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Research Article

Simultaneous Spectrophotometric Determination of Salbutamol by Coupling with Diazotized 4-Aminobenzoic acid

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ABSTRACT

A simple, rapid and sensitive spectrophotmetric method for trace determination of salbutamol (SAL) in aqueous solution and in pharmaceutical preparations is described. The method is based on the diazotization coupling reaction of the intended compound with 4-amino benzoic acid (ABA) in alkaline medium to form an intense orange, water soluble dye that is stable and shows maximum absorption at 410 nm. A graph of absorbance versus concentration indicates that Beer's law is obeyed over the concentration range of 0.5-30 ppm, with a molar absorbtivity 3.76×10^4 $L.mol^{-1}.cm^{-1}$ depending on the concentration of SAL. The optimum conditions and stability of the colored product have been investigated and the method was applied successfully to the determination of SAL in dosage forms.

Keywords: Salbutamol, 4-aminobenzoic acid, azo dye.

INTRODUCTION

Salbutamol sulphate (SAL), chemically known as bis [(1RS)-2- [(1,1-dimethylethyl) amino]-1-[4- hydroxy -3-(hydroxymethyl) phenyl]ethanol] sulphate, is an agonist of β_2 receptors which are present in the bronchioles of lungs of human body. Therefore, it acts as a bronchodilator and its cardiovascular effects are less than its bronchodilator actions[1]. Some different methods of analysis have been reported for the determination of SAL, including HPLC[2,3], capillary electrophoresis[4], flow injection analysis[5,6]. In addition, visible spectrophotometric methods have been described for the evaluation of salbutamol sulphate in pharmaceuticals, using different reactions[7-12]. However, these procedures possess some drawbacks such as lack of sensitivity, long extraction procedure or requiring critical working conditions and hence are unsatisfactory for routine analysis. The purpose of the present investigation is to develop a simple and sensitive method for the determination of SAL in pharmaceutical preparations using diazotization coupling reaction. The proposed method is based on a coupling reaction between SAL and DABA in alkaline medium to form an intense yellow-orange color product which shows an absorption maximum at 410 nm.

Reaction Mechanism of The Proposed Method

The aromatic amino group present in ABA is diazotized with nitrous acid ($NaNO_2$/HCl) and diazonium salt thus formed is coupled with SAL at room temperature. SAL forms an orange colored product (λ_{max} = 410 nm) with DABA in alkaline medium. Due to the phenolic nature of the drug, it can readily be coupled with DABA according to scheme 1[13].

Experimental

Apparatus

All spectral and absorbance measurements were carried out on a Shimadzu UV-visible 260 digital double beam recording spectrophotometer using 1-cm silica cells.

Reagents:

All chemicals used were of analytical reagent grade and pure salbutamol sulphate (SAL) drug sample was provided from state company for Drug Industries and Medical Appliance, SDI, Samara/Iraq. Dosage forms were obtained from commercial sources.

Salbutamol sulphate stock ($1000\mu gmL^{-1}$) and working solution ($500\ \mu gmL^{-1}$) The stock solution of SAL was prepared by dissolving 0.1000 g in distilled water and completed to 100 mL with the same solvent. Serial dilutions with distilled water were made to cover the working range.

Diazotized 4-aminobenzoic acid (DABA), 3 mM was prepared daily by dissolving 0.0411 g of ABA in about 20 mL of distilled water, add 2 mL of 1M hydrochloric acid in a 100 mL volumetric flask. Cool the mixture to 0-5 ºC for 5 min using an ice–bath. Add 0.0207 g amount of sodium nitrite (Merck) and stir the mixture. After 5 min the volume is made up to the mark with distilled water. More dilute solutions were prepared by suitable dilute with distilled water.

Hydrochloric acid solution (1M, BDH) Prepared by dilution of concentration hydrochloric acid and standardized against sodium carbonate.

Sodium hydroxide solution (0.1M, BDH) A 1.000g of sodium hydroxide was dissolved in distilled water and made up to the 250 mL volumetric flask with the same solvent.

