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Spectrophotometric Determination of Sulfacetamide Sodium in Pharmaceutical Preparation Using 8-Hydroxy-7-iodoquinoline-5-sulfonic Acid as Chromogenic Reagent

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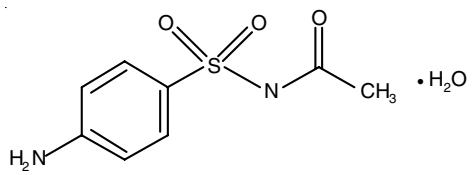
A simple, rapid and precise process have been presented for the analysis of sulfacetamide sodium in pure form as well as in pharmaceutical dosage. The process is based on the diazotization reaction of sulfacetamide sodium with sodium nitrite in the presence of hydrochloric acid to form diazonium salt, which is coupled with 8-hydroxy-7-iodoquinoline-5-sulfonic acid in alkaline medium to form azo dye, showing absorption maxima at 490 nm. Calibration plot was linear over the concentration range 2-28 μg mL^{-1} for sulfacetamide sodium with detection limit 1.9178 μg mL^{-1}. The molar absorptivity and Sandell's sensitivity are 6.6357×10^3 L mol^{-1} cm^{-1} and 3.8318×10^{-2} μg cm^{-2}, respectively. The method was successfully applied for analysis of sulfacetamide sodium in eye drops and did not require any preliminary separation or treatment of the samples. The results agree favourably with the Bratton-Marshall's method (standard method).

Keywords: Sulfacetamide sodium, 8-Hydroxy-7-iodoquinoline-5-sulfonic acid, Spectrophotometry, Diazotization coupling reaction.

INTRODUCTION

Sulfacetamide sodium (SCS) is a sulfonamide bacteriostatic antibiotic [1-3]. It is widely used in medicine because of its inhibitory effect on the growth in many bacteria [4] that was considered to be the major cause of death before the discovery of sulfa drugs and other antibiotics [5].

Sulfacetamide is sodium derivative of N-[(4-aminophenyl)sulfonyl]acetamide [6] whereas its chemical structure [7,8] is given as:



Its molecular weight is 254.2 g mol^{-1}. It is obtained in a monohydrate form and it is white, crystalline powder, freely soluble in water, slightly soluble in ethanol, sparingly soluble in acetone and partially soluble in ether and chloroform. It melts at 257 °C [9]. It is applicable effective treatment for bacterial conjunctivitis and as adjunctive therapy for trachoma [10]. Therefore, it is indicated for the treatment of the bacterial infections of the eyes [11]. Literature survey reveals that the drug can be determined by a variety of analytical techniques such as HPLC [12-14], liquid chromatography [15], capillary chromatography [16], micellar electro kinetic capillary chromatography [17,18], NMR [19], fluorescent probe study [20], electrophoresis [21] flow injection analysis [22], sequential injection analysis [23], colorimetry [24], spectrophotometric method [25-32]. The present work, is the description of a simple spectrophotometric method for the determination of sulfacetamide sodium in pure and eye drops based on diazotization of sulfacetamide sodium using sodium nitrite with hydrochloric acid, then coupled with 8-hydroxy-7-iodoquinoline-5-sulfonic acid as a new reagent in alkaline medium to form azo dye, showing absorption maxima at 490 nm The method has been proved successfully for the determination of sulfacetamide sodium in pure form and in eye drops.

EXPERIMENTAL

A Shimadzu UV-visible 1800 double beam spectrophotometer with 1 cm quartz cell was used throughout this research work.

Preparation of solutions

Sulfacetamide sodium (1000 μg mL^{-1}): Sulfacetamide sodium stock standard solution was prepared by dissolving 0.10 g of pure sulfacetamide sodium in distilled water and made up to100 mL volumetric flask with distilled water. Working standard solution were prepared by suitable dilution of the stock standard solution with distilled water.

Sodium nitrite (3.9×10^{-3} M): Sodium nitrite solution was prepared by dissolving 0.0269 g of sodium nitrite (Merck) in distilled water and diluting to the mark in 100 mL volumetric flask then (3.9×10^{-4} M) was prepared by diluting 10 mL of sodium nitrite solution (3.9×10^{-3} M) with distilled water in 100 mL volumetric flask.

