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Colorimetric estimation for salbutamol sulphate in pure form and in different types of pharmaceutical

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Abstract : Anew sensitive, simple and accurate colorimetric approach is suggested of the estimation of salbutamol sulphate drug in pure form ,also in different types of pharmaceutical. The approach is established on the conjunction of salbutamol (SLB) drug and the reagent 4-aminoantipyrine (4-AAP) reagent in basic medium to obtain a newly ligand that reacts with cobalt (II) to produce highly intensity red colour complex at 60°C. The water soluble dye is stable and estimated colorimetric ally with maximum absorption at(500nm).The calibration curve between the concentration and the absorbance shows that the range of concentration was applied by the Beer's law between (2-60µg/mL).The optimization of the experiential circumstances is examined. The precision and the accuracy for the approach are tested by the average relative standard deviation values (1.32%) and the average recovery values (100.23%) respectively. That it is based on the concentration. The approach sensitivity is obtained by molar absorptivity (0.6558×10^4 l. .cm^{-1}.mol^{-1}). the sensitivity of Sandell is calculated (0.036 µg.cm^{-2}). The analytical data for The approach is matched with the standard method. The general interference from drug additives was examined. The suggested approach is successfully applied on the estimation of (SLB) in various types of pharma.
Keywords : colorimetric; estimation; salbutamol sulphate ; pure form ; types of; pharmaceutical.

Introduction

Salbutamol sulphate (SLB), IUPAC name was bis [(1RS)-2-[(1,1-dimethylethyl) amino]-1-[4-hydroxy-3-(hydroxyl methyl) phenyl]ethanol]sulphate fig.(1), it is a 2-sympathicomimetic drugthatwas used as drug in the markets in1973s[1]. It is too known as albuterol. (SLB)is utilizedat first in the bronchial asthma treatment ,it is applied as drug for the other types of the disease of allergic airways ,It is worked as a β2adrenergic receptor agonist,. So(SLB) is acted as its cardiovascular ,and a bronchodilator influences are smaller than its bronchodilator actions drug is utilized in obstetrics forth on the premature labour prevention also as a nasal decongestant [2-4].

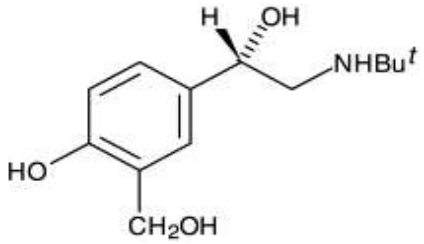


Fig.(1) The chemical structure of salbutamol.

Soluble freely in water, practically insoluble or so slightly soluble in ethanol (96 %) also in the methylene chloride[5].Different approaches have been utilized for the estimation of (SLB),involving liquid chromatography- tandem mass spectrometry[6],the gas chromatography conjugated with mass spectrometry flow injection analysis, high performance liquid chromatography[11], polarographic[12] derivative ultraviolet spectrophotometry[13], capillary electrophoresis[14]and the spectrophotometric (colorimetric) methods [15]. the colorimetric estimation procedures of (S such as charge-transfer complex formation[16], LB) in pharmaceuticals were dependent on the simple chromogenic diverse reactions diazotization coupling reaction[17], redox[18,19], reduction followed by chelation[20] , oxidative coupling[21,22], nitrosation[23] and nitration[24].The current investigation is aimed mainly for development A sensitive , new, simple and accurate colorimetric approach to the estimation of salbutamol depended on the coupling between the drug with (4-AAP) to obtain a newly ligand that combined with cobalt(II) to produce highly intensity red colour complex at 60°C degree. The approach is applied in pure drug form and in different types of pharmaceutical with highly accuracy and precision.

Experimental

Apparatus

Every spectral measuring's were carried out by UV-Visible double - beam 160 recording digital spectrometer.(Japan) and using 1cm silica cells. ice-water bath, sensitive balance, pH meter, Jenway 3020 .

