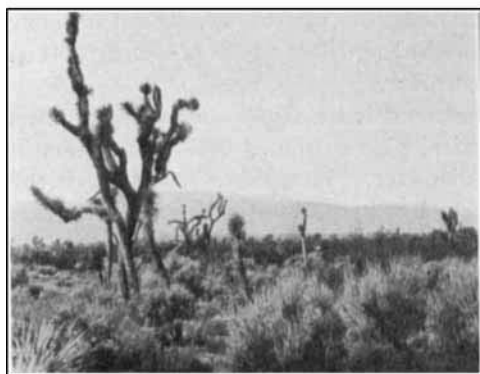


Fig. 1.—Mohave Desert. Darker colored plants in the foreground are *Ephedra nevadensis*.



Fig. 2.—Habit photograph of *Ephedra nevadensis*.



Fig. 3.—Habit photograph of clump of *Ephedra nevadensis*.



Fig. 4.—Habit photograph showing prostrate individual plant. *Ephedra nevadensis*.

50 to 90 centimeters in height, and has divergently spreading glaucous green, scabrous branches. Abrams continues describing it as follows (6):

“... leaf-like scales in 2's, 3 to 6 mm. long, sheathing to about the middle, obtuse or tapering at the apex, mostly deciduous in age; staminate ament sessile with 4 to 6 parts of the bracts; fruiting bracts of 4 to 5 parts, round-ovate, sessile; fruit exserted, acutish at apex.”

“... characteristic of the lower part of the Juniper-belt and the upper part of the Covillea belt of the desert regions, Upper and Lower Sonoran Zones: Nevada and Southern Utah southward through Arizona to Northern Mexico, and through the

Mohave and Colorado Deserts of California to Northern Lower California. Type: Pah Ute Mountains, altitude 5000 feet, and Carson City, Nevada."

The material used in the analysis made in this study was collected at the Eastern end of Cajon Pass, at a point about midway between the towns of Summit and Victorville, San Bernardino County, California. It was found growing in scattered colonies in the sandy soil of this area, and was intermingled with the Juniper and Joshua trees of this vicinity.

The method of collection consisted of simply pulling up the plants and spreading them out to air dry. In the commercial drug, the tips are usually cut into fine pieces approximately two to five centimeters in length by means of a drug cutter. The larger portions are removed by hand garbling.

Pharmacognostic Description.—**Macroscopical:** *Ephedra nevadensis* occurs in the market in the form of short cylindrical pieces, from 2 to 5 centimeters in length and from 1.5 to 4 millimeters in diameter. The most prominent of the external markings is the nodal portion, which consists of double opposite scars or adhering scale leaves. The internodal portions are finely longitudinally striate and are of peculiar roughened appearance usually associated with the members of the *Carex* group. The drug is of a light yellow-green color, and has a very fibrous fracture due to the large amount of bast in the cortex. The internal color is light brown for the cortex, and a deep red-brown for the pith area. The odor is slight, but rather aromatic, somewhat pine-like. The taste is aromatic and astringent.

The scale-like appendages are sometimes wanting, indicating that they do not function as the site of food production. On the other hand, the fact that the parenchyma cells are palisadal and radially arranged, and have numerous chloroplasts present, would indicate that, as is common in xerophytic plants, the functions of the leaves have been usurped by the stems.

Microscopical: In cross-section, the drug shows a single row of epidermal cells, square, and about 30 to 45 microns on a side. The outer walls consist of a very much thickened cuticle, rather even and about 25 microns in thickness. The cortex is made up of rectangular, palisade-like, parenchyma cells, 40 microns in width by 80 to 120 microns in length, and arranged radially. A number of small rounded bodies suggesting chloroplasts are still to be found in these cells. The parenchyma is somewhat loosely arranged, with air spaces showing beneath the stoma of the epidermis. The bast occur in three distinct rows, the outer being in contact with the epidermis, the middle being found about midway in the cortex, and the inner row at the cambium line. In the cross-section, the bast are circular or somewhat compressed, and show three or more distinct laminations. The lumen is rather small. From two to seven cells usually constitute a bundle, the members of which are arranged radially. The cambium area is made up of three to six rows of meristematic tissue, the individual cells being rather small. No distinct cambium is visible. The xylem consists of radial rows of rectangular tracheids, in two or three rows for each bundle. The medullary rays are made up of radially elongated parenchyma, and are usually two cells in width. They extend to the cambium, or barely into the inner bark area. In this xylem area, two distinct rows of tracheal-like tubes were observed, these being at the position of the spring growth of the annular rings. Large rounded parenchyma cells from 100 to 200 microns make