Hydrochloric acid (1 M): Hydrochloric acid solution was prepared by diluting (21.75 mL) of (11.49 M) of concentrated hydrochloric acid (BDH) in 250 mL of distilled water volumetric flask.

8-Hydroxy-7-iodoquinoline-5-sulphonic acid (0.1 %): 8-Hydroxy-7-iodoquinoline-5-sulphonic acid solution was prepared by dissolving 0.1 g of 8-hydroxy-7-iodoquinoline-5-sulphonic acid (BDH) in distilled water and diluting to 100 mL volumetric flask with the same solvent.

Ammonium hydroxide (2 M): Ammonium hydroxide solution was prepared by diluting 74.9 mL of 13.36 M of concentrated ammonium hydroxide (Fluka) with distilled water in 500 mL volumetric flask.

Diazotized sulfacetamide sodium solution (3.9×10^{-4} M): Prepared by transferring 10 mL of sulfacetamide sodium (1000 μg mL^{-1}) into 100 mL volumetric flask then add 10 mL of sodium nitrite (3.9×10^{-3} M) and 4 mL of HCl (1 M), shake well with cooling at 15 °C and diluting to the mark with distilled water.

More dilute solutions were prepared fresh daily by dilution of the stock solution with distilled water.

Pharmaceutical preparations: Two samples of sulfacetamide sodium eye drops obtained from commercial sources: (1) Apisulfa-20 eye drops (10 mL): (200 mg sulfacetamide sodium) - Amman pharmaceutical industries Co. Ltd. Jordan. (2) Apisulfa-10 eye drops (10 mL): (100 mg sulfacetamide sodium + 0.1 mg benzalkonium)-Amman Pharmaceutical Industries Co. Ltd. Jordan.

An aliquot corresponding to 100 mg of sodium sulfacetamide was diluted to 100 mL with distilled water in a volumetric flask to obtain 1000 μg mL^{-1} of sulfacetamide sodium. Further appropriate solutions of pharmaceutical preparations were made up by simple dilution with distilled water.

General procedure for calibration: An increasing volumes 1-7 mL of diazotized sulfacetamide sodium (100 μg mL^{-1}) was transferred into a series of 25 mL standard flask, followed by adding 2 mL of 8-hydroxy-7-iodoquinoline-5-sulphonic acid (0.1 %) and 1 mL ammonium hydroxide (2 M). The contents of the flasks were diluted to the mark with distilled water, mixed well and left for 10 min, the absorbance of the orange dye formed was measured at 490 nm against a reagent blank. For the optimization of conditions and in all subsequent experiments, a 5 mL of (100 μg mL^{-1}) of sulfacetamide sodium in a final volume of 25 mL was used.

RESULTS AND DISCUSSION

Absorption spectra: When a diluted aqueous solution of diazotized sulfacetamide sodium was mixed with 8-hydroxy-7-iodoquinoline-5-sulphonic acid in alkaline medium, an intense orange dyes produced directly, which became stable after 10 min and has a maximum absorption at 490 nm. Fig. 1 shows the spectra of the products formed.

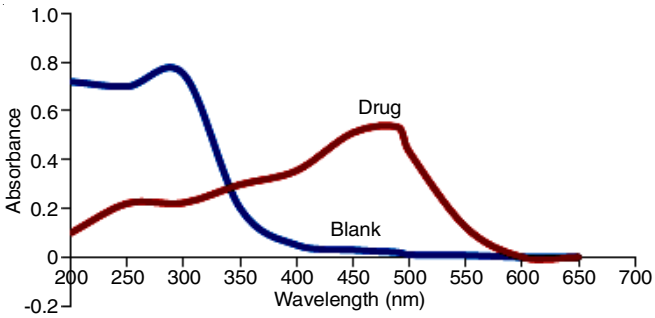


Fig. 1. Absorption spectra of azo dye (20 μg mL^{-1}) of sulfacetamide sodium against reagent blank and blank against distilled water

Optimization of the experimental conditions: The effects of various parameters on the absorption intensity of the formed product were optimized. A 20 μg mL^{-1} of sulfacetamide sodium was used in all optimization experiments.