Chemicals and reagents

All substances utilized were of analytical grade additionally It was supplied from BDH and Fluka companies and the pure drug salbutamol sample was supplied from(SDI) company, Samara, Iraq .Dosage forms were received from commercial resources.

Sodium hydroxide solution (0.05M) was made by dissolution (0.2 g) of (NaOH) in deionized water. After that palliated to (100 mL) in the volumetric flask.

Cobalt chloride ($CoCl_2.5H_2O$) (0.1%) solution was made with dissolution (0.1 g) from cobalt salt by deionized water after that, It was palliated to(100 mL) by using the volumetric flask.

(4-Aminoantipyrine(1%) (4-AAP)made with dissolution (1g)from (4-AAP) in little quantity of ethanol additionally palliated for the label in (100mL) calibrated flask by deionized water.

(Standard solution) of Salbutamol (500μg/mL) was made with dissolution (0.05g) of (SLB) pure in deionized water and palliated to the label in (100mL) calibrated flask with deionized water and putted in black container and leave in the refrigerator. This solution were utilized in the next experiments.

Procedure for pure drug[5].

Standard volumes (0.1 – 3 ml) from (500 μg/mL) of pure (SLB) drug, were transmitted into a chain of (25ml)calibrated flasks, after that added(1 mL) of (0.1%) cobalt salt,(1.5 mL) of (1% 4-AAP), and (0.5mL) of (0.05 M)(NaOH) .The result solution was putted in the water bath checked for(70 min) at (60°C). the red complex was produced, achieved and cooled to (25mL) with deionized water, thev alues of absorbance were computed at 500 nm versus the solution of blank.. The color for the dye formed is stable for the next day. The

working curve was built by utilizing the above approach utilizing standard drug solutions.(0.5 - 3 mL) volumes = (2 - 60 µg/mL) concentration.

Sample preparation Procedure.

1. Tablets samples[25]: finely powdered and weighed 20 tablets from kind of tablets(each tablet including (2 mg) of salbutamol). A powder amount was equivalent to (0.05) gm from each (SLB) was accurately weighed and transmitted into a beaker(25 ml). The completely powder was dissolute with deionized water, the filtered solution was making by utilizing a filter paper Whatmann (41). After that filtering to remove then on- dissolute ingredients. It was transmitted in the(100mL) volumetric flask and palliated to the final volume by the deionized water. A drug solution liquid was analyzed as examined in general approach.
2. Syrup sample[25]: The substance of two containers of (SLB) syrup (Butadin®syrup) [each (5mL) from syrup contains (5mg) (SLB)]were taken and mixed well, after that taken (125 mL) from the syrup solution that was containing (0.05 gm)from the (SLB). The standard working solutions were made by appropriate palliation from this solution and the recommended approach was utilized for the estimation for salbutamol.
3. Pressurized inhalation sample[5]:three canister s from pressurized inhalation sample of (SLB) (Vental inhaler) [each canister contains (0.02mg) (SLB) in(20 mL) volume]were taken and mixed well, after that taken (60 mL) from the sample that was including(0.05 gm) from the (SLB). the standard solution were prepared by suitable dilution from this solution that were analyzed by the studied approach.

Results and discussion

The optimization of the experiential circumstances influencing the reaction of salbutamol with (4-AAP) and cobalt chloride were examined accurately.

Absorption spectrum

(SLB) reacts with (4-AAP)) to obtain a newly ligand in the existence of sodium hydroxide that reacts with cobalt(II) to produce strongly intensity red colour complex after the heating for 70 min at 60°C, as appeared in fig.(2), the spectrum of absorption of which under optimum circumstances gives a maximum at 500 nm.