Analysis of commercial dosage forms: Fifty to 100 tablets were accurately weighed and powdered .An amount to

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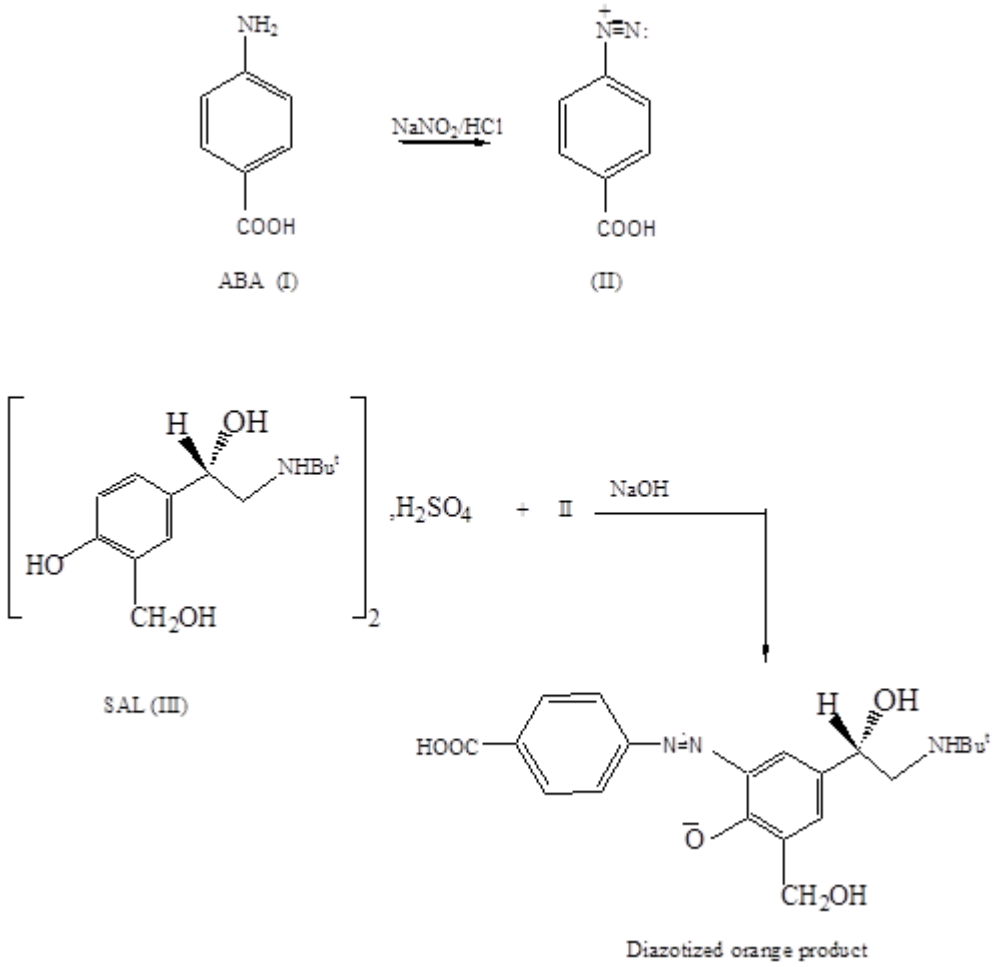

Scheme 1: Reaction mechanism

Table 2: Analytical data obtained from proposed method.

Parameter	value
Regression equation	y = 0.0652x + 0.0751
Beer's Low limits (µg.mL^{-1})	0.5-30
Molar absorbativity(lit.mole^{-1}.cm^{-1})	3.76×10^4
Slope(b)	0.0652
Intercept(a)	0.0751
Correlation coefficient (R^2)	0.9972
λ_{max} (nm)	410
R.S.D (%)	<2.63
Average of recovery (%)	102.214

Table 3: Accuracy and precision of the proposed method.

Conce. of SAL(µg/mL)		Rec.%	RSD%
Present	Found		
10	10.198	101.980	1.33
15	15.367	102.447	2.63

tablets equivalent to 100 mg of the pure drug, was dissolved in distilled water and transferred into a 100 ml calibrated flask and completed to the mark with the same solvent. The flask with its contents was shaked well and filtered. Samples of SAL were taken and the measurements were carried out as describe earlier under general procedure.

Procedure of pure drug

An aliquot of sample containing 5-300 µg of SAL was transferred into a series of 10 mL standard flasks to cover the range of 0.5-30 µg mL^{-1}. A volume of 2 mL of 3 mM DABA solution and 0.5mL of 0.1M sodium hydroxide solution were added. The contents of flasks were diluted to the mark with distilled water, mixed well and left for 5 min. The absorbance was measured at 410 nm (at room temperature 20°C). The color of the formed dye is stable for more than 3hr. For optimization of conditions and in all subsequent experiments, a solution of 250 µg was used and the final volume was 10 mL (i.e.25 µg mL^{-1}).

