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Short Communication

Spectrophotometric determination of hydroflumethiazide

YADVENDRA K. AGRAWAL,* RAJANI GIRIDHAR and SOBHANA K. MENON

Pharmacy Department, Faculty of Technology and Engineering, M. S. University of Baroda, Baroda 390 001, India

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Introduction

The wide use and therapeutic importance of saluretic agents have resulted in an increased number of chlorothiazide diuretics. A few methods have been developed for the analysis of hydroflumethiazide [1–4]. Bermejo *et al.* [5] developed a colorimetric method by diazotizing the drug and coupling the product with chromotropic acid and/or the Bratton Marshall reagent.

A simple, time-saving and sensitive method for the determination of hydroflumethiazide is needed. In the present communication a new spectrophotometric method for the determination of hydroflumethiazide is reported.

Experimental

Instruments

Absorbance measurements were made on a VSU 2-P C.Z. Jena spectrophotometer using 1-cm quartz cells. pH measurements were made on a Systronic digital pH meter, Model 355, equipped with glass and calomel electrodes.

Materials and reagents

All chemicals used were of Analar grade (BDH) unless otherwise specified.

Hydroflumethiazide BP was used. A 3.309 mg ml^{-1} solution was prepared by dissolving the requisite amount of the drug in 0.05 M sodium hydroxide. The solution was diluted with distilled water when necessary.

Potassium ferricyanide (0.01 M) was prepared by dissolving the requisite amount of potassium ferricyanide in distilled water. Hydrochloric acid (5 M) was prepared.

*To whom correspondence should be addressed.

Procedure and calibration curve

Three millilitres of a solution containing 330.9 μg ml^{-1} of hydroflumethiazide was placed in a boiling tube. To this solution 2.0 ml of 0.01 M potassium ferricyanide was added, followed by 3 ml of 4 M sodium hydroxide; the solution was then diluted to 10 ml with water. The contents of the test tube were then heated on a water-bath at 50°C for 30 min. The resultant solution was cooled and the pH was adjusted to 2.5 with 2 M hydrochloric acid. The contents were diluted to 25 ml with water. The absorbance of the greenish-blue complex was measured against the reagent blank at 725 nm. A calibration curve was plotted in the concentration range of 8.0–132.0 ppm of hydroflumethiazide.

Results and Discussion

Absorption spectra

The greenish blue complex of hydroflumethiazide with potassium ferricyanide had a maximum absorbance at 720 and 730 nm; hence all measurements were made at 725 nm. The molar absorptivity was 3.0×10^3 mol^{-1} cm^{-1}.

Effect of sodium hydroxide

The effect of molarity of sodium hydroxide on the colour development of hydroflumethiazide with potassium ferricyanide is shown in Table 1. It was observed that maximum colour intensity was obtained in 1.2–1.3 M sodium hydroxide. A higher or lower sodium hydroxide concentration decreased the colour intensity.

Table 1
Effect of sodium hydroxide molarity on the colour development of hydroflumethiazide with potassium ferricyanide

Sodium hydroxide molarity (M)	Absorbance	Molar absorptivity l mol^{-1} cm^{-1}
0.5	0.22	1.8×10^3
1.0	0.34	2.8×10^3
1.2	0.36	3.0×10^3
1.3	0.36	3.0×10^3
1.5	0.35	2.9×10^3
2.0	0.31	2.6×10^3
2.5	0.24	2.0×10^3

Hydroflumethiazide: 39.7 ppm; pH 2.5.
Potassium ferricyanide: 2 ml (0.01 M); λ_{max} 725 nm; colour, greenish-blue.

Effect of reagent concentration

The effect of reagent concentration on the colour intensity of the complex has been studied. It was found that 1.5–3 ml of the reagent, 0.01 M potassium ferricyanide, was sufficient for maximum colour development for 39.7 ppm of hydroflumethiazide. However, the absorbance decreased with higher and lower amounts of potassium ferricyanide (Table 2).

Effect of pH

The colour development of hydroflumethiazide with potassium ferricyanide was studied in the pH range 0.5–5.0. The results given in Table 3 show that the absorbance of

Table 2
Effect of reagent concentration on the colour development of hydroflumethiazide with potassium ferricyanide

Potassium ferricyanide, 0.009 M (ml)	Absorbance	Molar absorptivity $l\ mol^{-1}\ cm^{-1}$
0.5	0.17	1.4×10^3
1.0	0.30	2.5×10^3
1.5	0.36	3.0×10^3
2.0	0.36	3.0×10^3
2.5	0.36	3.0×10^3
3.0	0.36	3.0×10^3
4.0	0.34	2.8×10^3
5.0	0.31	2.6×10^3

Hydroflumethiazide: 39.7 ppm; pH 2.5.
Sodium hydroxide: 3 ml, 4 M; colour, greenish-blue; λ_{max}, 725 nm.