Effect of acids used in preparation of diazotization salt: The diazotization salt of sulfacetamide sodium was produced in acidic medium. So the effects of different acids solutions (1 M) were studied such as hydrochloric acid, sulfuric acid, phosphoric acid and acetic acid. It was found that hydrochloric acid was the most suitable acidic medium for a maximum absorbance and was used in all subsequent experiments. As a result the effect of various volumes of hydrochloric acid (1 M) were optimized on the maximum absorbance by variable the volumes of HCl and fixing the other parameters. It was found that 1 mL of HCl (1 M) gave the highest absorbance and was chosen for further use (Fig. 2).

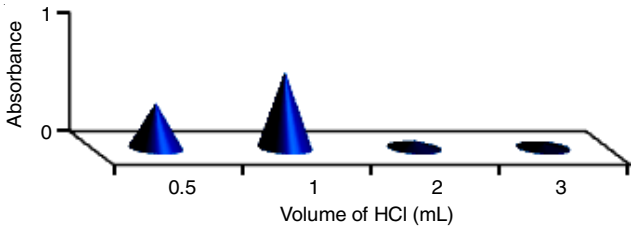


Fig. 2. Effect of the volume of HCl (1 M) for determination of sulfacetamide sodium (20 μg mL^{-1})

Effect of the alkaline medium (type and volume): Alkaline medium is essential for increasing the intensity of the colour. Accordingly, a different alkaline solutions (2 M) were examined such as sodium carbonate, ammonium hydroxide, sodium hydroxide and potassium hydroxide. It was found that ammonium hydroxide was the most appropriate alkaline medium for a maximum absorbance and was used in all following experiments. Consequently, the effect of different volumes of ammonium hydroxide (2 M) was studied on the maximum absorbance by changeable the volume of ammonium hydroxide solution between (0.5-4 mL) with fixing the other parameters. A volume of 1 mL of ammonium hydroxide (2 M) was enough to obtain the maximum absorbance (Fig. 3).

Effect of coupling reagent concentration: Different volumes of reagent 8-hydroxy-7-iodoquinoline-5-sulphonic acid (0.1 %) was studied in the range of 0.5-3 mL with fixing the other parameters. Maximum absorbance intensity was obtained with 2 mL of 8-hydroxy-7-iodoquinoline-5-sulphonic acid (Fig. 4).

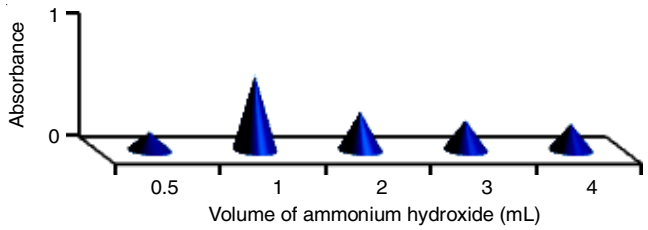


Fig. 3. Effect of the volume of NH_4OH (2 M) for determination sulfacetamide sodium (20 µg mL^{-1})

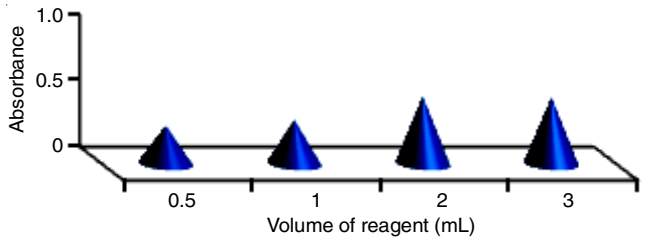


Fig. 4. Effect of the volume of 8-hydroxy-7-iodoquinoline-5-sulphonic acid (0.1 %) for determination of sulfacetamide sodium (20 µg mL^{-1})

Order of addition of reagents: The order of reagents addition is very necessary, so different orders of addition of reagents were examined and it was found that the order of addition of reagents by mixing sulfacetamide sodium with sodium nitrite then HCl, 8-hydroxy-7-iodoquinoline-5-sulphonic acid and ammonium hydroxide gave the highest absorbance and was used in all further experiments.

Effect of reaction time: The resulting colour product of the proposed method was found to be formed quickly but the colour intensity reached a highest absorbance for 10 min, therefore a 10 min development time was chosen as optimum in the general procedure.

Composition of the product: Continuous variation (Job's) method [33], had been studied under the suggested optimum conditions using equimolar solutions of the drug and reagent (1.57×10^{-3} M). The result obtained in Fig. 5 shows that 1:1 azo dye was formed between diazotized sulfacetamide sodium and reagent at 490 nm.

