

Colorimetric Microdetermination of Some Sulfa Drugs

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A colorimetric method has been developed for microdetermination of some sulfa drugs. The proposed method is based on the diazotization of the drug with sodium nitrite and hydrochloric acid. The diazonium salt was then coupled with 8-hydroxyquinoline in alkaline medium and the developed color was measured at its wavelength of maximum absorbance. The proposed colorimetric method of analysis is as accurate as the USP method (USP XX. The National Formulary, NF XV, 1980, p. 925. Mack Easton, Pa., 1980) and further being simpler than the official one. Application of the suggested method to a representative pharmaceutical sulfa drug is presented and the validity of the method was assessed by applying the standard addition technique. © 1986 Academic Press, Inc.

INTRODUCTION

The colorimetric methods are currently used for the analysis of sulfa drugs either in biological fluids or in various dosage forms. Among these methods are the phenol hypochlorite reaction using chloramine T (14) and thymol (2). Other methods assessed by aldehydes, such as *p*-dimethylaminobenzaldehyde (15), 4-aminocinnamic aldehyde (12), vanilline (9), and the color reaction with 1,2-naphthoquinone-4-sulfonate (16).

Several methods have been proposed for the colorimetric determination of sulfanilamides based upon diazotization of the free amino group with nitrous acid and the subsequent coupling of the diazo compound with either amines or phenols. The phenol coupling agents used were thiocol, thymol, phloroglucinol, and resorcinol (1, 5, 17, 18). Dimethyl α -naphthylamine, substituted diphenyl amine (4), *N*- α -naphthyl ethylenediamine (3), and chromotropic acid (10) are examples of the amines used.

An improved colorimetric method for the determination of sulfonamides (11) was described by Bratton and Marshall's reaction. Also it is possible to stop the diazotization reaction at the diazonium salt step and then spectrophotometric measurements were carried out in the UV region at 380 nm (7).

o-Diacetyl benzene was found to give colored compounds with aromatic primary amines in acetic acid medium (8).

In this work, 8-hydroxyquinoline, a new coupling agent that has been introduced by the authors (6), is tried for the microdetermination of some sulfa drugs. The optimum conditions for the maximum color development were studied. The proposed procedure was compared with official method of analysis and was used for the determination of a representative sulfa drug in tablets.

EXPERIMENTAL

Apparatus

A Unicam SP 600 Series 2 spectrophotometer, with a matched pair of 1-cm glass cells was used throughout.

Reagents and Materials

- (1) 1% Sodium nitrite solution.
- (2) 0.1% 8-Hydroxyquinoline in 1% sodium hydroxide solution in 50% aqueous ethanol.
- (3) 10% Aqueous hydrochloric acid.
- (4) 20% Aqueous sodium hydroxide.
- (5) Stock solution of sulfa drugs (1 ml equivalent to 1 mg of sulfa drug) prepared by dissolving 100 mg sulfa drug in a few milliliters of distilled water with the aid of a few drops of 0.1 *N* sodium hydroxide solution, then the volume was completed, in a 100-ml volumetric flask, with distilled water.
- (6) Dilute standard solution of sulfa drugs (1 ml equivalent to 20 μg of sulfa drugs) prepared by dilution from the stock solution, with distilled water.

Procedure

For authentic samples. Prepare working standard solutions by measuring suitable volumes of dilute standard sulfa drugs solutions into 10-ml volumetric flasks. To each flask add 1 ml of 10% hydrochloric acid, followed by 3 ml of 1% sodium nitrite solution. Mix the contents of each flask and allow to stand for 10 min. Add to each flask 3 ml of 0.1% 8-hydroxyquinoline solution and allow to stand for another 10 min. Render the solution alkaline by adding 1 ml of 20% sodium hydroxide solution and complete to volume with 50% aqueous ethanol. Measure the absorbance of the developed color at its λ_{max} , in a 1-cm cell and against a reagent blank simultaneously prepared.

For tablets. Weigh and powder 20 tablets of the drug to be analyzed. Weigh accurately an amount equivalent to 100 mg of the active constituent into a 100-ml volumetric flask. Dissolve in a few milliliters of ethanol with the aid of a few drops of 0.1 *N* sodium hydroxide then adjust to volume with distilled water. Carry out the suitable dilution and proceed as described above for color development.