Table 3
Effect of pH on the colour development of hydroflumethiazide with potassium ferricyanide

pH	Absorbance	Molar absorptivity $l\ mol^{-1}\ cm^{-1}$
0.5	0.36	3.0×10^3
1.0	0.36	3.0×10^3
2.0	0.36	3.0×10^3
3.0	0.36	3.0×10^3
4.0	0.30	2.5×10^3
5.0	0.18	1.5×10^3
6.0	0.09	0.8×10^3

Hydroflumethiazide: 39.7 ppm; λ_{max}, 725 nm.
Potassium ferricyanide: 2 ml, 0.01 M.
Sodium hydroxide: 3 ml, 4 M.

the coloured complex was maximum in the pH range 0.5–3.0. Above pH 3.0 the absorbance of the blank was relatively higher.

Effect of temperature and time of heating

The development of colour of hydroflumethiazide with potassium ferricyanide and sodium hydroxide was studied at various temperatures. It was found that the complex had a maximum absorbance when the contents were heated at 40–60°C for 30 min. However, the colour intensity was decreased when the solution was heated above 60°C. The heating time of 30 min was sufficient for colour development.

Beer's law

The hydroflumethiazide ferricyanide complex obeyed Beer's law at 725 nm in the concentration range of 8–132 ppm of hydroflumethiazide. The Sandell [6] sensitivity was 0.11 $\mu g\ cm^{-2}$.

Stoichiometry of the complex

The ratio of ferricyanide to hydroflumethiazide in the complex was determined by Job's continuous and molar ratio methods [7, 8]. It was found that the ratio was 1:4.

Determination of hydroflumethiazide in pharmaceuticals

To evaluate the accuracy of the results recovery experiments were carried out. The results were compared with the BP method [9, 10]. The accuracy of the present method was relatively greater than that of the BP method. Moreover, the present method can be

Table 4
Analysis of hydroflumethiazide tablets

Sr. no.	Labelled amount mg/tablet	Hydroflumethiazide found (mg) Present method, mean	Present method, standard deviation*	BP method
1	25	25.05	0.2	24.97
2	25	25.05	0.1	24.99
3	25	24.03	0.1	25.05
4	25	24.98	0.2	25.07
5	25	25.03	0.1	25.05

*Five determinations.
Potassium ferricyanide: 2 ml (0.01 M); colour, greenish-blue.
Sodium hydroxide: 3 ml 4 M; pH 2.5; λ_{max}, 725 nm.

Table 5
Analysis of hydroflumethiazide in the presence of various excipients in synthetic mixtures

Sr. no.	Excipients	Recovery* (%)
1	Propylene glycol	100.0
2	Talc	100.2
3	Glycerin	100.1
4	Magnesium stearate	100.5
5	Starch	100.6
6	Calcium carbonate	100.3
7	Lactose	100.4
8	Acacia	100.2
9	Tragacanth	100.2

*Mean of eight determinations.
Potassium ferricyanide: 2 ml (0.01 M); colour, greenish-blue; pH 2.5.
Hydroflumethiazide: 25 mg.
Sodium hydroxide: 3 ml, 4 M; λ_{max}, 725 nm.

Table 6
Analysis of hydroflumethiazide in pharmaceutical preparations

Sr. no.	Dosage form	Labelled (mg)	Recovery* (%)	Standard deviation* (%)
1	Hydroflumethiazide tablets	25	99.99	0.15
2	Hydroflumethiazide + spironalactone tablets (25 mg)	25	100.01	0.02
3	Hydroflumethiazide + reserpine tablets (0.25 mg)	25	100.02	0.03

*Mean recovery and standard deviation of seven determinations.
Potassium ferricyanide: 2 ml (0.01 M); colour, greenish-blue; pH 2.5.
Sodium hydroxide: 3 ml, 4 M; λ_{max}, 725 nm.

used even for very low concentrations of hydroflumethiazide, thus giving a wide range for determination of the drug. The results are presented in Table 4.

In order to test the suitability and specificity of the present method, hydroflumethiazide was determined in synthetic mixtures containing common tablet excipients. The results in Table 5 show that the excipients did not interfere with the determination.

The proposed method was successfully applied to the determination of hydroflumethiazide in pharmaceutical preparations. Each tablet was powdered and dissolved in 10 ml of TM sodium hydroxide solution; the solution was filtered and diluted to 50 ml with distilled water. A 2-ml aliquot of this solution was analysed by the recommended procedure. The results are presented in Table 6.

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