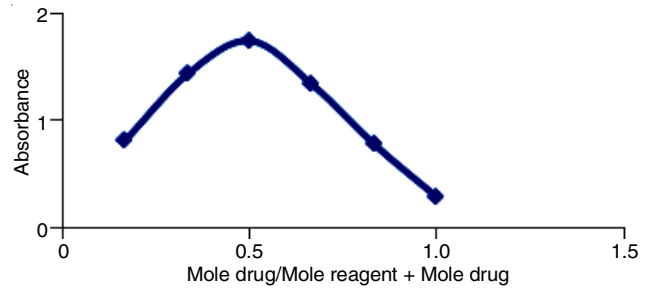
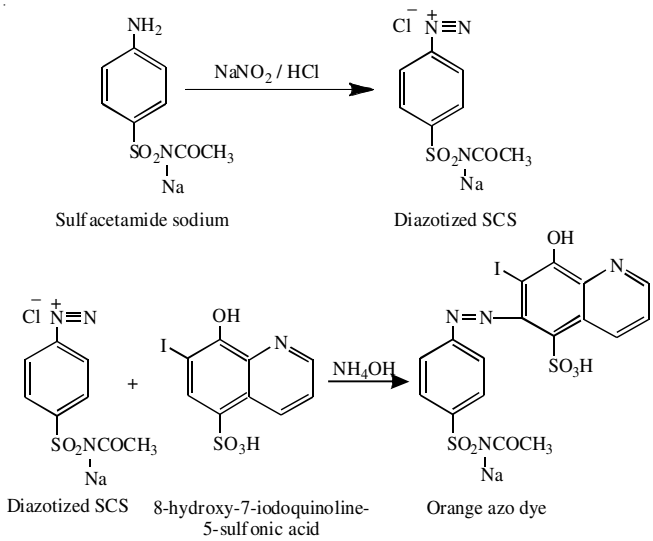


Fig. 5. Continuous variation plot

Reaction mechanism: The reaction between diazotized sulfacetamide sodium and 8-hydroxy-7-iodoquinoline-5-sulfonic acid occurs in two steps: in the first step, the reaction of the drug with sodium nitrite occurs in an acid medium producing the diazonium salt. In the second step, the diazonium salt in alkaline medium coupled with 8-hydroxy-7-iodoquinoline-5- sulfonic acid to produce azo dye that was monitored at 490 nm. The proposed mechanism is shown in **Scheme-I** [34].



Scheme-I: Proposed mechanism of the reaction between diazotized sulfacetamide sodium with 8-hydroxy-7-iodoquinoline-5-sulfonic acid

Determination of stability constant: The apparent stability constant [35] was calculated by comparing the absorbance of a solution containing stoichiometric amount (1.57×10^{-3} M) of diazotized sulfacetamide sodium and reagent 8-hydroxy-7-iodo-quinoline-5-sulphonic acid (A_s) with that of a solution containing a five-fold excess of reagent (A_m) and according to analytical procedure. The average stability constant (K) = 0.953 $\times 10^4$ L mol^{-1} where [$K = (1-\alpha)/\alpha^2C$; $\alpha = (A_m - A_s)/A_m$].

Analytical characteristic of spectrophotometric method: For the proposed method, a calibration diagram was obtained by the method described before and a sequence of standard solutions was analyzed in triplicate to examine the linearity (Fig. 6). The slope (a), the intercept (b), the molar absorptivity (ε) and Sandell's sensitivity (S), were determined and included in Table-1. The accuracy and precision for the proposed method was examined by analyzing four replicate of sulfacetamide sodium by proposed method for three different concentrations of sulfacetamide sodium. The values of recovery, relative standard deviation (RSD) % and relative error E_{rel} % are summarized in Table-1. These values indicated the high accuracy and precision for the proposed method. Statistical evaluation [36] of the regression line gave the values of standard deviation for residuals ($S_{y/x}$), slope (S_a) and intercept (S_b) at 95 % confidence are shown in the same table. The limit of detection (LOD) and limit of quantitation (LOQ) were determined by using the formula: LOD or LOQ = k $S_{y/x}$/b; where k = 3 for LOD and 10 for LOQ. The values are shown in Table-1.

