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A note on a micro and a semimicro method for the assay of ephedrine

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Two colorimetric methods for the assay of ephedrine are proposed. One is a semimicro method in which the intensity of red colour produced by the oxidation of ephedrine with hydrogen peroxide is measured. The other is a micro method in which measurement is made of the intensity of the brown colour of the respective copper dithiocarbamate, produced by interaction of ephedrine, carbon disulphide and ammoniacal copper sulphate, the limit of sensitivity being 100 μg. Both methods gave reproducible results when used to assay ephedrine in pharmaceutical preparations. Results were compared with those from the Egyptian pharmacopoeial method.

WITH the aim of devising a simple and precise colorimetric estimation for ephedrine, the colour tests for ephedrine with hydrogen peroxide (Snell & Snell, 1954) and with copper dithiocarbamate (Fiegel, 1960) were found to be a suitable starting point.

The hydrogen peroxide method uses as a basis the oxidation by hydrogen peroxide of ephedrine in alkaline medium to give a red colour. This colour, we found to obey Beer's law in the range 2·5–15 mg.

The dithiocarbamate method depends upon the reaction of ephedrine with carbon disulphide and ammoniacal copper sulphate solution. A water-insoluble brown copper salt of the dithiocarbamic acid is produced which, when dissolved in benzene or chloroform, gives a brown solution obeying Beer's law in the range of 100–900 μg.

Experimental and results

HYDROGEN PEROXIDE METHOD

Reagents. Ephedrine hydrochloride, hydrogen peroxide (30 vol.), sodium hydroxide (0·1N), sodium chloride 16%, ether, all of analytical grade.

Procedure. A standard curve is plotted, using varying concentrations of ephedrine hydrochloride solution.

To 1·5 ml of ephedrine hydrochloride solution containing 2·5–15 mg/ml, add 16% sodium chloride (4 ml), 0·1N sodium hydroxide (0·5 ml) and hydrogen peroxide (6 drops). Mix thoroughly, heat on a water bath for 5 min and cool. Measure the colour developed in a Unicam S.P. 1300 colorimeter using filter No. 1 (370–515 mμ). The colour developed obeys Beer's law when ephedrine hydrochloride is present in amounts ranging from 2·5–15 mg. The colour is stable for over 3 hr.

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DITHIOCARBAMATE METHOD

Reagents. Ephedrine hydrochloride, concentrated ammonium hydroxide, benzene, copper sulphate 5% solution, carbon disulphide, all of analytical grade.

Procedure. A standard curve is plotted using varying concentrations of ephedrine hydrochloride solution.

To 1 ml of an aqueous solution of ephdrine hydrochloride containing 100–900 μg/ml add 5% copper sulphate solution (1 ml), concentrated ammonium hydroxide (3 drops) and carbon disulphide–benzene (1 : 3) (5 ml). Shake the mixture thoroughly for 5 min. Separate the organic layer and measure the colour with a Beckman DU spectrophotometer at a wavelength of 440 mμ. The colour obeys Beer's law over a concentration range of 100–900 μg/5 ml of organic layer. The colour reaches its maximum in the organic layer after 10 min and remains stable for a further 15 min.

Experiments made on solutions containing different added amounts of ephedrine hydrochloride show the reproducibility of the two methods (Table 1). From Table 1 it is obvious that the amounts of ephedrine recovered by both methods were almost quantitative.

TABLE 1. ESTIMATION OF EPHEDRINE HYDROCHLORIDE BY THE HYDROGEN PEROXIDE METHOD AND THE COPPER DITHIOCARBAMATE METHOD

Hydrogen peroxide method				Copper dithiocarbamate method			
Ephedrine HCl (mg)				Ephedrine HCl (µg)			
Added	Found	Recovery (%)	Error (%)	Added	Found	Recovery (%)	Error (%)
2·5	2·425	97	−3	100	100	100	0·0
				200	198	99	−1
5	4·91	98·2	−1·8	300	303	101	+1
				400	396	99	−1
7·5	7·80	104	+4	500	511·5	102·3	+2·3
				600	607·2	101·2	+1·2
10	9·84	98·4	−1·6	700	700	100	0·0
				800	793·6	99·2	−0·8
12·5	12·5	100	0·0	900	911·7	101·3	+1·3
15	14·81	98·7	−1·3	1000	965	96·5	−3·5

ASSAY OF EPHEDRINE IN SOME PHARMACEUTICAL PREPARATIONS

Some preparations of ephedrine (official in the Egyptian Pharmacopoeia and British Pharmaceutical Codex) were assayed by the proposed methods and the results compared with those from the Egyptian Pharmacopoeia method of analysis.

Preliminary treatment. A. Tablets of ephedrine hydrochloride, 30 mg (Memphis Co.). A weighed quantity of the powdered tablets equivalent to 15 mg of ephedrine salt was transferred to a separator with water, made alkaline with strong ammonium hydroxide and extracted successively with ether (4 × 20 ml quantities), the final volume being adjusted to a concentration of 2·5–15 mg/ml for the hydrogen peroxide method or of 100–90 μg/ml for the copper dithiocarbamate method.

B. Ampoules of ephedrine sulphate 50 mg/ml (Misr Co.). The sample was diluted with distilled water to give the optimum concentration for either method.

C. Elixir of ephedrine B.P.C. 1963. A measured volume of the elixir was transferred to a separator, made alkaline with ammonium hydroxide and extracted successively with ether. The final volume was adjusted to give a suitable concentration for each method.

The ephedrine content of the tablet and elixir was also determined by the copper dithiocarbamate method directly without extraction.

The data are in Table 2. These show that the proposed methods are comparable with the E.P. method of assay. Moreover, the copper dithiocarbamate method is applicable directly to the filtrate of the tablet and diluted elixir without previous treatment.

TABLE 2. COMPARATIVE ANALYSIS OF SOME OFFICIAL PREPARATIONS OF EPHEDRINE OFFICIAL IN THE EGYPTIAN PHARMACOPOEIA AND BRITISH PHARMACEUTICAL CODEX

Preparations and its ephedrine content	E.P. Method		Hydrogen peroxide method		Copper dithiocarbamate method			
	Ephedrine content (%)	devn (%)	Ephedrine content (%)	devn (%)	Ephedrine content by extraction (%)	devn (%)	Ephedrine content without extraction (%)	devn (%)
Tablet 0·5 gr	97·2	−2·8	99·52	−0·48	98·5	−1·5	98·82	−1·18
Ampoule 50 mg/ml ..	101·95	+1·95	104·2	+4·2			103·57	+3·57
Elixir 0·46 g/100 ml ..	100·4	+0·4	99·1	−0·9	99·0	−1·0	98·3	−1·7

References

Snell, F. D. & Snell, C. T. (1954). *Colorimetric Methods of Analysis*, p. 35, 3rd edn, New York: D. Van Nostrand.

Fiegel, F. (1960). *Spot tests in Organic Analysis*, p. 274, 6th edn, New York: Elsevier.