up the pith. Some of these show chloroplast-like bodies, while others are filled with a brownish colored substance suggestive of phlobane nature by its reaction.

In cross-section, *Ephedra californica* presents much the same appearance, except that the cuticle is very wavy and is irregularly thickened. The parenchyma of the cortex is somewhat longer than in *Ephedra nevadensis*, being as high as 275 microns in length. The bast occur in bundles of from three to seven cells and are somewhat less in diameter. There are few vessel-like openings in the xylem area, and the medullary rays are slightly more prominent. The pith shows the same deposit of brownish material, but in this case, the chloroplast-like bodies are distinctly green. The wood has somewhat less in amount and does not show over two annular rings.

Powder Description.—The powder is of a light brown color, darkening somewhat with aging and exposure to light. Under the microscope, it consisted of very irregular fragments, none of distinct diagnostic value. The pith cells with their brownish material were occasionally present, and this substance itself occurred in irregular broken fragments throughout the mount. The bast occurred singly or in groups of twos, showing the very small luminæ and the tapering ends. They were fifty microns in diameter and from two hundred to eight hundred microns long. A number of shortened bast cells of the nature of stone cells were present, something like the stone cells of *Prunus Virginiana*. In all, the powder does not present a sufficiently distinctive feature to be used in identifying the drug.

In longitudinal section, the xylem may be separated into long tapering cells with spiral markings and shorter tracheids, with the characteristic bordered pores of the gymnosperms. Some of the spiral markings are of the nature of closely twisted strands, while others are more loosely twisted.

Drug Preparation.—In the grinding of *Ephedra nevadensis* the large amount of bast present in the cortex interfered greatly in obtaining a uniform powder. The following table indicates the method employed in preparing the drug for analysis for this study:

TABLE SHOWING THE RESULTS FROM PREPARING EPHEDRA BY THE BALL MILL, HAND MILL, AND GYRATOR MILL PROCESSES.

	Ball mill.	Hand mill.	Gyrator mill.
Amount of drug taken.....	125 Gm.	125 Gm.	25 Gm.
Weight of No. 60 or finer powder.....	80 Gm.	70 Gm.	18.6 Gm.
Per cent of powder.....	62	56	74.4
Weight of No. 20 to No. 60 powder.....	8 Gm.	20 Gm.	6.1 Gm.
Per cent of powder.....	6.2	16	24.4
Residue (gruffs).....	35 Gm.	35 Gm.	0.3 Gm.
Per cent of residue.....	28	28	1.2

The lack of uniformity in results would seem to indicate that the preparation of the sample drug for analysis must be arranged so that it is uniform. Considerable care was here exercised to include representative portions of each of the three fractions of the whole drug.

CHAPTER IV.

CHEMICAL ASPECTS OF EPHEDRA NEVADENSIS.

Proximate Analysis.—Following the methods outlined under the Vegetable Drug Analysis section of the United States Pharmacopœia X (8), the following proximate analyses of *Ephedra nevadensis* were made:

- | | |
|-----------------------------|--------------------------------------|
| 1. Moisture | 6. Alcohol soluble extractive |
| 2. Total ash | 7. Dilute alcohol soluble extractive |
| 3. Acid insoluble ash | 8. Chloroform soluble extractive |
| 4. Crude fiber | 9. Tannin |
| 5. Ether soluble extractive | 10. Volatile oil |
| (a) Volatile at 100° C. | 11. Resin |
| (b) Non-volatile | |

TABLE SHOWING THE DETERMINATION OF MOISTURE, ASH AND ACID-INSOLUBLE ASH IN THE
UNGROUND DRUG EPHEDRA NEVADENSIS.