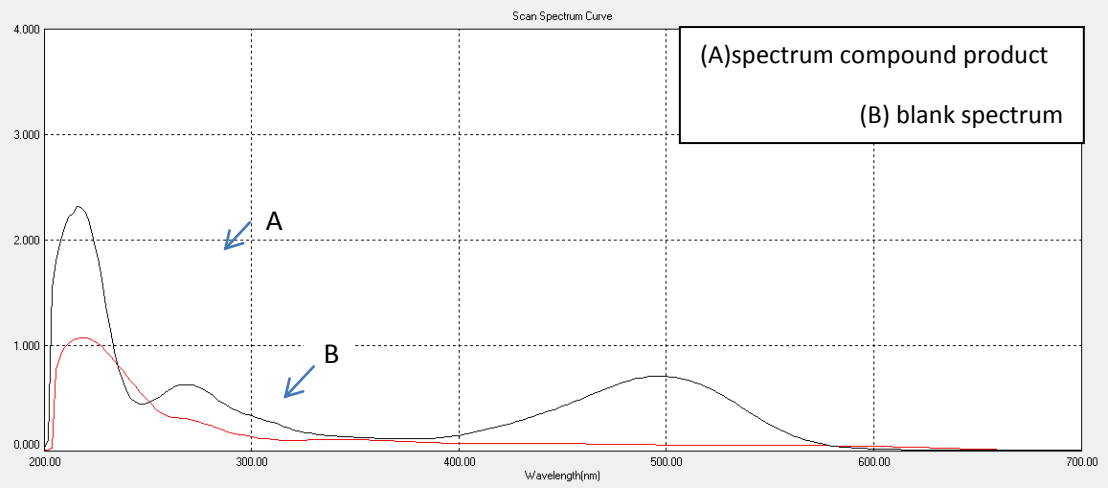


Fig.(2)(A)Absorption spectra of (20 µg/mL) of (SLB) processing as studied by the approach and computed versus blank,(B) Absorption spectra of blank that was including (4-AAp) ,$CoCl_2$ and NaOH .in the final volume (25 mL).

3.2 Medium influence

The medium of medium on the absorbance of the product solution was examined, the basic medium was the best for the reaction. bases like hydroxide ammonia, ammonium, potassium hydroxide, sodium hydroxide and sodium carbonate were realized and given that sodium hydroxide highly sensitivity than other

bases, that used in the examined approach, the influence of additional volumes for (NaOH) As appeared by fig.(3), it was showed that the highly absorbance for the chelating complex product gave at λmax (500nm)by utilizing (0.5 mL) of(0.05 M NaOH).So that ; the pervious constant amount of sodium hydroxide was utilized in every next tests.

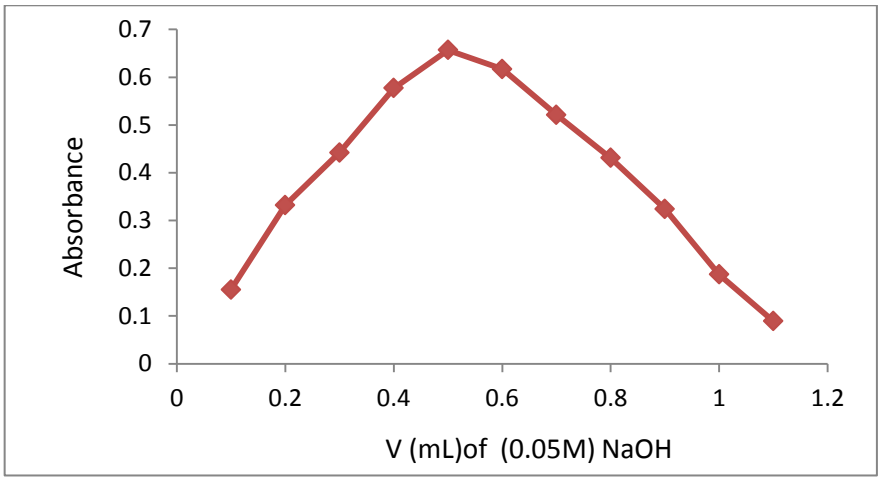


Fig.(3) the influence of additional volumes for NaOH on the absorbance of the coloring product

3.3 Influence of the quantity of (4-AAP)

By using constant quantity of the drug solution, the different concentrations of the solution of (4-AAP) were utilized to the volume (1.5 mL) from (1%) solution was show sufficient on the colour increasing of the product to give highly intensity fig.(4), with a minimal value blank also was assumed to be prefect.