Salbutamol sulphate stock solution (1000 µg mL^{-1})

Stock solution (1000 µg mL^{-1}) was prepared by dissolving 0.1000 g of the pure compound in a sufficient amount of distilled water and complete to 100 mL in a volumetric flask with the same solvent. Working solution (500 µg mL^{-1}) for the drug was prepared by a simple dilution with the same solvent. The measurement was carried out as described earlier under general procedure using suitable volume of last solution.

RESULTS AND DISCUSSION

Absorption Spectra

Table 4: Application of the proposed method for the determination of SAL in pharmaceutical forms.

Drug Sample	SAL (µg.mL^{-1})		Rec. % *	Aver. Rec.	R.S.D%*
	Taken	Found			
Butadin	10	10.21	102.10	99.65	2.34
(Tablets 2 mg)SDI	15	14.58	97.20		3.23

* Average of four determinations.

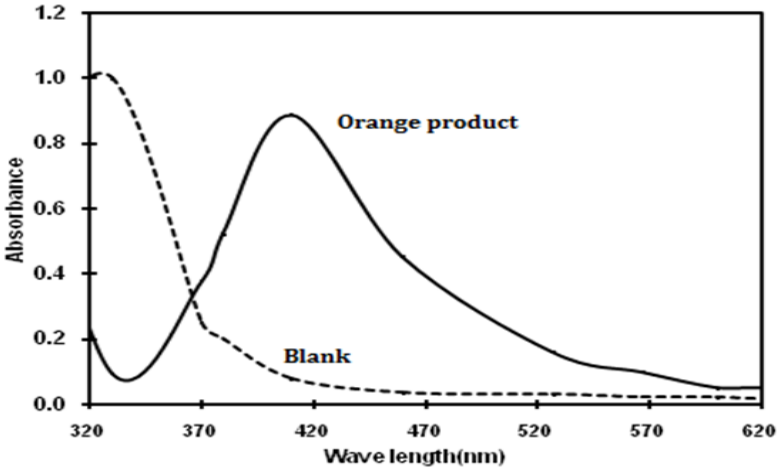

Figure 1: Absorption spectra of A (25 µg mL^{-1}) of SAL treated as described under procedure and measured against blank , B the reagent blank measured against distilled water.

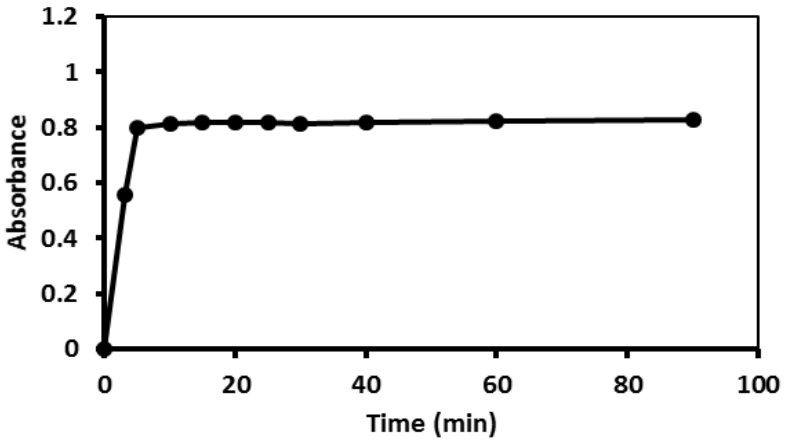

Figure 2: Effect of reaction time.