Unground drug.	Moisture.	Ash.	Acid-insoluble ash.
a-	5.5%	6.8%	0.25%
b-	5.59%	7.3%	0.31%
c-	5.6%	7.43%	0.275%
d-	5.14%	7.35%	0.29%

TABLE SHOWING THE DETERMINATION OF MOISTURE, ASH AND ACID-INSOLUBLE ASH IN THE
GROUND DRUG EPHEDRA NEVADENSIS.

Ground drug.	Moisture.	Ash.	Acid-insoluble ash.	Excess ash.
a-	8.04%
b-	8.34%	14.62%	6.67%	6.37%
c-	8.26%	14.56%	6.71%	6.41%
d-	6.41%	0.31%
e-	6.92%	0.34%

TABLE SHOWING THE DETERMINATION OF MOISTURE, ASH AND ACID-INSOLUBLE ASH IN THE
DRUG EPHEDRA CALIFORNICA.

Drug.	Moisture.	Ash.	Acid-insoluble ash.
a-	6.57%	6.82%	0.40%
b-	6.69%	6.55%	0.39%
c-	6.43%	6.01%	0.36%

TABLE SHOWING THE DETERMINATION OF CRUDE FIBER IN THE WHOLE DRUG EPHEDRA
NEVADENSIS.

	(1).	(2).
Weight of drug.....	2.250 Gm.	2.325 Gm.
Weight of crude fiber and ash.....	0.934 Gm.	1.013 Gm.
Weight of ash.....	0.028 Gm.	0.033 Gm.
Weight of crude fiber.....	0.906 Gm.	0.980 Gm.
Per cent of crude fiber.....	42.6	42.15

TABLE SHOWING THE DETERMINATION OF CRUDE FIBER IN THE GROUND DRUG EPHEDRA
NEVADENSIS.

	(1).	(2).
Weight of powdered drug.....	2.080 Gm.	2.060 Gm.
Weight of crude fiber.....	0.307 Gm.	0.345 Gm.
Per cent of crude fiber.....	14.76 %	16.75 %

TABLE SHOWING THE DETERMINATION OF CRUDE FIBER IN THE POWDERED DRUG EPHEDRA
CALIFORNICA.

	(1).	(2).
Weight of powdered drug.....	2.112 Gm.	2.030 Gm.
Weight of crude fiber.....	0.430 Gm.	0.416 Gm.
Per cent of crude fiber.....	20.36 %	20.49 %

TABLE SHOWING THE DETERMINATION OF ETHER EXTRACTIVE CONSTITUENTS OF EPHEDRA NEVADENSIS.

	(1).	(2).	Average per cent.
1. Total ether-soluble constituents			
(a) Market sample.....	6.24%	6.42%	6.33%
(b) Personal sample.....	8.00%	8.20%	8.1 %
2. Volatile ether-extractive drug.....	0.5 %	0.7 %	0.6 %
3. Non-volatile ether-extractive.....	7.5 %	7.5 %	7.5 %
4. Resin content.....	0.5 %	0.3 %	0.4 %

TABLE SHOWING THE ALCOHOL SOLUBLE EXTRACTIVE CONSTITUENTS OF EPHEDRA NEVADENSIS.

	(1).	(2).	Average per cent.
Market sample.....	17.7%	17.5%	17.6%

TABLE SHOWING THE COLD WATER SOLUBLE EXTRACTIVE CONSTITUENTS OF EPHEDRA NEVADENSIS.

	1.	2.	Average per cent.
Market sample.....	8.24%	8.33%	8.28%

Attempted Isolation of the Alkaloid.—1. Using the method employed by Chen (3), 100 Gm. of the powdered drug were exhausted with 80 per cent alcohol. The percolate was evaporated to a thick syrup under reduced pressure, diluted with water made alkaline with ammonium hydroxide and filtered. Two portions of the filtrate were shaken with chloroform, and the chloroformic washings were added to the washings from the filtrate residue. Upon evaporation a green resinous residue was left. This was treated with *N*/10 hydrochloric acid, the solution was filtered and evaporated. At this point, Chen was able to obtain crystals of ephedrine hydrochloride.