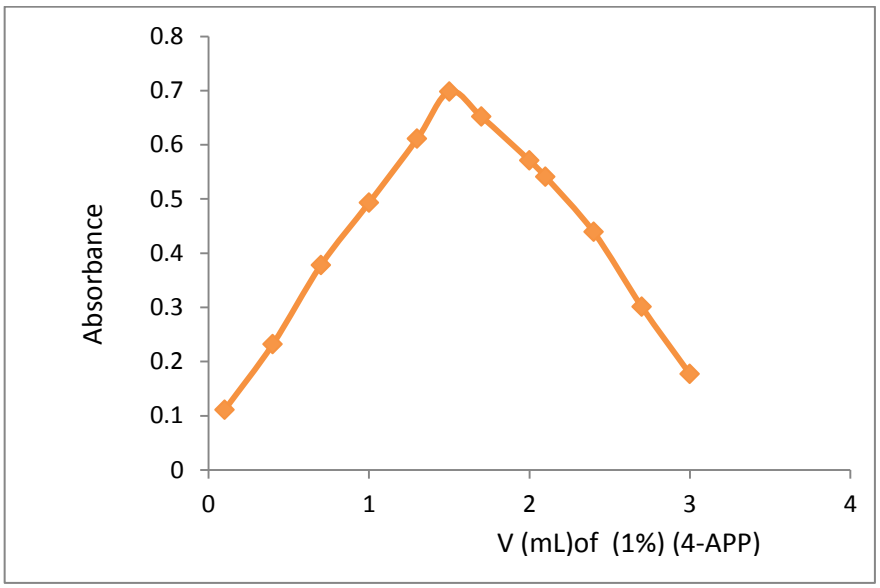


Fig.(4) the influence of (4-AAP) concentration on the absorbance of the coloring product

Influence of($CoCl_2.5H_2O$)concentration

The coloring complex product was given with highly absorbance when (1 mL)of (0.1%)concentration of($CoCl_2.5H_2O$) solution were utilized with a mixture of 4-AAP ,salbutamol and sodium hydroxide fig.(5), so that , this quantity was utilized in the approach since it obtains highly sensitivity and minimal blank value.