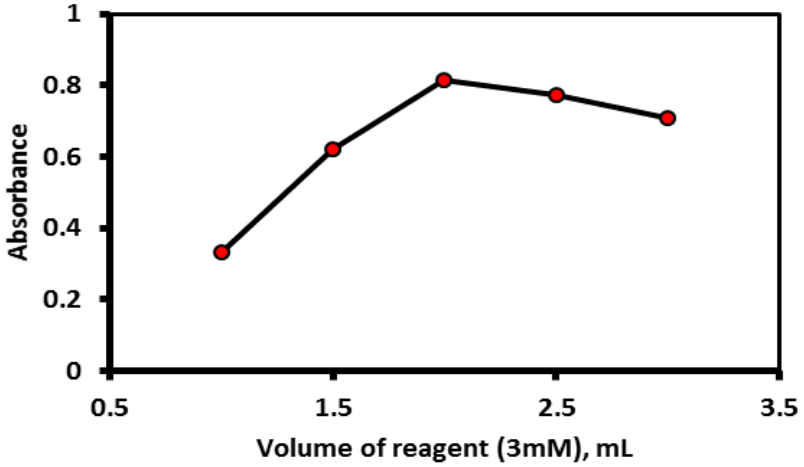

Figure 3: Effect of reagent.

When a very diluted aqueous solution of SAL was mixed with DABA reagent in alkaline medium, an intense orange azo dye formed immediately, which became stable after 5min. The orange product has a maximum absorption at 410 nm. Fig.1 shows the spectra of the product formed and of the reagent blank, the maximum absorption at 410 nm was used in all subsequent experiments.

Study of The Optimum Reaction Conditions

The effects of various parameters on the absorption intensity of the formed product were studied and the reaction conditions were optimized.

Effect of Reaction Time

In spite of the rapid color development (formed immediately) the color intensity reached a maximum after SAL solution had been reacted with DABA and sodium hydroxide for 5 min, therefore 5 min development time was selected as optimum in the general procedure. The color obtained was stable for 3hr (Fig.2).

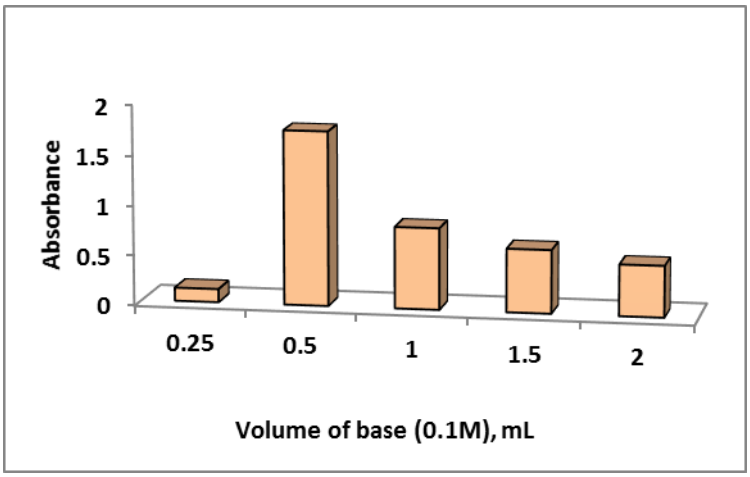

Figure 4: Effect of volume off base.

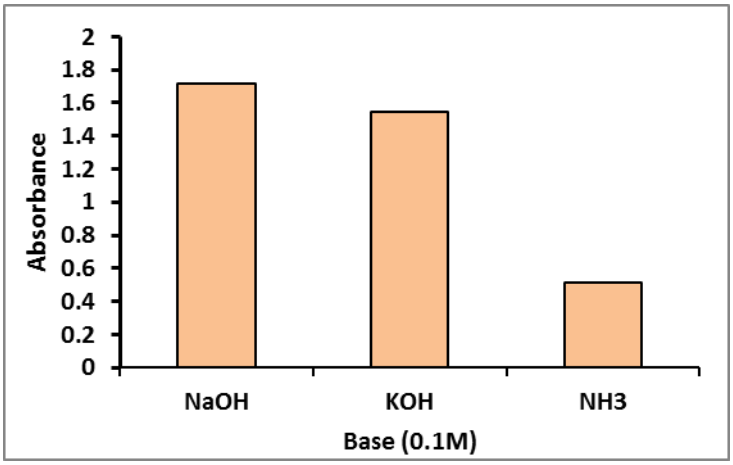

Figure 5: Effect of type of base.

