IASJ المجلات الاكاديمية العراقية

Tikrit Journal of Pure Science

ISSN: 1813 – 1662 (Print) --- E-ISSN: 2415 – 1726 (Online)

Journal Homepage: http://tjps.tu.edu.iq/index.php/j

Determination of Salbutamol Using Spectrophotometric Method Depending on Chromium-1,5-diphenylcarbazide Complex

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https://doi.org/10.25130/tjps.v25i5.290

ARTICLE INFO.

Article history:

-Received: 20 / 4 / 2020

-Accepted: 28 / 7 / 2020

-Available online: / / 2020

Keywords:

Salbutamol, spectrophotometric, 1,5-diphenylcarbazide.

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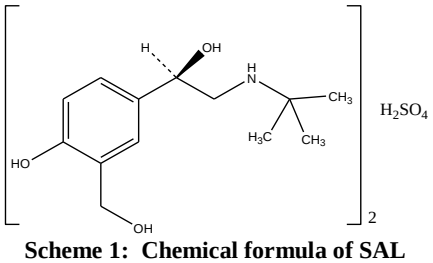
ABSTRACT

A rapid, simple, accurate, and economized spectrophotometric method for the determination of salbutamol sulfate(SAL) has been suggest using an oxidation-reduction reaction. This method depends on the oxidation of SAL medication with an excess amount of chromate (CrO_4^{2-}) as an oxidant agent in the acidic medium of 2N Sulphuric acid and the presence of Sodium oxalate as a catalyst of the oxidation process. Then the remaining quantity of chromate will be reacted with 1,5-diphenylcarbazide to form a pink-reddish and stable water-soluble complex which is exhibiting maximum absorption at 543 nanometers. The optimum conditions for the present work were studied experimentally. The linearity of the proposed method follows Beer's law in the concentration range of 50 to 900 µg in a final volume of 25ml with a molar absorptivity which is equal to 0.538×10^4 $l.mol^{-1}.cm^{-1}$. The proposed method shows good recovery values, accuracy, and precision. The present method was so good to be successfully applied for the determination of SAL medication in its pure form and pharmaceutical preparations.

Introduction

Salbutamol sulfate is one of the adrenergic bronchodilators medications that have a geat important due to their selectivity of beta2-adrenergic receptor agonists. Its use to treat asthma and other lung diseases. SAL has been used also to treat high blood levels of potassium. SAL found as a racemic mixture (R(-) salbutamol and S(+) salbutamol) and it was discovered in 1966; since that time it still has great importance. Salbutamol (SAL)[1], chemically named Bis [(1RS)-2-[(1,1-dimethylethyl)amino]-1-[4-hydroxy-3-(hydroxymethyl)phenyl]ethanol]sulfate (Scheme 1), SAL is used at first in treatment of bronchial asthma, SAL was freely soluble in water while it was slightly soluble in ethanol.

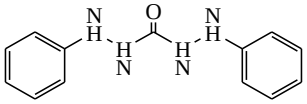


Scheme 1: Chemical formula of SAL

Bis [(1RS)-2-[(1,1-dimethylethyl)amino]-1-[4-hydroxy-3-(hydroxymethyl)phenyl]ethanol]sulfate $C_{26}H_{44}N_2O_{10}S$,M.wt.=576.7 g/mol

Many spectrophotometric approaches have been reported for estimating SAL in various pharmaceuticals products. One of these methods has used 4-amino antipyrine in basic with maximum absorption at 500nm [2], Another method has studied the determination of SAL in tablets[3] or using N-Bromo succinimide to assay SAL in bulk and tablet dosage forms [4]. Moreover, fluorescence method was β-cyclodextrin with SAL at emission wavelength 609.8 nm[5], charge-transfer reaction with o-chloranil has been used for estimating of SAL[6], or on the coupling between N, N-diethyl-p-phenylenediamine Sulfate with SAL in the presence of KIO_4[7], Also, ion-pair formation between SAL and Hematoxylin at pH 9.5 [8]. The spectrophotometric method has been developed for the determination of SAL in tablet [9], 2-chloro-4-nitroaniline was reacted with Nitrite in acidic medium to form produce diazonium ion, which is finally coupled with SAL in basic medium forming azo dyes [10], Other researches were described a new method to determine SAL in bulk drug and tablet

dosage[11], coupling reaction was used with diazotized O-nitroaniline in alkaline medium to estimate SAL [12], flow injection methods with spectrophotometric detection have been used for determining of SAL in pharmaceutical formulations[13]. An oxidative-coupling reaction was used 2,4-dinitrophenylhydrazine with Sodium periodate for SAL determination Also, oxidative coupling reaction of SAL with P-aminobenzoic acid at pH=11.96 was carried out in the presence of N-chlorosuccinimide [14]. An organic compound 1,5-diphenyl carbazide (DPC) (Scheme 2) was usually used for colorimetric methods in analytical chemistry. DPC was used in photochemical reactions as an artificial donor and also photosynthesis transport of electron [15].