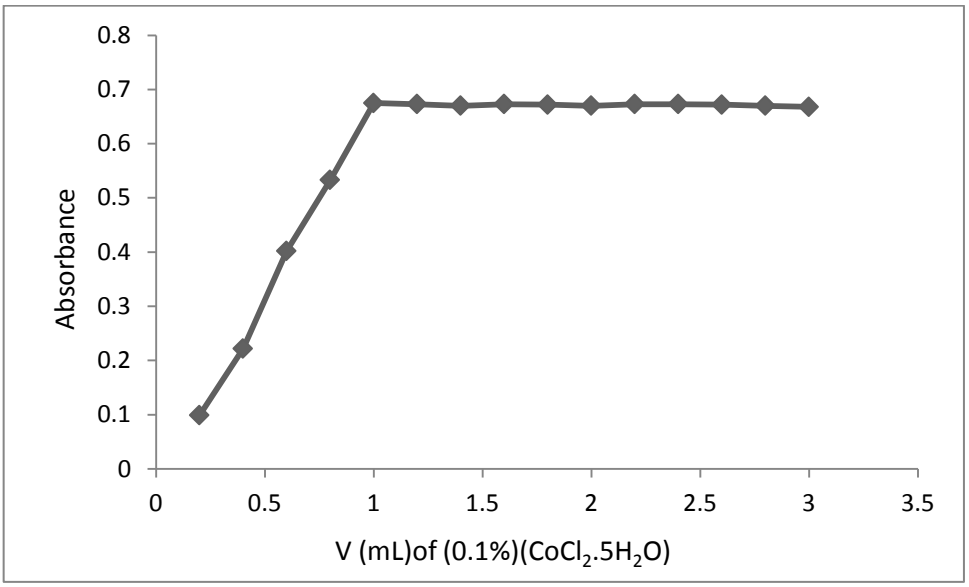


Fig.(5)the influence of ($CoCl_2.5H_2O$) concentration on the absorbance of the coloring product

Temperature and Reaction time influence

The time of reaction was investigated with the showing of the colour improvement at temperature of room and at the various of temperatures in water-bath (thermostatically controlled). The value of absorbance was computed at 5 min periods versus reagent of blank treated in the same method. As appeared in fig.(6), the figure was saw that production of the product complex for (SLB) was carried out ultimate at (60°C)after (70 min) and fixed for at least 3 hour.

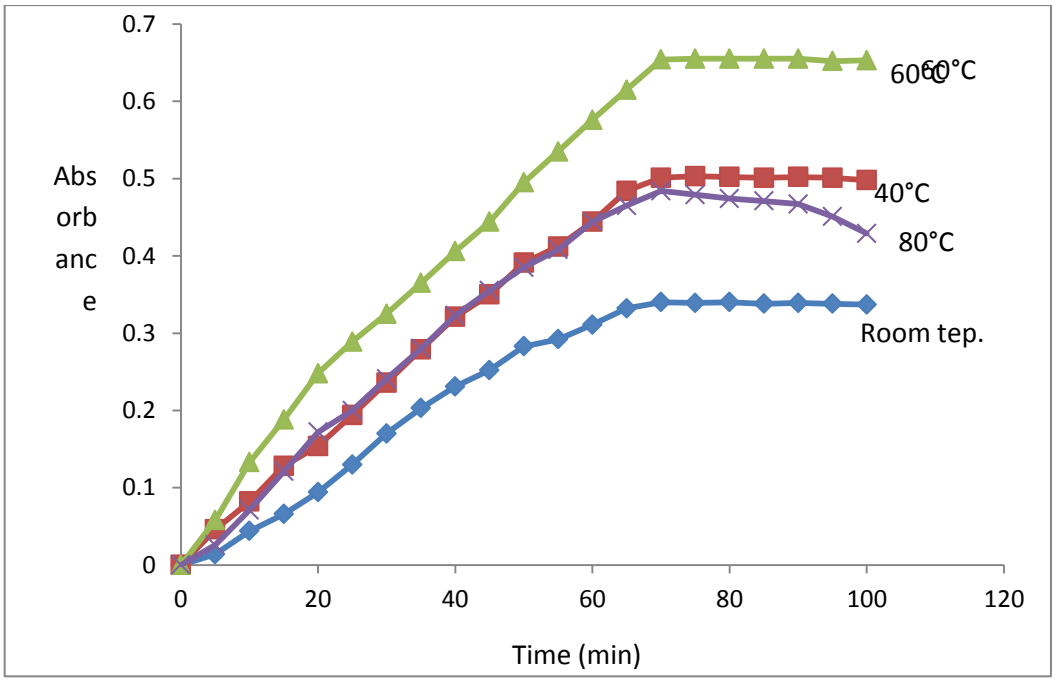


Fig.(6)the influence of improving time and temperature on the absorbance of a coloring product

Order of addition influence

To get the prefect results, the addition order of reagents must be pursued as obtaining by utilized the examined approach, moreover a decrease in the colour intensity was noted.

