# QUALITATIVE TESTS FOR EPHEDRINE AND ITS DERIVATIVES*,[1]

BY C. T. FENG AND B. E. READ.

In the course of our research upon the best quantitative method of assay for ephedra and its alkaloids we undertook a large number of qualitative tests with a view of possibly finding one which would prove of worth in quantitative work. While this has not been definitely attained much useful information has been brought together concerning the reaction of ephedrine and its derivatives toward various laboratory reagents which we herewith report.

Chen in 1925 (1) in one of his first reports from these laboratories gave a list of reactions of ephedrine with several of the commoner laboratory reagents, and later Chen and Kao (1926) (2) summarized the various tests known q. v., which it is unnecessary for us to go over again now.

Tsiang and Brown (1927) (7) gave a more complete report upon the gold and platinum salts made with solutions of ephedrine varying in strength from 1 in 10,000 to 1 in 1000. With Krant's reagent they obtained a characteristic crystalline precipitate.

On account of the fact that Chinese ephedra has been shown to contain (*a*) ephedrine, (*b*) pseudoephedrine (6), and (*c*) methyl-ephedrine (5), we have carefully extended our tests to all three of these compounds; also to the (*d*) butyl, (*e*) benzyl and (*f*) quaternary halide compounds which have been synthesized in these laboratories (4).

Unless indicated otherwise, solutions of the above compounds were found to give their best reactions in the following concentrations: (*a*) and (*b*) five to ten per cent, (*c*) two and a half to five per cent, (*d*) and (*e*) one to two and a half per cent, and (*f*) one-tenth to one per cent.

### 1. BIURET TEST (MODIFIED) (3).

(*a*) *Ephedrine Hydrochloride.*—A violet pigment very soluble in ether giving a brilliant solution, which when evaporated to dryness yields a gelatinous residue (3).

(*b*) *Pseudoephedrine Hydrochloride.*—The pigment is more slowly soluble in ether yielding a solution of dull appearance, which when air dried produces beautiful violet crystals (3).

(*c*) *Methyl-Ephedrine Hydrochloride.*—Vigorous shaking of the reaction mixture showed that the pigment was not extractable by ether, but before shaking the ether dissolved some of the pigment.

(*d*) *Butyl-Ephedrine Hydrochloride.*—Identical with (*c*).

(*e*) *Benzyl-Ephedrine Hydrochloride.*—The pigment was absolutely insoluble and was not extractable by ether.

(*f*) *Quaternary Halide.*—No biuret coloration produced.

### 2. POTASSIUM IODIDE TEST. A SATURATED SOLUTION ADDED TO A FIVE PER CENT SOLUTION OF EACH COMPOUND.

(*a*) Prisms or rhombic bars. (Fig. 1.)

(*b*) Hexagonal rhomboid plates. (Fig. 2.)

(*c*) Slowly producing thin flaky crystals. (Fig. 3.)

(*d*) Producing oily drops immediately, from which rosettes separate later. (Fig. 4.)

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Fig. 1.

Fig. 2.

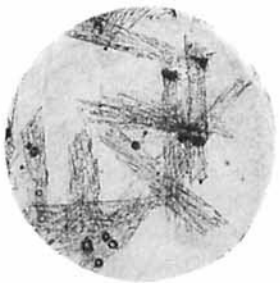

Fig. 3.

Fig. 4.

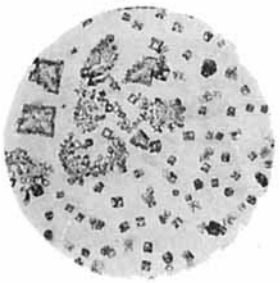

Fig. 5.

Fig. 6.

Fig. 7.

Fig. 8.

Fig. 9.

Fig. 10.

Fig. 11.

Fig. 12.

Fig. 1.—Potassium iodide and ephedrine hydrochloride. Fig. 2.—Potassium iodide and pseudoephedrine hydrochloride. Fig. 3.—Potassium iodide and methyl-ephedrine hydrochloride.

Fig. 4.—Potassium iodide and butyl-ephedrine hydrochloride. Fig. 5.—Cadmium potassium iodide and ephedrine. Fig. 6.—Cadmium potassium iodide and methyl ephedrine.

Fig. 7.—Picric acid and ephedrine. Fig. 8.—Picric acid and pseudoephedrine. Fig. 9.—Picric acid and methyl ephedrine.

Fig. 10.—Ammonium thiocyanate and ephedrine. Fig. 11.—Ammonium thiocyanate and pseudoephedrine. Fig. 12.—Ammonium thiocyanate and methyl ephedrine.