1,5-Diphenyl carbazide
M.wt. = 242.28

Scheme 2: Chemical structure of DPC

It is well known that the chelate chromate-1,5-diphenylcarbazide shows a pink-violet color intense at pH = 0.2 [15], when SAL was reduced chromate to chromium (III) the excess of chromate was reacted with 1,5-diphenylcarbazide. The aim of this present work is to use to develop a simple, rapid, and sensitive spectrophotometric method for the estimation of SAL in pharmaceutical formulations.

Materials and Method

Instruments

The figure of salbutamol final spectra and absorbance measurements were carried out using JASCO V – 630 UV-Visible double-beam computerized spectrophotometer with 1-cm matched cells. The pH readings were carried out using HANA pH meter.

Analytical chemical materials

Salbutamol (1000 µg/ ml) solution. The solution was prepared by dissolved 0. 1000 g of SAL in distilled water then the volume was completed to 100 ml with distilled water in a dry and clean volumetric flask. Then, the solution was relocate to a dark bottle to be settled fully 4 days. SAL working solution of 100 µg/ml solution was prepared by suitable alleviation of the stock solution with distilled water.

Potassium chromate solution (8.6×10^{-4} M) solution. potassium chromate was weighed equal to 0.0167 g, then dissolved it in distilled water using a 100 ml volumetric flask. This solution was kept to be stable for more than one month.

Sodium oxalate solution, 0. 1 M. 0.1M of sodium oxalate , the solution was prepared by weighing 1.34 g, then dissolved in distilled water and completed to 100 ml with distilled water using a volumetric flask.

1,5-diphenylcarbazide solution 1×10^{-3} M:

Dissolved 0.0605 gm of 1,5-diphenylcarbazide (DPC) in enough amount of pure acetone, then complete the volume to 250 ml with distilled water in a suitable volumetric flask.

Sulphuric acid 2N:

98% concentration Sulphuric acid solution has been used for preparing 2N of Sulphuric acid solution in a 250 ml volumetric flask.

Interferences solutions, 1000 µg.ml^{-1}: interferences solutions have been prepared by dissolving 0.1g of each one of them in 100 ml of distilled water by using a volumetric flask.

Butadin syrup solution, 100 µg .ml^{-1}: Diluting 25 ml of Butadin syrup (2 mg Salbutamol Sulfate per 5 ml) to 100 ml in a volumetric flask with distilled water.

Butadin a tablets solution, 100 µg .ml^{-1}: five tablets of Butadin were powdered (each tablet contains 2 mg Salbutamol Sulfate), Then dissolved in 80 ml of distilled water, after shaking well, the solution was filtered into a 100-ml volumetric flask, and diluted to the mark with distilled water to obtain 100 µg .ml^{-1} Salbutamol Sulfate solution.

Results and discussion:

In final volumes are 25 ml ,100 µg of SAL have been taken for subsequent experiments.

Study of Optimum conditions:

The various analytical related to the oxidation – reduction reaction and the intensity of the resulted coloured product was studied and optimum conditions have been chosen.

Studying Sulphuric acid H_2SO_4 amount:

Different volumes (0-5.0) ml of 2N H_2SO_4 were chosen, The optimum amount of H_2SO_4 on the reaction of SAL with the oxidant agent (Chromate) was selected, Table 1 showed that 2.5 ml of 2N Sulphuric acid was chosen an optimum volume because, it gives a stable colored complex more than other volumes [11], therefore 2.5 ml was recommended for later experiments.

Table 1: Effect of Sulphuric acid amount.

Volume (ml) of 2N Sulphuric acid	Absorbance	Final pH
0.0	0.206	1.75
0.5	0.257	0.89
1.0	0.279	0.60
1.5	0.289	0.51
2.0	0.299	0.38
2.5	0.304	0.26
3.0	0.308	0.20
4.0	0.306	0.18
5.0	0.309	0.14

Effect of Oxidizing agent

The proposed method depends on using as excess of chromate as an oxidant , so that, chromate ions were oxidized SAL in presence of sodium oxalate, the unreacted amount of chromate was then reacted with DPC in acidic medium, therefore, different volume (0.5-3.0) ml of 8.6×10^{-4} M chromate solution was studied and the results indicated a 1.0 ml of chromate solution was selected as an optimum volume for the next experiments.