Quantification

So as to estimate the concentration range for the coloured product involve to the Beer's law, a computed absorbance of the product was at the value of λmax(500 nm) after the color increasing by utilized the examined approach for the solutions sequence including increase quantities of (SLB)fig.(7).molar absorptivity, Sandell's sensitivity, additionally. The Beer's law limits were estimated and showed in Table (1), it was appeared the sensitivity for the studied approach. The linear was computed from the corresponding correlation coefficient also the regression equation for (SLB) estimation into the studied approach appears premium linearity. the precision(relative standard deviation) (RSD) and The accuracy (average recovery %) for the five replicates analysis of every three various concentrations fro(SLB)(30, 15 and 5µg/mL) showed that the approach is accurate additionally precise. LOQ and LOD is computed for the studied approach. surely, the LOQ a little bit passes the minimum of the Beer's law range. However, LOD is as well as less the minimum of the Beer's law range [26] .

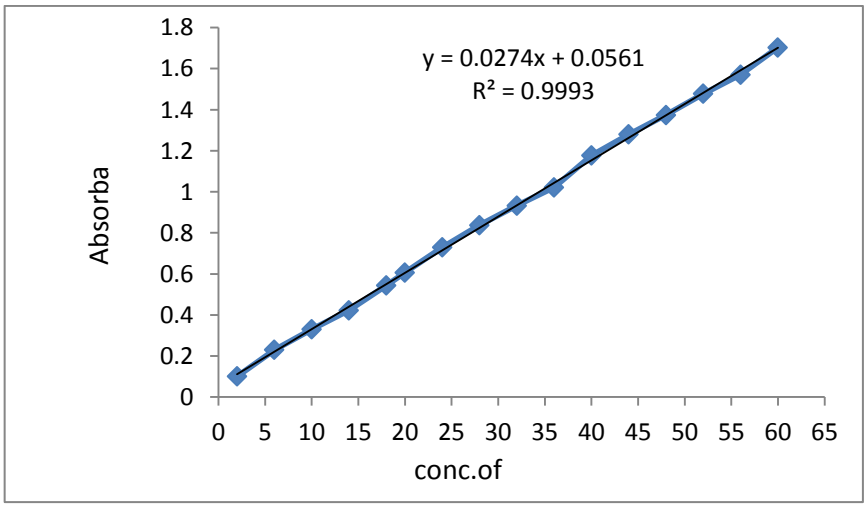


Fig.(7) The Calibration curve of(SLB)

Table(1)Synopsis of visual properties also the analytical information for the examined approach.

Parameter	Values of approach
limits of Beer's law	(2.0 - 60.0) (µg/ml)
Correlation coefficient	0.9993
Sandell's sensitivity	0.036 (µg. cm^{-2})
Molar absorptivity	0.6558×10^4 ($L.mol^{-1}. cm^{-1}$)
Limit of quantitation	1.3412 (µg/ml)
Limit of detection	0.5510 (µg/ml)
Regression equation	(*Y*)*
Intercept,	*b* 0.0561
Slope,	*a* 0.0274
Average recovery	% 100.23
RSD**	% 1.32