(*e*) Oily droplets which do not crystallize in one or two hours.
(*f*) Readily producing clusters of characteristic rhombic crystals (4).

3. AURIC CHLORIDE. THREE PER CENT, MICRO-TEST (7).

(*a*) Golden-yellow sharp needles, soluble in water and alcohol.
(*b*) Golden-yellow feathery needles, soluble in water and alcohol.
(*c*) Yellow prisms, soluble in water and alcohol.
(*d*) Yellow oily drops, slightly soluble in water, readily in alcohol.
(*e*) Similar to (*d*).
(*f*) Characteristic crystals.

The butyl-ephedrine mixture (*d*) evaporated to dryness yields a gelatinous mass which in several days crystallizes out, benzyl-ephedrine yields no crystals.

4. PLATINIC CHLORIDE. TWO PER CENT, MICRO-TEST (7).

(*a*) Pale yellow silky needles, very soluble in water or alcohol.
(*b*) Pale yellow bunches of long needles, very soluble in water or alcohol.
(*c*) Characteristic yellow needles, soluble in water or alcohol.
(*d*) Pale yellow rhombic-hemihedral crystals. Slightly soluble in water and very soluble in alcohol. A quicker reaction than that with auric chloride.
(*e*) Pale yellow drops. Slightly soluble in water, very soluble in alcohol.
(*f*) Characteristic fine needles (already published, Feng 1932 (4)).

5. CADMIUM POTASSIUM IODIDE. TWENTY PER CENT.

(*a*) Oily droplets separate which on standing crystallize out. (Fig. 5.) Readily soluble in water.
(*b*) Similar to (*a*).
(*c*) On standing clusters of characteristic needles are formed. Soluble in water. (Fig. 6.)
(*d*) Oily droplets first appear, which later crystallize out in irregular forms. Slightly soluble in water.
(*e*) Similar to (*d*).
(*f*) Fine flakes readily separate out which are almost insoluble in water.

All of the above crystalline precipitates are soluble in alcohol or acetic acid.

6. PICRIC ACID. ONE PER CENT, MICROCHEMICAL TEST.

(*a*) Yellow needle-shaped crystals, readily soluble in water. Shaped like pine needles. (Fig. 7.)
(*b*) Yellow needle-shaped crystals, soluble in water. Less fine than (*a*), shaped like thorns. (Fig. 8.)
(*c*) Yellow feathery leaflets, soluble in water. (Fig. 9.)
(*d*) Yellowish flakes, slightly soluble in water.
(*e*) Yellowish globules, slightly soluble in water.
(*f*) Characteristic yellowish needles, very soluble in water.

These results are sufficiently characteristic to be used to distinguish these six compounds one from the other. It is important to use the strengths of solutions given at the beginning of this report, earlier workers using weaker solutions reported negative results (1); ephedrine in strong solution certainly yields a crystalline precipitate with picric acid one per cent.

7. AMMONIUM THIOCYANATE. SATURATED SOLUTION. MICROCHEMICAL TEST.

(*a*) (Ephedrine in ten per cent solution.) Elongated prisms. (Fig. 10.)
(*b*) (Saturated solution of pseudoephedrine hydrochloride.) It sets to a glassy paste not showing discrete crystals. (Fig. 11.)
(*c*) (Five to ten per cent.) Rhombic hemihedral plates. (Fig. 12.)
(*d*) (Two and a half to five per cent.) Leaflets crystallize out on standing from the oily droplets which first separate out.
(*e*) (Two and a half to five per cent.) Oily droplets, which do not crystallize, separate out.

(*f*) (One to two and a half per cent.) Prismatic hemihedral plates. All of the above were readily soluble on the addition of water.

8. PHOSPHOMOLYBDIC ACID. TEN PER CENT.

All of the compounds with this reagent yielded a pale yellow precipitate, which became blue on standing for a definite length of time varying, with the compound tested:

| | | |
|---|---|---|
| (*f*) | Methyl-ephedrine-methyl-iodide | In 1 to 2 days |
| (*d*) | Butyl-ephedrine hydrochloride | In 2 to 3 days |
| (*e*) | Benzyl-ephedrine hydrochloride | In 3 to 4 days |
| (*a*) | Ephedrine hydrochloride (2) | In 4 to 6 days |
| (*b*) | Pseudoephedrine hydrochloride | In 6 to 20 days |
| (*c*) | Methylephedrine hydrochloride | In 6 to 20 days. |

9. POTASSIO-MERCURIC IODIDE. MAYER'S REAGENT.

The compounds all yielded a whitish precipitate, the solubility in water or dilute acids varying with the compound used.