When this same procedure was here applied, there no crystals resulted from the hydrochloric acid washings of the alkalinized chloroform; this tends to indicate the absence of any alkaloid of the nature of ephedrine. In order to check thoroughly this finding, two more extractions were made by the use of this method. The results in both of these cases were negative, thus proving that *Ephedra nevadensis* does not contain the alkaloid ephedrine. The residue obtained from each of the four extraction methods was treated with 5 cc. of *N*/10 HCl, and divided into three portions. Each of these portions was treated with an alkaloidal reagent. The results in all cases were negative, as is shown in the following chart:

Reagent.	Extraction.			
	1.	2.	3.	4.
Mercuric-Potassium Iodide T. S. (Mayer's)...	Neg.	Neg.	Neg.	Neg.
Tannic Acid T. S.....	Neg.	Neg.	Neg.	Neg.
Picric Test Solution.....	Neg.	Neg.	Neg.	Neg.

2. Five cubic centimeters of ammonia water were added to 25 Gm. of the ground drug, and then ether was used to extract the supposed alkaloid. The ether extract was treated with *N*/10 Sulphuric Acid V. S. to form the water soluble sulphate of the alkaloid. This solution was then made alkaline with ammonia and extracted with more ether. Upon separation of the ether layer and evaporation of the ether, no residue was left: this indicated the absence of any alkaloid in the original material.

3. The above procedure was employed with chloroform in the place of ether; the results in this case were also negative.

4. Two lots of 25 Gm. each of the powdered drug were mixed with calcium hydroxide and thoroughly dried. This mixture was extracted with ether in a Soxhlet extractor for three hours. The ether of the solution was allowed to evaporate spontaneously, and the residue was treated with 10 cc. of *N*/10 hydrochloric acid. The acid solution was then treated with ammonia until neutralization was effected. The solution was then extracted with ether, and the separated ether was allowed to evaporate spontaneously. A slight residue remained in the watch crystal. After the sodium decomposition method for the detection of nitrogen gave negative results, the conclusion may be drawn that the supposed alkaloid cannot be extracted by this method.

THE IDENTIFICATION, ISOLATION, AND APPROXIMATE QUANTITATIVE ANALYSIS OF THE ACTIVE CONSTITUENTS OF EPHEDRA NEVADENSIS.

The Tannin Content.—The extremely astringent taste of the stems of *Ephedra nevadensis* would indicate that a large amount of a tannin is present. A quantitative method of analysis was attempted, using the following procedure (9):

Ten Gm. of the drug were macerated with 100 cc. of distilled water at 20° C. The solution was filtered from the drug and saturated with sodium chloride. The tannin was then extracted by means of ethyl acetate, but it gave extremely variable results.

This would tend to indicate that the tannin is not of the exact nature of gallotannic acid, such as is present in the various tanning materials.

An alternate method was attempted, in which one Gm. of Gilt-Label French gelatine was dissolved in 100 cc. of distilled water. The solution was standardized against a 1 per cent solution of gallotannic acid which conformed to the standards of the U. S. P. X. One Gm. of *Ephedra* was extracted by maceration with 10 cc. of distilled water at 20° C. and filtered. Five cc. of the filtrate representing 0.5 Gm. of the drug were added to 20 cc. of the gelatine solution. The resultant precipitate was collected on a tared filter, washed with cold water and dried at 60° C. to constant weight. This method did not produce concordant results so that it may be concluded that the quantitative analysis cannot be performed by this method.

Identification of the Nature of the Tannin.—Using the classification outlined by Proctor (10), the tannin from *Ephedra nevadensis* seems to fall into the pyrogallol group, inasmuch as it responds to the following reactions:

1. The production of a blue-black precipitate upon the addition of ferric chloride test solution.
2. A transient pink color results from the addition of diluted iodine solution.
3. Upon the addition of the solution obtained by macerating the powder in cold water to a solution of gelatine, a dense flocculent precipitate results (distinction from gallic acid).
4. The aqueous solution produces a precipitate when lead nitrate solution is added (distinction from pyrogallol and gallic acid).

