E. distachya (genuina). All three forms have the same aspect and differ only by botanic characters." In the U. S. Dispensatory 20th Edition, mention is made of *E. distachya*, L., stating that the branches and roots are used in Siberia as a remedy in gout and syphilis; also that the alkaloid of the species has been isolated and is different from ephedrine.

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EPHEDRINE: ITS ISOLATION AND DETECTION FROM THE TOXICOLOGICAL STANDPOINT.*

BY KUEN TSIANG AND E. D. BROWN.

Ephedrine, an alkaloid obtained from an old Chinese drug, Ma Huang (*Ephedra vulgaris*) has been recently introduced as a new therapeutic agent and gives promise of possessing considerable merit. In 1924, Chen and Schmidt published a report on "The Action of Ephedrine" pointing out especially its effect

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upon the circulation and its similarity to epinephrine in its chemical structure and in its action. Since this time, Chen has reported further results of his experimental investigation which has led to its clinical use in a number of conditions where it might rationally be expected to produce the desired result.

There is a fairly wide margin between the therapeutic dose and the toxic dose and there is little probability that death may result from its administration.

So far as we know, there has been no published report on the identification of the alkaloid, ephedrine, so we undertook to develop tests of identity. Ephedrine sulphate was used in making the tests which came to us from the Peking Union Medical College where it had been prepared as a product of their laboratory. Tests made by treating the dry alkaloid with the commonly employed reagents which in many cases give color reactions with certain alkaloids, were negative. This group consisted of the concentrated mineral acids: sulphuric, nitric and hydrochloric, and a group of other reagents including sulphuric acid with sugar, sulphuric acid with potassium dichromate, Froehde's reagent, and a solution of ferric chloride. A solution of the alkaloid was prepared and attempts made to

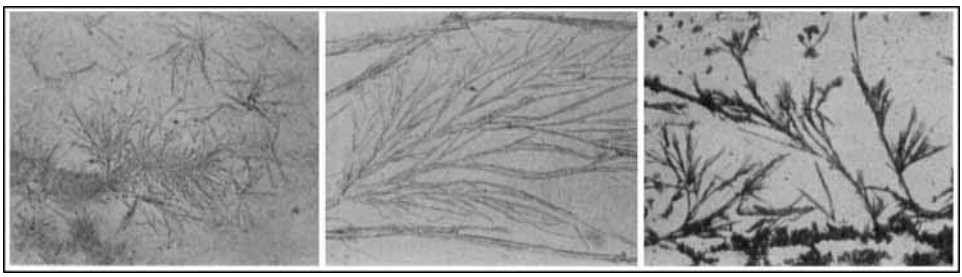

Fig. 1.—Ephedrine 1:1000. Gold chloride.

Fig. 2.—Ephedrine 1:1000. Platinic chloride.

Fig. 3.—Krauts reagent 1:1000.

obtain a characteristic crystalline precipitate with a group of alkaloidal reagents. Amorphous precipitates were produced by a large number of these reagents, but these would not serve as a means for the identification of the alkaloid. Four of the reagents employed gave crystalline precipitates which were very satisfactory. These crystalline precipitates appeared to be fairly characteristic for the alkaloid and may be employed as a means for identification. The reagents employed for these tests are described as follows:

Millon's Reagent.—This reagent when added to a drop of a solution of the alkaloid on a glass slide in dilutions of 1–100 or preferably 1–50, forms beautiful, star-like or leaf-like crystals. The crystals are slow in forming and are variable in shape depending on the concentration.

Gold Chloride.—This is a sensitive test. Fine needle-like crystals, some in the form of rosettes, were given by a 1–2500 solution. A 1–1000 solution, however, gave crystals possessing a more striking appearance, Fig. 1.

Platinic Chloride.—This reagent was also found to be very sensitive. Crystals were formed in a dilution of 1–10,000, but a 1–1000 solution gave better results. The crystals are inclined to be acicular, but have a strong tendency to branch or to be so arranged as to resemble the branches of a bush or tree, Fig. 2.

Kraut's Reagent.—With this reagent there is also produced what might be

considered a characteristic crystalline precipitate. In dilutions of 1–1000 or 1–500, needle-like crystals are formed which have a marked tendency to branch, giving the appearance of bushes, Fig. 3. In dilutions of 1–100 the tendency is for the crystals to be arranged in the form of rosettes.

In all the above tests it is well to emphasize that the formation of crystals occurs slowly.

In view of the fact that ephedrine bears a close relationship in chemical structure to both epinephrine and tyramine, the same tests were made with these substances.

In some instances, especially with Kraut's reagent, there is a similarity in the crystals formed which might be confusing. Any doubt, however, may be overcome by the use of ferric chloride solution which gives a color reaction with epinephrine and tyramine owing to the presence of the OH group on the benzol ring. This is not the case with ephedrine.

Caffeine also gives a somewhat similar precipitate with gold chloride and Kraut's reagent, but the absence of a precipitate with platinic chloride and Millon's reagent, as well as many of the other alkaloidal reagents, makes it easy to rule it out.

In order to determine whether the ephedrine could be isolated and detected when mixed with animal tissue, the following experiment was made.

A small amount of the alkaloid was thoroughly mixed with a liberal amount of ground meat and the alkaloid extracted by the Stas-Otto method. The alkaloid was recovered in a very pure form and gave the same microchemic tests as the original drug.

This experiment would give no indication as to how long the drug might remain in the body before being broken down, but it serves to show that it may be recovered and identified if present.

EDITORS NOTE: "A Study of Ephedra Nevadensis," by Ralph E. Terry will follow in the May issue of the JOURNAL.

THE STANDARDIZATION AND STABILIZATION OF ACONITE PREPARATIONS.—PAPER III.

BY EDWARD E. SWANSON AND CHESTER C. HARGREAVES.

1. Review of previous data.
2. Methods of assay.
3. The assay of five series of tinctures and fluidextracts.
4. The hydrogen-ion concentration or p_H value.
5. Conclusions.

In two previous articles (1, 2) by comparing the chemical method U. S. P. IX with the biochemical method now official in U. S. P. X, on a number of aconite drugs, tinctures and fluidextracts, it was found that the chemical method is unreliable. This method assays the total ether-soluble alkaloids, which are similar in chemical properties toward solvents and precipitants, but not similar in toxicity and pharmacological action. The biochemical method, which has been found to be more accurate, determines the total amount of toxic alkaloids in terms of a standard aconitine, which is regarded pharmacologically and therapeutically