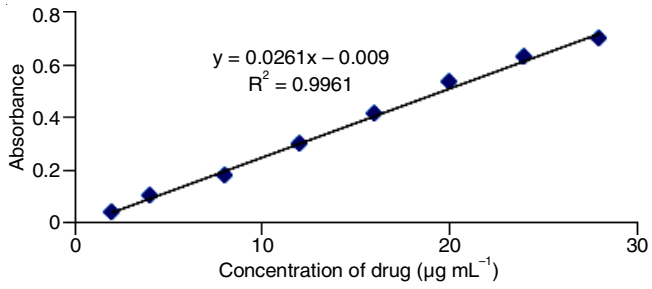


Fig. 6. Calibration graph of sulfacetamide sodium

TABLE-1
ANALYTICAL DATA OBTAINED FROM THE DETERMINATION OF SULFACETAMIDE SODIUM

Parameter	Value
λ_{max} (nm)	490
Beer's law limits (μg mL^{-1})	2-28
Molar absorptivity (ε, L mol^{-1} cm^{-1})	6.6357×10^3
Sandell's sensitivity (S, μg cm^{-2})	3.8318×10^{-2}
Regression equation	Y = 0.0261 [SCS μg mL^{-1}] - 0.009
Slope (a)	0.0261
Intercept (b)	-0.0090
$S_{y/x}$	1.6685×10^{-2}
Standard deviation of slope (S_a)	2.7347×10^{-2}
Standard deviation of intercept (S_b)	0.4580
Correlation coefficient (R)	0.9980
Relative standard deviation (RSD %)	1.1328
Average of recovery (%)	99.195
Relative error (%)	-0.805
Limit of detection (LOD) (μg mL^{-1})	1.9178
Limit of quantitation (LOQ) (μg mL^{-1})	6.3927
Molar ratio (D:R)	1:1
Colour	Orange

Pharmaceutical application: The suggested method was applied to the determination of sulfacetamide sodium in eye drops formulation. Two types of eye drops preparations containing sulfacetamide sodium were analyzed and they gave a good accuracy and precision as shown in Table-2. The proposed method was compared successfully with the Bratton-Marshall's method (standard method) using N-(1-naphthyl)-ethylenediamine dihydrochloride (NED) [37].

TABLE-2
APPLICATION OF THE PROPOSED AND STANDARD METHOD FOR THE DETERMINATION OF EYE DROPS CONTAINING SULFACETAMIDE SODIUM

Pharmaceutical preparation	Proposed method		Standard method
	Recovery (%)	RSD (%)	Recovery (%)
Apisulfa-10 eye drop	99.342	1.569	98.475
Apisulfa-20 eye drop	100.211	1.877	99.283

Statistical analysis [38] was performed by applying F-test and t-test at 95 % confidence level. The calculated values for F (1.9303) and t (0.608) did not exceed the critical values of F =19.0 and t = 2.776 ($n_1 + n_2 - 2 = 4$).These confirming that there are no significant differences between the proposed methods with the standard method with respect to precision and accuracy in the determination of sulfacetamide sodium in pharmaceutical preparations.

A standard additions method was used to correct the chemical interferences that present in eye drops preparations. It involves adding increment volumes (0-2 mL) of standard solution of 100 μg mL^{-1} to a fixed volume sample (1 mL of 100 μg mL^{-1}) and employing the conditions described under procedure. It gave a good accuracy and precision (Table-3).

Conclusion

The proposed method was found to be easy, fast, low cost and fairly selective than some of the reported methods. It had an advantage of being accurate, did not require the removal of excipients, pH control and solvent extraction step. The proposed method was applied to the analysis of sulfacetamide sodium in eye drops and can be used for the routine analysis.

TABLE-3
APPLICATION OF THE STANDARD ADDITIONS METHOD AND BRATTON-MARSHALL'S METHOD FOR THE DETERMINATION OF EYE DROPS CONTAINING SULFACETAMIDE SODIUM

Eye drops samples	[SCS] depend on standard addition	Standard additions method		Bratton-Marshall's method
		Recovery (%)	RSD (%)	Recovery (%)
Apisulfa-10	3.98	99.50	1.47	98.475
Apisulfa-20	4.1	99.75	1.93	99.283

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