From the fact that a cold water extract of the drug gave no reaction with alkaline cupric tartrate in the form of Benedict's solution, the tannin was in the form of a glucoside. This was verified when it was found that the cold water extract when hydrolyzed with acid, heating or standing, yielded an abundant precipitate with the test solution, indicating the presence of glucose. Upon carefully subjecting

some of the powdered drug to sublimation, pyrogallol was detected in the condensate by the usual tests for this material.

CHAPTER V.

THE PHYSIOLOGICAL ASPECTS OF EPHEDRA NEVADENSIS.

From the high tannin content, it would seem that the best form in which to administer the drug would be in the type of preparation known as fluidextract. Employing the process outlined in the Pharmacopœia, and known as Type Process A, two fluidextracts were made, one using 85 per cent alcohol, and the other, 50 per cent alcohol. In addition, one thousand cubic centimeters of an infusion (modified by the addition of 15 per cent alcohol) were prepared.

The use of the residues obtained from the determination of the alcohol-soluble and ether-soluble constituents gave fractions somewhat unlike. In case of the ether-soluble extractive, the residue consisted largely of chlorophyll in which was embedded the resin and some volatile oil. Therefore, the administration of this material should be of distinct variance from that of the extract made with alcohol, for the alcohol extract necessarily would contain considerable tannin in addition to the chlorophyll and resin. A third extract made with chloroform as a solvent was employed. This preparation was essentially of the same nature as the one made with ether. However, the chloroformic solution did not have the physical characteristic of swelling when heated, the ether extract behaving very much as rubber does, when heated. This would tend to prove the ether extract to be of a slightly different nature than the chloroformic one.

TABLE SHOWING THE DIURETIC EFFECTS OF THE ADMINISTRATION OF VARIOUS PREPARATIONS OF EPHEDRA NEVADENSIS.

Preparation.	Subject.	Size of dose.	Results by days.			
			1.	2.	3.	4.
Fluidextract 50% alcohol	A	0.75 cc.	Slight			
		1.0 cc.	+	Slight		
		1.5 cc.		+	Slight	
		2.5 cc.			+	+
Fluidextract 50% alcohol	B	Same range of doses	Slight			
			+	+	+	+
Fluidextract 80% alcohol	C	Same range of doses	Slight	Slight	Slight	
			+	+	+	+
Fluidextract 80% alcohol	D	Same range of doses	Very slightly	Slight	Slight	Slight
			+	+	+	+
Infusion 5% strength	E	100 cc.	Strongly			
			+			
Infusion 5% strength	F	100 cc.				
			+			
Alcoholic extract— 0.065 of extract represents the alcohol soluble constituents of 1 Gm. of the drug	G H I J K	0.375 Gm. 0.8 Gm. 1.25 Gm. 2.0 Gm. 3.0 Gm.	—	All extracts were divided into 3 doses given about 3 hours apart.		
			—			
			—			
			—			
			Slight			
Chloroformic extractive	L M	0.8 Gm. 2.0 Gm.	+			
			—			

+ = Positive reactions.
- = Negative reactions.

The mode of administration varied with the preparation, except that all were given by mouth. In case of the fluidextract the liquid was given undiluted. The infusion presented some difficulties because of its extreme astringency. It was thought that some of the astringency might be overcome by the addition of sugar dissolved in the infusion at the time of administration, and this method was used. On the other hand, the administration of the solid extracts was best made by enclosing them in gelatine capsules.

The method of physiological assay was largely of the clinical type. A number of persons were given graduated doses of the various preparations, and the results noted in the foregoing table. There is considerable difficulty because of the personal factor which can only be eliminated by the use of a large number of subjects and observations carried over a number of years. Obviously it would be impossible in a study of this nature to carry on such investigation.