(*a*) and (*b*) Readily soluble.
(*c*) Soluble.
(*d*) and (*e*) Not very soluble.
(*f*) Almost insoluble.

10. POTASSIUM TRI-IODIDE. WAGNER'S REAGENT.

A strong solution of iodine five per cent and potassium iodide five per cent gave brown precipitates with all the compounds. The reagent diluted 0.2 per cent, gave no permanent precipitate with ephedrine in one per cent solution and only a cloudy effect with pseudoephedrine one per cent. Butyl and benzyl-ephedrine in dilute solution of 0.1 per cent gave heavy precipitates.

11. POTASSIUM BISMUTH IODIDE. KRANT'S OR THRESH'S REAGENT.

A reddish precipitate insoluble in water is produced by all the compounds but on the addition of acetic acid (*a*), (*b*) and (*c*) were readily soluble, (*d*) and (*e*) were difficultly soluble and (*f*) was almost insoluble. (Tsiang and Brown (7) used this test with ephedrine 1 in 1000 solution.)

12. MERCURIC CHLORIDE. FIVE PER CENT.

No precipitate was obtained from (*a*), (*b*) or (*c*) in five per cent solutions, (*d*), (*e*) and (*f*) yielded white precipitates soluble in excess of the reagent, or on the addition of water and weak acids.

13. SODIUM NITROPRUSSIDE. FIVE PER CENT.

Only butyl-ephedrine and benzyl-ephedrine in five per cent solution formed flesh-white precipitates, soluble in excess of water.

14. BISMUTH NITRATE. FIVE PER CENT, SLIGHTLY ACIDIFIED WITH NITRIC ACID.

They all yield white precipitates soluble in excess of nitric acid. This test is more sensitive than some, especially with the quaternary halides (*f*), each of which give a characteristic result described in another report (4). One of these quaternary compounds might be used to estimate bismuth.

15. AMMONIUM MOLYBDATE. FIVE PER CENT.

All the compounds form white precipitates soluble in excess of the reagent or on the addition of water, the solubilities decreasing in the order cited, as was the case in other tests.

16. PHOSPHOTUNGSTIC ACID. TEN PER CENT.

White curdy precipitates of nonspecific character were produced by all the compounds.

17. ZINC-CHLOR-IODIDE. STEPHENSON'S REAGENT.

There was obtained in all cases a brownish white precipitate insoluble on the addition of water, but soluble in dilute acetic acid.

18. REAGENTS WITH NO VISIBLE REACTION.

Tannic acid, barium nitrate, cobalt chloride, glucose, glycerine, manganese chloride, nickel chloride, phthalic acid, potassium ferri and ferrocyanides, sodium benzoate or nitrite. The reactions with potassium permanganate and chromic acid were so unstable that they seem worthless as test reagents for this class of compound.

NOTE.

Many of the above tests confirm earlier reports upon the various reactions of ephedrine, but this is the only comprehensive statement dealing with solutions of known strengths.

LITERATURE CITED.

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# A NOTE ON THE WATER CONTENT OF MAGNESIUM OXIDE.*,[1]

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## INTRODUCTION.

The Pharmacopœia recognizes dual standards for magnesium oxide and heavy magnesium oxide. The rubric requires 96 per cent purity after ignition and permits 10 per cent water to be present in the compounds in general use. In the preparation of the monographs for these compounds for the forthcoming edition of the Pharmacopœia, the authors had occasion to examine several commercial samples of each variety of magnesium oxide. The percentage of water found in the specimens showed great variation. In many instances the water content of the light variety exceeded the Pharmacopœial limit. The highest quantity of water found was 22 per cent.

On account of these findings, the authors investigated the problem and recorded their observations in this communication.

TABLE I.—PERCENTAGE OF WATER IN COMMERCIAL SAMPLES OF MAGNESIUM OXIDE.

| No. | Light. Per Cent Water. | Heavy. Per Cent Water. | No. | Light. Per Cent Water. |
|---|---|---|---|---|
| 1 | 22.0 | 7.8 | 8 | 11.5 |
| 2 | 20.3 | 7.8 | 9 | 18.0 |
| 3 | 20.3 | 7.8 | 10 | 21.9 |
| 4 | 19.2 | 3.4 | 11 | 19.3 |
| 5 | 19.4 | 6.5 | 12 | 22.5 |
| 6 | 14.0 | | 13 | 14.5 |
| 7 | 17.9 | | Mean 18.5 per cent | |

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