RESULTS AND DISCUSSION

A proposed method for the microdetermination of some sulfa drugs has been developed. The proposed method is based on the diazotization of sulfa drugs with sodium nitrite in hydrochloric acid medium. The diazonium salts thus formed were then coupled with 8-hydroxyquinoline. The medium was then rendered alkaline with sodium hydroxide and the developed color was then measured against a reagent blank at the wavelength of maximum absorbance.

It is noteworthy that there was no need for decomposing the excess nitrous acid, since no interference with the subsequent color development was observed. The optimum conditions for maximum color development were studied and applied for the analysis of nine sulfa drugs. All the analyzed sulfa drugs exhibited

TABLE 1
Analytical Data for the Determination of Authentic Samples of Sulfa Drugs by the Proposed Procedure, Percentage Recovery Being Compared with USP XX and NF XV (13)

| Authentic samples | λ_{\max} (nm) | Used (μg) | % Recovery | |
|----------------------|--------------------------|---------------------------|------------------------------|------------|
| | | | Proposed method ^a | USP method |
| Sulfanilamide | 500 | 2-25 | 99.86 \pm 1.03 | 100.2 |
| Sulfaguanidine | 500 | 2-25 | 99.86 \pm 0.83 | 99.8 |
| Sulfacetamide sodium | 500 | 5-35 | 100.46 \pm 0.95 | 100.0 |
| Sulfamerazine | 500 | 5-35 | 100.85 \pm 0.80 | 99.7 |
| Sulfadimidine sodium | 500 | 10-35 | 100.20 \pm 0.93 | 100.6 |
| Sulfadiazine | 500 | 2-35 | 100.81 \pm 1.74 | 99.7 |
| Sulfathiazole | 500 | 10-40 | 100.71 \pm 0.66 | 100.0 |
| Sulfasomidine | 504 | 10-40 | 100.58 \pm 1.33 | 99.8 |
| Sulfapyridine | 500 | 10-40 | 100.05 \pm 0.85 | 99.9 |

^a Results are the average of 10 experiments.

maximum absorbance at wavelength ranging between 500 and 504 nm (Table 1). The concentration ranges over which the studied sulfa drugs obeyed Beer's law are shown in Table 1.

Comparison of the obtained percentage recovery by the proposed method with the purity of the studied compounds as determined by the USP XX and NF XV, 1980 (13) showed similar accuracy of the two methods (Table 1). The proposed colorimetric procedure being simpler than the official one.

Application of the proposed method to a representative single sulfonamide tablet was performed. Elkosine tablets, Swiss pharma S.A.A., Cairo, Egypt, labeled as containing 500 mg of sulfasomidine per tablet, showed a found percentage of 99.8% of the labeled amount by the proposed colorimetric method. The validity of the proposed procedure was assessed by applying the standard addition technique. The obtained results are shown in Table 2.

Results shown in both Tables 1 and 2 indicate that the proposed colorimetric

TABLE 2
Accuracy of the Recovery of Standard Addition of Authentic Sulfasomidine to Elkosine Tablets by the Proposed Method

| Experiment No. | Added (μg) | Found (μg) | Recovery (%) |
|----------------|-------------------------|-------------------------|-----------------|
| 1 | 10 | 10.0 | 100.0 |
| 2 | 10 | 9.9 | 99.0 |
| 3 | 12 | 11.8 | 98.3 |
| 4 | 12 | 12.0 | 100.0 |
| 5 | 18 | 18.0 | 100.0 |
| 6 | 18 | 17.8 | 98.9 |
| | Mean | | 99.4 \pm 0.78 |
| | ($P = 0.05$) | | |

method is accurate and precise for the determination of the studied sulfa drugs, both in pure and dosage forms. However, the procedure adopted cannot be applied for mixture of sulfa drugs, since the color developed in all cases exhibited nearly the same wavelength of maximum absorbance. Preliminary separation would be, therefore, necessary for the analysis of a mixture of sulfa drugs.

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