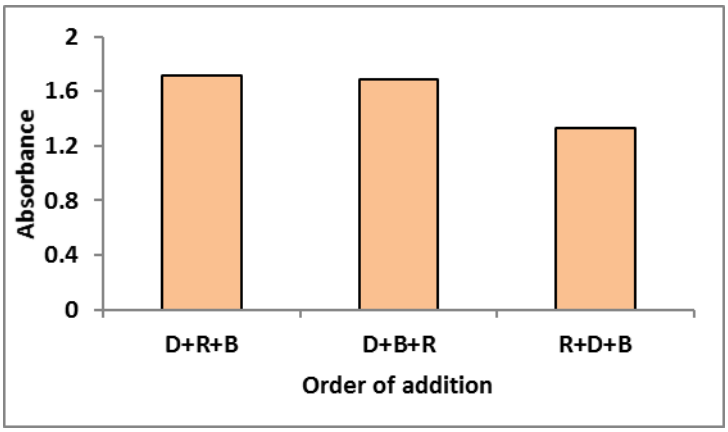

Figure 6: Effect of order of addition.

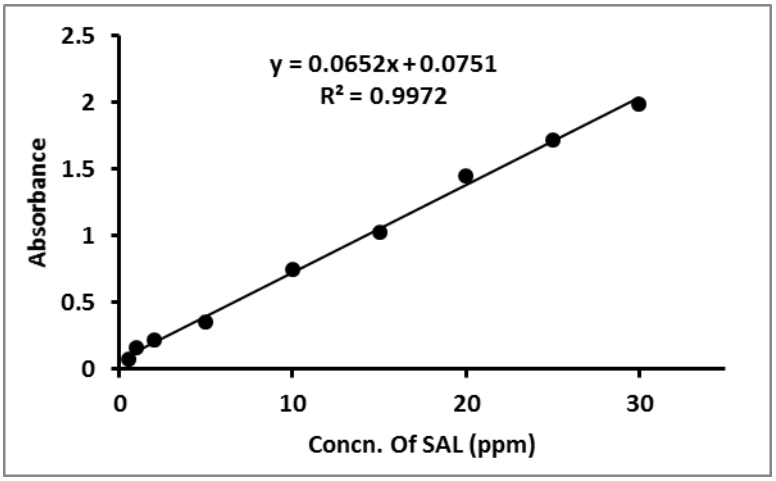

Figure 7: Calibration curve.

Effect of Diazotized Reagent Concentration

When various volumes of DABA solution were added to a fixed concentration of SAL, 2mL of 3mM DABA solution was sufficient to develop the color to its full intensity and give minimum blank value; above 1.5 mL the absorbance of blank value increased, causing a decrease in the absorbance of sample. Therefore, 2mL of 3mM DABA solution was found optimum and was used in all subsequent experiments (Fig.3).

Effect of Alkaline Solution

Preliminary results indicated that the presence of an alkaline in the reaction mixture is essential for developing a more intense orange color. Different volumes of sodium hydroxide were examined and it was found that 0.5mL of 0.1M solution gave a high sensitivity and minimum blank value (Fig.4). In this respect, sodium hydroxide, potassium hydroxide, and ammonia were examined (Fig.5). It was found that the best results were obtained with sodium hydroxide, therefore, sodium hydroxide was chosen.

Effect of Order of Addition

Different orders of addition of reagents were experimented and it was found that the order of addition of reagents cited under general procedure (Drug + reagent + base) was optimum and was used in all subsequent experiments (Fig. 6).

Working Curve

Under the recommended conditions described above and mentioned in the general assay procedure, a linear calibration graph (Fig.7) for SAL was obtained, which shows that Beer's law obeyed over the concentration range of 0.5-30 ppm with a correlation coefficient of 0.9972. The conditional molar absorpativity of the product formed with SAL was found to be 3.76×10^4 $L.mol^{-1}.cm^{-1}$ with reference to the SAL [Table (2)].

Accuracy and Precision

To determine the accuracy and precision of the method, SAL was determined at three different concentration. The overall relative standard deviations and recoveries were summarized in Table (3). Small relative standard deviation and a good recovery indicated high precision and accuracy of the proposed method.

Analytical Applications

The suggested method was applied to the quantitative determination of SAL in pharmaceutical formulations. One type of tablets containing SAL have been analyzed and they gave a good accuracy and precision as shown in Table (4).

CONCLUSION

A simple, rapid and sensitive spectrophotometric method has been developed for the determination of trace amount of SAL in aqueous solution based on diazotization coupling reaction with DABA reagent in the presence of sodium hydroxide. The proposed method does not require temperature control or solvent extraction step, the method was applied successfully to pharmaceutical tablets containing.

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