*** *Y = a X+ b*, where the concentration is *X*of (SLB) with (µg/mL).**
**** five Average for the estimations .**

Interference

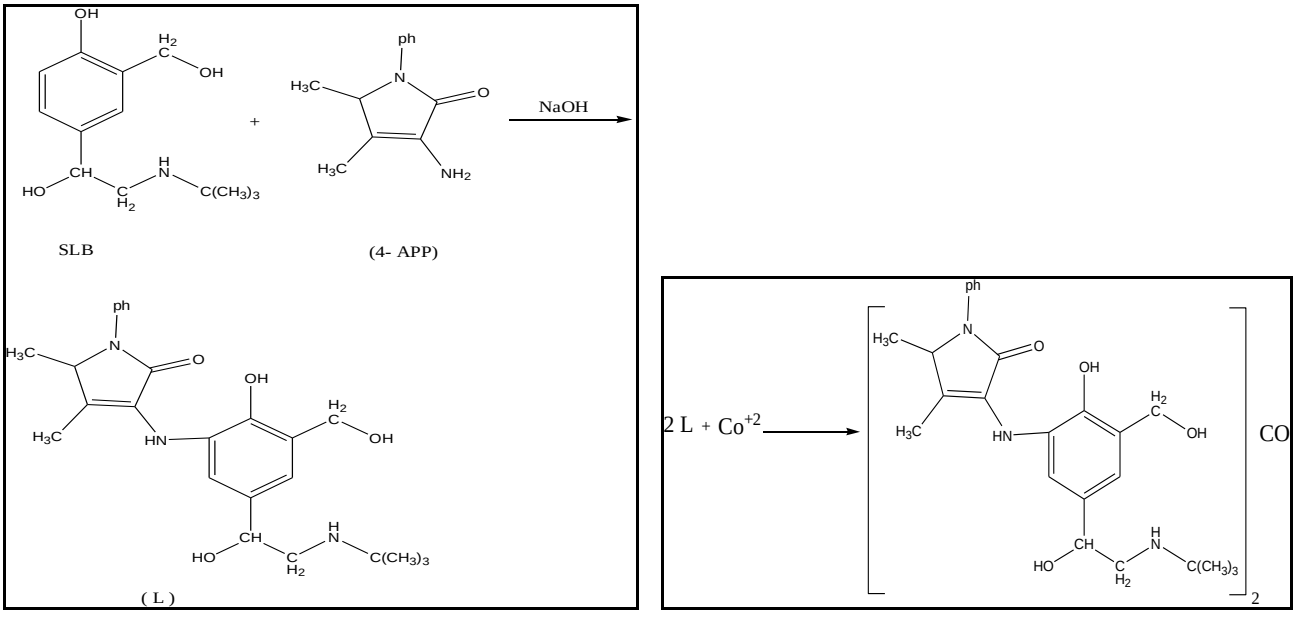
The interferences by several excipients that predominant in glycombined with the pharmaceutical dose forms were examined by computing the absorbance for the solutions including (20 µg/mL) of (SLB) and every one of the excipients was taken separately in concentration(200 µg/mL) .It were tested by utilizing the like approach in the calibration curve in the end volume of (25mL). the results was showed that the examined excipients do not influence in the estimation of salbutamol in its different dosage forms. (Average of three estimations).

Table 2.Investigation of (20 ppm)salbutamol(SLB) in the being of excipients.

Excipients	% Error	% Recovery
Acacia	+ 2.400	102.400
Talc	- 3.100	96.900
Glucose	+2.200	102.200
Starch	- 2.200	97.800
lactose	+4.100	104.100
Vitamin C	-3.400	96.600
Sucrose	+.2.250	102.250
Glycerin	2.850-	97.150
magnesium stearate	- 4.100	95.900
PVP	- 1.550	98.850
Aspartate	+ 2.100	102.100
Sodium chloride	- 2.650	97.350

Structure of the product

It is obvious from the literatures [27-29] that a mole ratio and continuous variation method (Job's method) of phenolic compound : 4AAP was 1:1 formation a new ligands existence minimum absorbance. The absorbance sensitivity has been improved by its reaction with (Co(II)) to give the intensity of color for The resulting complex. By utilizing the continuous variation method (Job's method) and the method of molar ratio .The results obtained appeared that the colored complexes with stoichiometric ratio of 2:1 [4-AAP-phenolic drug] ligand:Co(II). The obvious stability constant for the resulting complex were computed by comparison the absorbance of solution that involving equivalent amounts of new ligand [4-AAP-phenolic drug] and Co(II) and other solution containing a five-fold excess of Co(II) ion from the starting concentration. the perfect amount for the utilizing solution was (1mL) of (2×10^{-3}M). The average conditional stability constants the resulting complex in water under the examined experiential circumstances is(5.34×10^{5}) . The reaction may proceed as given in the following Scheme fig(8):



Fig(8) scheme of possible reaction pathway for the complex formation of (SLB) drug with (4 - APP)and Co(II).