From the results shown in the foregoing table, it will be seen that for the diuretic effect, an infusion form of the drug is best. This would indicate that the water soluble substances were active in stimulating the kidneys. The uniformly negative results obtained from both the alcoholic and chloroformic extracts indicate that the wax resins and chlorophyll are inactive in this respect. In the continued administration of *Ephedra nevadensis* in the fluidextract form some slight constipating effect was noted. This was probably due to the tannin present in these preparations. In no conditions were any untoward symptoms reported, such as any mydriatic action or heart stimulation. This further tends to prove the absence of any alkaloid of the nature of Ephedrine, for in the extracts sufficient of the material was administered to show these reactions if the alkaloid be present.

CHAPTER VI.

SUMMARY.

The characteristic appearance of the commercial form of the drug, *Ephedra nevadensis*, makes its identification rather easy, when in the whole form. The mounted cross-sections are distinctive in having the tracheals in the xylem composed largely of tracheids. This would make it an easy matter to distinguish it from a cross-section of pine wood, which would be the only possible cause for confusion. On the other hand, when in powder form, *Ephedra* would be rather difficult to identify because of the absence of distinctive elements other than the peculiarly marked tracheals. Pith parenchyma filled with the brownish material might also be listed as a somewhat rather distinctive constituent.

This study indicates that the astringency in the taste of *Ephedra* is due to tannin. This tannin is gallotannic acid as proven by its various reactions and reduction products. Resin was found in the drug to a very limited extent. The amount was so small that no attempt was made to separate out a quantity large enough to analyze for its properties. The rather distinctive odor and some of the taste may be due to the volatile oil. This, too, was of such a small amount that a study of its exact composition was postponed until further supplies of the material could be secured. No doubt the most important function of this study has been to prove that *Ephedra nevadensis* contains no alkaloid. Systematic analysis, confirmed by a number of different methods, has proved the absence of ephedrine.

CONCLUSIONS.

In the study of the physiological qualities of *Ephedra nevadensis*, the following points seem especially pertinent:

1. The drug seems to be possessed of some slight diuretic effects. This characteristic is best shown in the infusion form. From this, it may follow that the water-soluble constituents are of a blenorrhetic nature. The fact that the alcoholic and chloroformic extracts do not possess this property further proves the fact that these constituents are of the water-soluble group.

2. The drug is not strongly active, for doses representing from 5 to 15 Gm. of the drug produce only slight stimulation. This proves that the drug does not belong to the exceedingly active class of medicinal plants.

3. The slight constipating after-effects following the prolonged administration of the fluidextract mitigates its ability to increase excretion through the kidneys. This may be said to be due to the tannin present.

4. The absence of the alkaloid, *Ephedrine*, precludes the use of *Ephedra nevadensis* as a circulatory stimulant, and the other effects ascribed to *Ephedrine*.

From the recapitulation of the evidence, there seems to be no distinct advantage to be gained by the introduction of *Ephedra nevadensis* into medicine. The properties usually ascribed to it are such that the need is well supplied by some well established therapeutic agent. Outside of its domestic use, very little may be said in its favor.

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- (7) W. H. Foster, "Ephedra for Diseases of the Blood," pamphlet.
- (8) "Pharmacopœia of the United States of America, X," p. 463-6.
- (9) "Agricultural Analysis," A. A. O. A. A.
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EXAMINATION OF ASARUM CAUDATUM.

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A year ago a preliminary report (1) on a few Northwestern plants contained reference to one of the wild gingers. We have now submitted this herb to a more extended examination, with special regard to the interesting volatile oil. Since other members of the genus are now used to some extent in medicine and in perfumery, it was deemed important to learn whether the Washington variety might be employed in the same way.

Asarum caudatum (Lindl.), *Aristolochiaceæ*, is a perennial, possessing stem-like rhizomes, 2 to 8 mm. thick, with branches 10 to 30 cm. long, having a penetrating, ginger-like odor, and a spicy, acrid taste. The roots are thick, fibrous and fleshy. The leaves are evergreen, reniform, cordate, entire, sparsely hairy throughout, and with long petioles. The flowers are solitary, peduncled, brownish