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Development of new spectrophotometric methods for the estimation of levosalbutamol in tablet dosage forms

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ABSTRACT

Two simple, sensitive and cost-effective spectrophotometric methods have been developed for the estimation of levosalbutamol(LSB) in bulk drug and pharmaceutical dosage forms. Methods were based on the formation of reddish yellow colored and bluish green colored chromogens, which were measured at 555 nm and 425 nm, respectively and are stable for more than 12 hours in case of both methods. Beer's law is obeyed at concentration of 20-100 μg mL^{-1} in method 'A' and 30-110 μg mL^{-1} in method 'B' at wavelength of maximum absorbance. Common excipients used as additives in pharmaceutical preparations do not interfere in the proposed method. The results obtained with the proposed methods are in good agreement with labeled amounts when tablet dosage forms were analyzed.

KEYWORDS

Spectrophotometry;
Levosalbutamol (LSB);
1,10-phenonthrolin;
Potassium ferrocynide;
Ferric chloride.

INTRODUCTION

Levolin is trade name of levosalbutamol is an effective and safe drug for treat wheezing and shortness of breath that commonly occur with lung problems (e.g. asthma, chronic obstructive pulmonary disease). Chemically levosalbutamol is 2-(hydroxymethyl)-4-[(1*S*)1-hydroxy-2-(tert-butylamino)ethyl]phenol (represented in Figure 1). Levosalbutamol[1] is a bronchodilator (β-2 receptor agonist) that works by opening breathing passages to make breathing easier. Levosalbutamol has better side effect profile and more efficacious than racemic salbutamol in the management of acute as well as chronic asthma[2]. A large clinical study demonstrated that inhaled levosalbutamol, 0.625mg or 0.125mg three times daily, provides effective relief from the symptoms of asthma[3]. It is not official in any pharmacopoeia and spectrophotometric analytical reports are not found in literature for its quantitative estimation in bulk drug and tablet dosage forms.

Two simple, sensitive and low-cost spectrophotometric methods have been developed for the quantitative estimation of levosalbutamol (LSB).

Procedure

Method A is based on the oxidation of LSB with ferric chloride in the presence of 1,10-phenonthrolin and orthophosphoric acid to form reddish yellow colored chromogen with absorption maximum at 555nm and obeyed Beer's law in concentration range of 20-100 μg/ml.

Method B is based on the oxidation followed by complex formation reaction of LSB with potassium ferrocynide in the presence of $FeCl_3$ to form bluish green colored chromogen with absorption maximum at 425nm and Beer's law range of 35-120 μg/ml.

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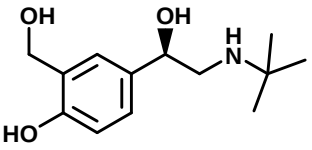

Figure1 : Structure of Levosalbutamol

Spectrophotmetric parameters are established for the standardization of the methods including statistical analysis of data. These methods have successfully extended to tablets containing LSB.

EXPERIMENTAL

Shimadzu UV/Visible double beam spectrophotometer (model 2450) with 1 cm matched quartz cells were used for all the spectral measurements. All the chemicals used were of A.R.grade.

About 100 mg of LSB (pure (or) equivalent formulation) was accurately weighed and dissolved in 20 ml of methanol and filtered, the filtrate was diluted with methanol upto 100 ml (1 mg/ml). The final concentration of the LSB was brought to 100 (μg/ml) with methanol.

In case of formulations, commercially available tablets (Levolin® 250mg) was analysed by the proposed methods. 20 tablets of the LSB, each containing 250mg of the drug, were accurately weighed and powdered. Tablet powder equivalent to 100 mg of LSB, was transferred to a 100ml volumetric flask. The contents were dissolved in methanol and made volume made to 100 ml methanol. The resulting solution was filtered through the whatmann No.41 filter paper and volume made to 100 ml with methanol and dilution was carried out in the same manner as described for standard solution. Working standard solutions were prepared by appropriate dilution of standard stock solution with methanol for Method A & B.

RESULTS AND DISCUSSION

Method A

Fresh aliquots of standard drug solution of LSB ranging from 0.1-0.5 ml (1 μg/ml) were transferred into a series of 10ml volumetric flasks. To each flask, 1 ml of ferric chloride (0.5%, w/v), 1 ml of 1,10-phenonthrolin (0.5% w/v), 1 ml of orthophosphoric acid(0.5%, w/v) was kept on waterbath for 15 min, for complete colored development. The volumes were made up to the mark with methanol. The absorbance of the reddish yellow colored chromogen was measured at 555nm against the reagent blank. The colored species was stable for more than 12 hours. The amount of LSB present in the sample was computed from the calibration curve.