Effect of catalyst amount

Sodium oxalate has been added to the colored product as a catalyst of the oxidation process, so that, 2 ml of 0.1 M sodium oxalate is considered to be an optimum amount as it resulted from the experimental work.

Effect of time

A study of time effect on the reducing process of CrO^{4-}_2 to Cr(III) by SAL in the presence of oxalate ions as a catalyst and the absorbance intensity of the colored complex was investigated. The results showed a 2 min of reaction time was considered to be optimum and selected for the later experiment.

Effective amount of 1,5-diphenylcarbazide(DPC)

From the experimental results 2 ml of DPC 1×10^{-3}M was found to be an optimum amount ,as the value of the correlation coefficient was equal to 0.9903, so that, 2 ml of DPC was selected for the next experiments.

Effect of various kinds of surfactants

Frequently the addition of all kinds of surfactants (sodium dodecyl sulfate an anionic surfactant, cetyltrimethylammonium bromide, cetylpyridinium chloride as cationic surfactants and Triton X-100 as a non-ionic surfactant) to the colored system does not increase the intensity of absorbance or lead to shift wavelength to higher values.

Order of addition effect:

varied orders of addition have been studied, Table 2 shows that the first order of addition was considered to be an optimum because it gives the lowest absorbance, thence it was dependent in the later experiment.

Table 2: Effect of order of addition

Component of the colured system	Order number	Absorbance
S+C+Ox+H+R	I	0.302
S+H+Ox+C +R	II	0.329
S+Ox+R+H+C	III	0.326
S+H+R+Ox+C	IV	0.333
S+C+R+H+Ox	V	0.327
S+Ox+R+C+H	VI	0.331

S= SAL, Ox=Sodium oxalate, C=Chromate, H= Sulphuric acid, R= DPC.

Stability period

under optimum conditions, the effect of time on the intensity of absorbance for the coloured complex product at the maximum selected wavelength at 542 nm, The absorbance has been measured at several period of time, which was showed that the coloured complex was immediately developed and remains maximum and constantly more than 2 hr. as shown in figure 1.

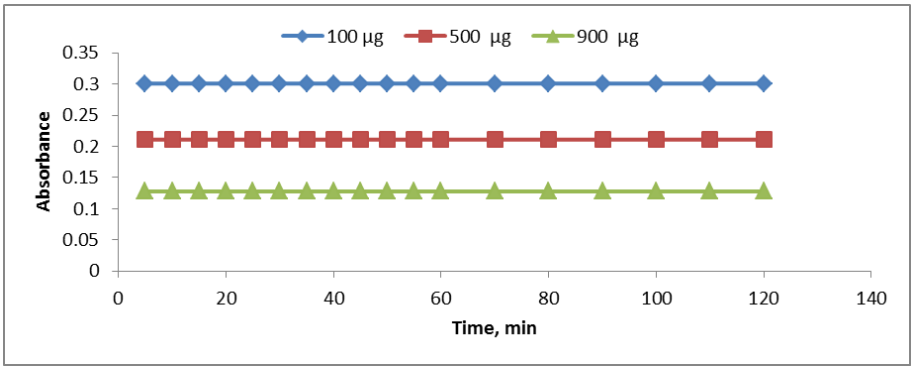


Fig.1 : Stability of the product coloured complex

Beer's law, molar absorptivity and sensitivity

Aliquots of 25 ml dry and clean flask contained (0.5-9.0) ml of 100 µg of SAL, 1 ml of chromate solution 8.6×10^{-4} M, 2 ml of 0.1 m sodium oxalate solution, 2.5 ml of 2N H_2SO_4 and 2 ml of 1×10^{-3} M 1,5-diphenylcarbazide reagent. the absorbance was measured at the selected wavelength at 542 nm, Beer's law was follow over the range of 2-36 ppm of SAL (Fig.2). The molar absorptivity being 1.256×10^4 $l.mol^{-1}.cm^{-1}$, and the Sandell sensitivity is 0.001905 µg $.cm^{-2}$.

