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Method Development and validation of *Levosalbutamol sulphate* by Derivative Spectroscopy

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Abstract

***Plan**: An analytical method for estimation of levosalbutamol in bulk and pharmaceutical formulation.*
***Preface:** The developed method is simple, fast and accurate and can be used for routine analysis of Market formulations.*
***Methodology:** In this study zero, first and second order derivative spectrophotometric method were developed for the estimation of Levosalbutamol sulphate. In zero order spectrophotometery, absorbance value was measured at 277nm. In first derivative spectrophotometry amplitudes were measured at 233nm.In second derivative spectrophotometry amplitudes were measured at 237nm. Calibration curves were linear between the concentration range of 20-60µg/ml, 5-30µg/ml and 35-60µg/ml respectively. The % RSD value is less than 2% and the recovery were near 100% for all methods.*
***Outcome:** All the developed methods were applied on pharmaceutical formulations.*
***Key words:** Spectrophotometric method, Levosalbutamol sulphate, Derivative spectroscopy.*

1. Introduction

Levosalbutamol sulphate (LSS) is the R - enantiomer of short acting β_2-adrenergic receptor agonist of Salbutamol. Chemical it is 4[(1R)-2-(tert-butylamino)-1-hydroxyethyl]-2-(hydroxy methyl) phenol and its Molecular formula $C_{13}H_{21}NO_3$, Molecular wt. 239.311 g/mol. As a bronchodilator, it is used to treat asthma and COPD [1, 2]. Literature survey reveals that, only few spectrophotometric [3 ,4,5,6,7] and bio-analytical methods by HPLC was found using human plasma urine, blood and biological fluids[8,9,10] , GC-MS-SIM [11] and HPLC[12] for the quantitative estimation of Levosalbutamol sulphate in bulk and pharmaceutical formulations have been developed. Hence an attempt has been made to develop new method for its estimation in bulk and pharmaceutical formulation with good accuracy, simplicity and precision.

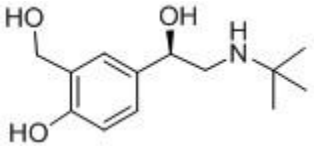

Fig.1 Levosalbutamol sulphate

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2. Material and Methods

2.1 Apparatus

A shimadzu model 1800 double beam UV/ Visible spectrophotometer with spectral width of 1 nm, wavelength accuracy of ± 0.1 nm and a pair of 10 mm matched quartz cell was used to measure absorbance of all the solutions. Spectra were automatically obtained by UV-Probe system software (ver.2.34).

2.2 Reagents and Materials

All chemicals and reagents were used of AR grade. Authentic of LSS was obtained as gift samples from Cipla Pharmaceutical Pvt., Ltd. Mumbai.

2.3 Selection of detection wavelength

Solutions of drug were scanned over the range of 200-400 nm. It was observed that the drug showed considerable absorbance at 277nm, 232nm and 237nm for zero, first and second order were selected as the wavelength for detection. The spectra of LSS show in fig. 5, 6 and 7.

2.4 Preparation of standard stock solutions

LSS was weighed (100mg) and transferred to 100ml volumetric flasks and make up the volume up to the mark with distilled water and the final concentration of solution containing 1000 µg/ml of LSS.

2.5 Preparation of working solutions

Aliquot from the stock solutions of LSS was appropriately diluted with distilled water to obtain working standard of LSS.

3. Method Development and Validation

The method was validated for accuracy, precision, linearity, detection limit, quantitation limit and specificity.

3.1 Linearity

The linearity of levosalbutamol was found to be 20-60µg/ml, 5-25µg/ml and 35-55µg/ml for zero, first and second order respectively. The r^2 values were near about 0.999 for all orders which shows good correlation between analyte concentration and response area. The data of regression analysis was shown in table 1 and figure 2, 3, 4.