Method B

Fresh aliquots of standard drug solution of LSB ranging from 0.3-1.0 ml (1 μg/ml) were transferred into a series of 10 ml volumetric flasks. To each flask, 1 ml of ferric chloride (0.5%, w/v) and 1 ml of potassium ferrocynide(0.5% w/v) was kept on waterbath for 15 min for complete colored development, cool. Then transferred the colored solution into 125 ml separating funnel and the total volume of aqueous phase was adjusted to 5 ml chloroform(10 ml) was added to each separating funnel. The contents were shaken for through mixing of two phases and were allowed to stand for clear separation of the layers. The absorbance of the separated chloroform layer was measured against their reagent blank at 425 nm. The colored species was stable for more than 14 hours. The amount of LSB present in the sample was computed from the calibration curve.

The results of the above methods were compared with the results obtained with UV-Visible spectrophotometric method. Solution of LSB in methanol either pure or formulation (1 $\mu g.ml^{-1}$) was prepared. Aliquots of LSB ranging from 0.1-1.0 ml were transferred into a series of 10 ml volumetric flasks. The volumes were made upto the mark with methanol and the absorbance of the solutions was measured at 400 nm against the solvent blank. The amount of LSB present in the sample was computed from the calibration curve.

The optical characteristics such as absorption maxima, Beer's law limits, molar-absorptivity and sandell's sensitivity[4]. Least square method[5] was applied for regression analysis such as slope (b); intercept (a) and correlation(r) values (represented in Figure 2 & 4) obtained from different concentrations and the results were summarized and cited in TABLE 1. The percent relative standard deviation and percent range of error (0.005 and 0.001 level of confidence limits) cal-

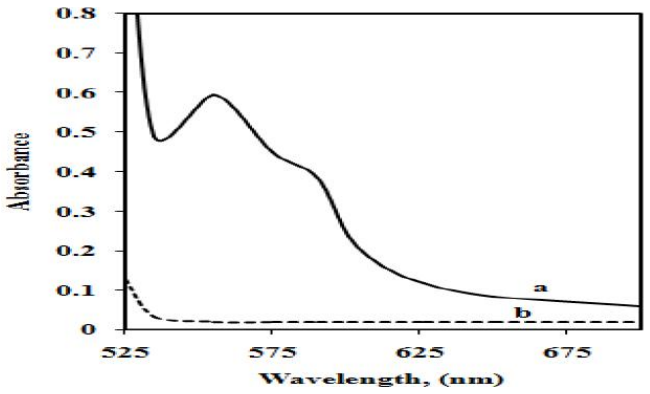

Figure 2 : Absorption spectrum of
a) LSB with (Ferric chloride + 1, 10-phenonthrolin + ortho-phosphoric acid)
b) Ferric chloride + 1, 10-phenonthrolin+orthophosphoric acid