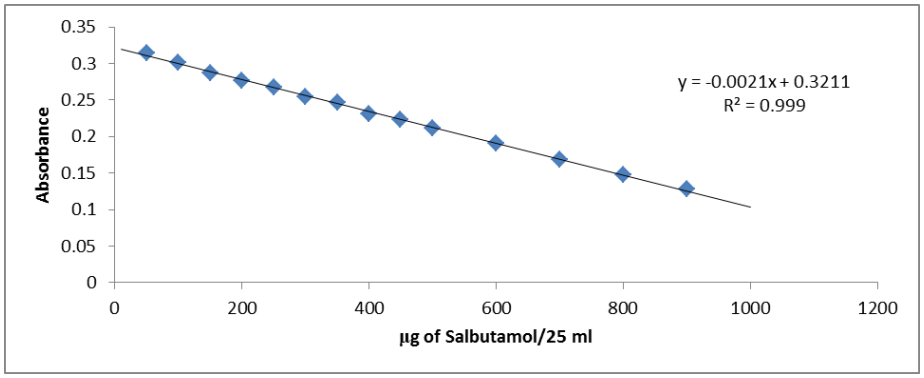


Fig.2 : Calibration graph for SAL determination

Absorption spectra

SAL was treated according to the optimum conditions, so that the absorption spectrum was showed in Fig.3 indicate that sample solution showing maximum absorption at 542 nm for chromate-DPC chromophore in contrast to blank solution which was showed slightly absorption at the same wavelength.

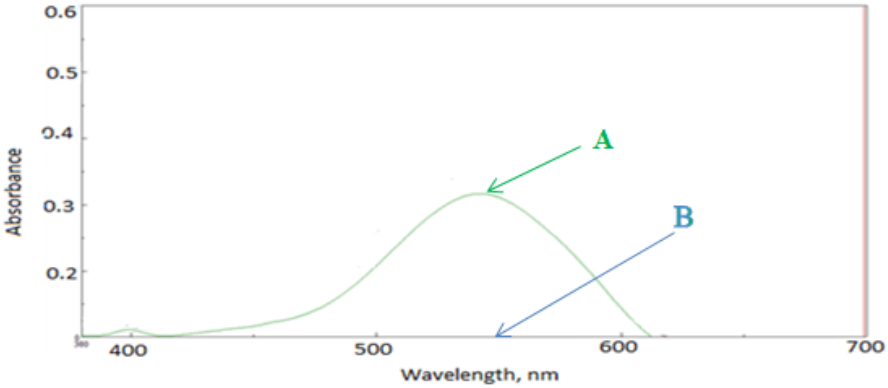


Fig 3. Absorption spectra of 100 µg of SAL/25 ml measured against (A) reagent blank, (B) Chromate against reagent blank.

Accuracy and precision

SAL has been determined at 3 concentrations, in order to check the values of accuracy and precision of the present method, Table 3 indicated that the suggested method was an almost reliable method.

Table 3 : Accuracy and precision

SAL µg/25ml	Rec.* %	RSD* %
100	99.29	± 0.0024
300	98.88	± 0.0023
500	98.50	± 0.0026

Rec.=Recovery, RSD=Relative standard deviation, * = Average of 5 readings.

Nature of the reaction between chromate and (DPC) reagent.

Job's method was used for the determination of the reaction ratio of SAL with chromate. From the expermintal results obtained that 1:1 SAL to chromate ratio(Fig.4), while the chromate-DPC ratio is 1:2 [15].

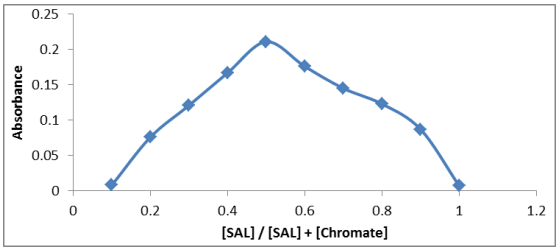
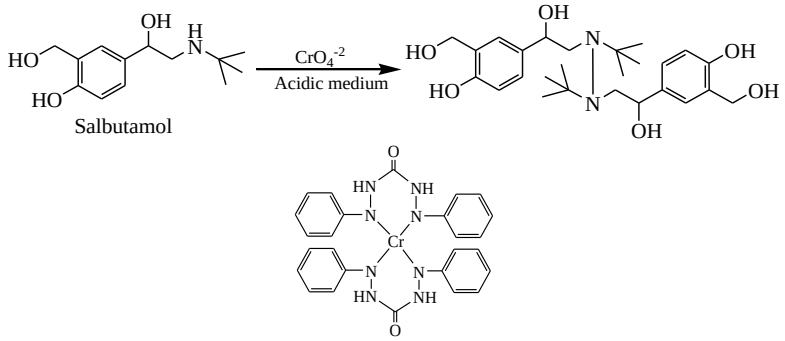


Fig 4: Job's plot for SAL – Chromate

Hence the suggested mechanism of the SAL oxidation process may have the following structure:



Effect of foreign materials

The effect of some foreign species which was usually accompanied with pharmaceutical preparations was studied. The absorbance of solutions containing 100 µg.ml^{-1} SAL and (50,100 and1000) of interferences were measured, the results showed in Table 4 was found that the studied excipients don't interfere seriously in the determination of SAL in its dosage forms.