Analytical applications

The studied approach was felicitously utilized to estimate(SLB) in its pharmaceutical dose forms. The results obtained were made statistical comparison by a variance ratio (*F*-test) for precision and a Student's(*t*-

test) for accuracy with the standard approach[5] (basing on the titration for pure (SLB)potentiometric ally by utilizing perchloric acid (0.1 M) at the confidence level (95%) by the five degrees of freedom, as seen with table (3). The produced results appeared that the *F*-test and *t*-test were below the theoretical value of *(F*=6.39 , *t*=2.31), pointing there was no clear distinction between the examined approach and standard approach. (Average of three investigations)[31]. Furthermore ,the studied approach are compared favorably with other reported approaches as appeared in table(4).

Table 3. Estimation of (SLB) in pharmaceutical dose forms utilized the examined approach and comparing with the standard approach.

(SLB) pharmaceutical preparations	Examined approach		Standard approach		Nominal Values (t),(F)
	Recovery %	RSD%	Recovery %	RSD%	
Pure salbutamol	100.23	1.32	99.92	1.21	(F)Value =1.93 (t)Value=1.07
Butadin (tablets) (2mg/Tab) S.D.I,Iraq	99.84	1.83	99.77	1.66	
Butadin tablets (2mg/Tab) (Dijla),Iraq	100.44	1.65	99.89	1.04	
Butadin (syrup) (2mg/5ml) S.D.I,Iraq	100.04	1.21	99.93	1.21	
Vental inhaler(SLB) (0.1/DOSE) (Arab drug company) Cairo ,Egypt	100.14	1.51	99.88	1.47	

Table 4: results Comparing for the estimation of (SLB) with the examined approach additionally with the reminded approaches

Reagent used	λmax (nm)	Beer's law limit ($\mu g.ml^{-1}$)	Molar absorptivity ($L.mol^{-1}cm^{-1}$)	Application	Remarks
Cerium(IV)– MBTHa [18]	530	0-15	2.4×10^{-4}	-	contains extraction and an expensive reagent
Ferricyanide 4-Aminophenazone[32]	505	25-175	-	-	Heating waiting, for 30 min
Diazotized 4-minoacetophenone[33]	463	0.5-30	2.72×10^{-4}	Table, syrup	-
Chloramine-T N,N-Dimethyl-pphenylenediamine[34]	620	10-40	-		Extraction with butan-2-ol
Diazotized o-nitroaniline[35]	448	2-40	1.58×10^{4}	Table, syrup	
BrO3 —Br– /methyl orange [21]	510	0.5-5	7.17×10^{4}	Tablet	Includes some reagents and difficult conditions
F–C reagentb [16]	750	1-15	-------	Tablet, urine	Uses flow injection and extraction
sodium carbonate, hydroxyl ammonium[36]	701	100-500	6.24×10^{3}	Table, injection	-
diazotized 2,4-dinitroaniline[37]	558	2 - 6	9.33×10^{4}	Table, syrup	-
4-AAP-Co	500	2 - 60	0.6558×10^{4}	Tablet, syrup Vental inhaler	Examined approach

aMBTH, 3-methylbenzothiazolin-2-one hydrozone.
b Folin–Ciocalteu reagent, F–C reagent.

Conclusion

The studied approach is fairly sensitive, simple and economic when comparison with previously reported approaches specially those established on non-aqueous midst and costly technicality such as(HPLC)that do not need any treatment for the drug or the approach of extraction and give a perfect precision and accuracy. The approach is necessary for the estimation of pharmaceutical specimens of (SLB) (syrup and tablet), and the producing data founded there is no interference with the additive existent in common dose forms.

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