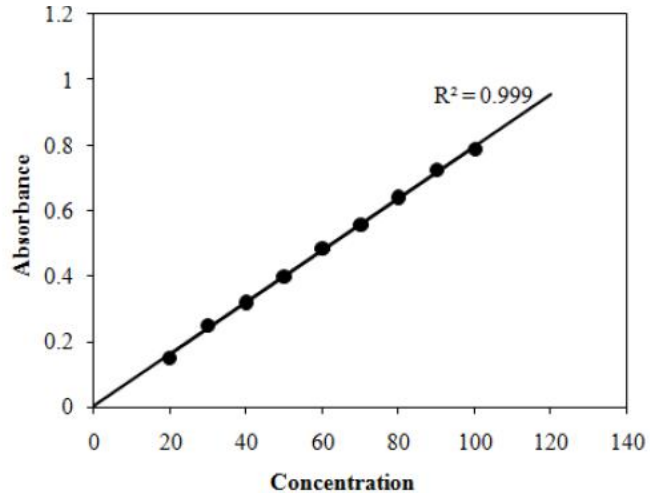

Figure 3 : Beers Law plot of method A

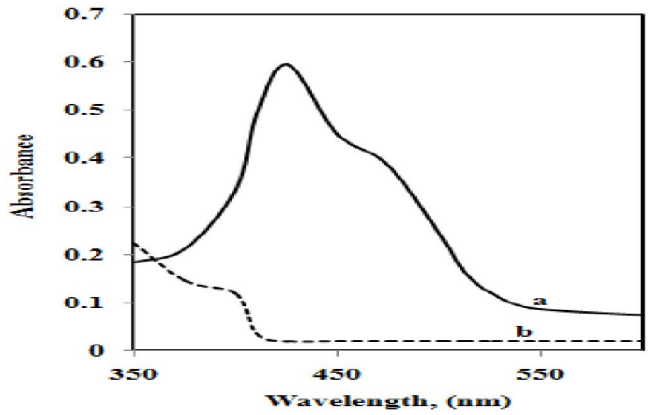

Figure 4 : Absorption spectrum of
a) LSB with (Ferric chloride + Potassium fe rrocynide + Chloroform)
b) Ferric chloride + Potassium ferrocynide + Chloroform

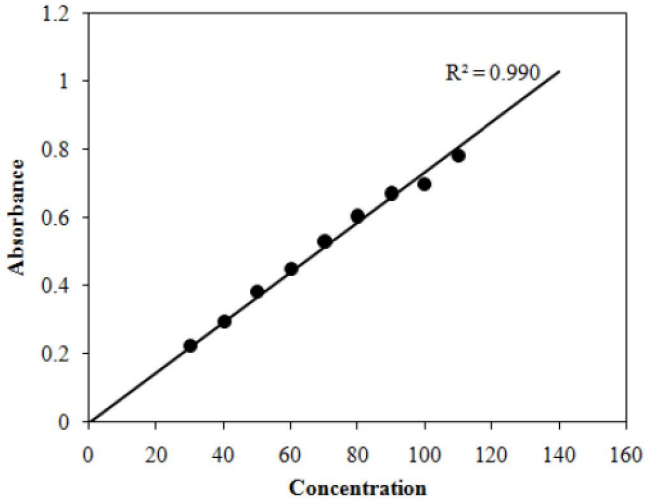

Figure 5 : Beers Law Plot of Method B

TABLE 1 : Optical Characteristic of Proposed Methods

Parameters	Method A	Method B
λ max (nm)	555	425
Beer's Limit(μg. ml^{-1})	20-100	30-110
Molar absorptivity (L. mol^{-1} cm^{-1})	1.897×10^3	1.6661×10^3
Specific absorptivity	0.00739	0.006962
Sandell's sensitivity (μg.cm^{-2}/ 0.001 A.U)	0.135	0.144
Correlation coefficient (r^2)	0.999	0.990
Regression equation(Y=mX+C)	-	-
Slope (m)	0.00739	0.00696
Intercept	0.00233	0.02857
Confidence limit with 0.05 level (95%)	±0.6432	±0.4582
Confidence limit with 0.01 level (95%)	±0.8386	±0. 6218

Sandell sensitivity (S)=10^{-3}/a; S=Number of micrograms of the determined per ml of a solution having a cross section of 1 cm^2 and absorbance of 0.001 and a=absorbance of 1 μg/ml solution determined in a cuvette with an optical path length of 1 cm.

TABLE 2 : Assay of recovery studies of Levosalbutamol in tablet dosage form

Pharmaceutical formulations#	Labeled amount (mg/tablet)	Amount found in mg* by		Percent recovery	
		Method A(mg) Mean±SD	Method B(mg) mean±SD	Method A	Method B
Tablet	2	1.96±0.5	1.89±0.3	98	94.5

***Mean of six determinations.**
#the commercial preparations used were, Tablet-Levolin

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culated from the eight measurements 3/4 f the upper Beer's law limits of LSB are given in TABLE 1. The results showed that these methods have reasonable precision. Comparison of the results obtained with the proposed and UV methods for the dosage forms (TABLE 2) confirms the suitability of the methods for pharmaceutical dosage forms when compared to UV method. The proposed methods are reaction specific and eliminate interference from impurities.

The optimum conditions for color development for methods A and B were established by varying the parameters one at a time and keeping the other parameters fixed and observing the effects of product on the absorbance of the colored species and incorporated in the products. To evaluate the validity and reproducibility of the methods, know amounts of the pure drug were added to the previously analysed pharmaceutical preparations and the mixtures were analysed by proposed methods. The percent recoveries were given in TABLE 2.

The proposed methods are found to be simple, sensitive, selective, accurate, precise, economical and can be used in the determination of levosalbutamol (LSB) in bulk drug and its pharmaceutical dosage forms (tablets) in a routine manner.

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