Table 4 : Effect of interferences

Interferences, µg	Recovery (%)/100 µg of SAL added		
	100	500	100
Acatia	99.49	100.46	97.89
Lactose	99.83	100.23	98.31
glucose	100.17	99.76	98.73
Menthol	99.66	99.54	99.15
Starch	100.34	99.31	99.57

Application of the method: The present method was utilized satisfactorily for estimation of SAL in pharmaceutical preparation as shown in Table 5.

Table 5: determination of SAL

Drug	µg of SAL present/25 ml	µg of SAL measured/25 ml	Rec.* %	R.E * %
Butadin syrup 2 mg SAL/ 5 ml (S.D.I Iraq)	50	50.08	100.17	± 0.0017
	100	100.35	100.35	± 0.0035
	300	299.39	100.20	0.0020
Butadin tablet 2 mg SAL/ tablet (S.D.I Iraq)	50	49.92	99.83	± 0.0017
	100	100.53	100.17	± 0.0070
	300	298.79	99.61	± 0.0041

R.E=Relative error. * = Average of 5 readings.

The results tabulated in Table 6 indicated that the calculated value of t-test [16] at a 95% confidence level for five degrees of freedom ($N_1+N_2-2=5$) didn't exceed the theoretical values so, there is no significant difference between the present method and the literature method.

Table 6: The value of t-test

drug	Pharmaceutical reparation	t-test	Tabulated value of t-test
Butadin tablet 2 mg SAL/ tablet (S.D.I Iraq)	Tablet	± 1.426	± 2.571

Comparison of the present method: Table 7 shows the comparison of spectrophotometric methods for SAL determination.

Table 7: Comparison of the method

Analytical parameters	Present method	Literature method [14]
Reaction	Oxidation reduction	oxidative coupling
pH	0.2	11.96
λ_{max} (nm)	542	622
Temperature, ^oC	Rome temperature	45
Time of developed color complex	Immediately	20
Beer's law range (ppm)	2-36	2-25
Molar absorptivity ($l.mol^{-1}.cm^{-1}$)	1.256×10^4	1.828×10^4
R.S.D. (%)	not more than ±0.0023	not more than ±3.34%
Color of the product	Pink-violet	Blue
Application of the method	Pharmaceutical preparations	Pharmaceutical preparations

Conclusion

SAL was determined by the suggested spectrophotometric method which was considered to be a rapid, sensitive, and inexpensive method without any requiring of expensive instrumentation or needed temperature controlling or extraction process. Good recovery values of SAL are achieved using the proposed method from the successful application of the proposed method to determine SAL in pharmaceutical preparations.

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تقدير السالبيوتامول باستخدام طريقة طيفية اعتمادا على معقد الكروم−5,1 ثنائي كاربازايد

ايناس سمير ذنون ، باسمة احمد عبد الهادي ، ناجح حسن شيخو

قسم الكيمياء ، كلية العلوم ، جامعة الموصل ، الموصل ، العراق

الملخص

في هذا البحث تم اقتراح طريقة طيفية لتقدير كبريتات السالبيوتامول باستخدام تفاعل الاكسدة والاختزال. توصف الطريقة المقترحة بانها سريعة وبسيطة ودقيقة واقتصادية.الطريقة المقترحة تعتمد على اكسدة دواء السالبيوتامول بوجود كمية زائدة من (CrO^{-2}_4) كعامل مؤكسد بوسط حامضي (2N) من حامض الكبريتيك وبوجود اوكزالات الصوديوم كعامل محفز لعملية الاكسدة والكمية المتبقية من الكرومات سوف تتفاعل مع الكاشف 5,1−ثنائي فنيل كاربازايد ليكون معقد وردي محمر ذائب بالماء والذي يظهر اعلى امتصاص عند طول موجي 543 نانوميتر. تم دراسة الظروف المثلى للتفاعل مختبريا وكانت العلاقة الخطية لهذه الطريقة تتبع قانون بير بمدى تركيز 50−900 مايكروغرام في حجم نهائي 25 مليليتر وامتصاصية مولارية مساوية ل$0,539\times10^{4-}$لتر.مول$^{-1}$.سم$^{-1}$,وكانت قيم الاسترجاعية والدقة لهذه الطريقة جيدة , بالاضافة الى ذلك طبقت هذه الطريقة بنجاح لتقدير دواء السالبيوتامول بشكله النقي وفي مستحضراته الصيدلانية.