Table 1 Analytical performance parameters of levosalbutamol

Parameters	*Zero order*	*First order*	*Second order*
Wavelength Maximum	277	232	237
Linearity range (µg/ml)	20-60	5-30	35-65
Correlation coefficient	0.998	0.999	0.996
LOD (µg/ml)	1.84	1.18	2.13
LOQ (µg/ml)	5.48	3.57	6.45
Sandell's sensitivity (mg/cm^2/0.001 absorbance unit)	0.107	0.071	0.198

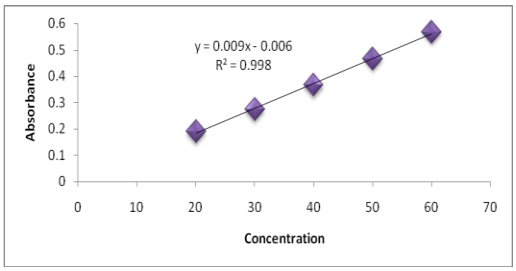

Fig.2: Calibration curve for zero order for levosalbutamol

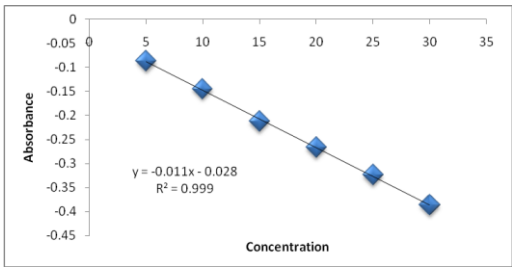

Fig. 3 Calibration curve for first order for levosalbutamol

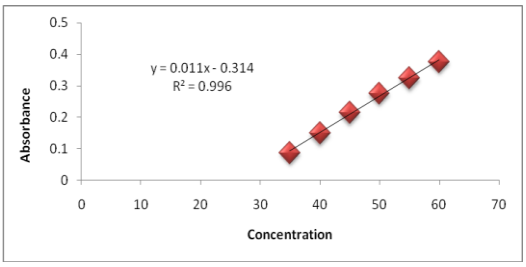

Fig. 4 Calibration curve for second order for levosalbutamol

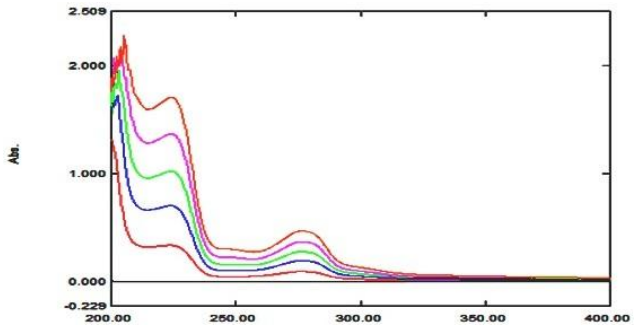

Fig 5 .Zero order spectra of levosalbutamol

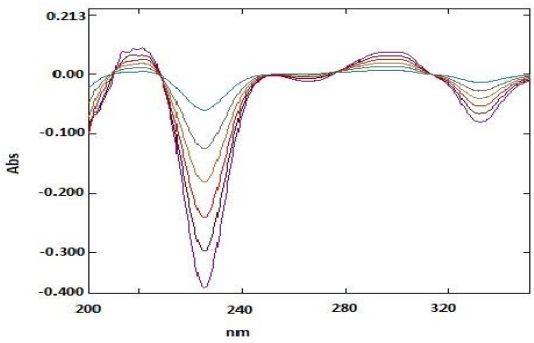

Fig 6 .First order spectra of levosalbutamol

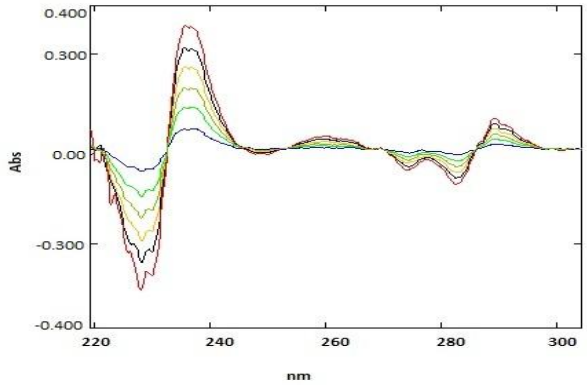

Fig 7 Second order spectra of levosalbutamol

3.2 Precision

The %RSD obtained for repeatability studies were found to be -0.53-0.73 carried out by estimating response for levosalbutamol. The %RSD for intra-day and inter-day precision was found to be 0.154-1.13 and 0.21-1.5 respectively for levosalbutamol. The RSD values which are well below 2% indicate that the precision of the method is satisfactory. (Table 2 and 3).

Table 2 .Repeatability study for levosalbutamol

Parameters	*Zero order (30µg/ml)*	*First order (10µg/ml)*	*Second order (40µg/ml)*
Mean	0.274	-0.195	0.147
SD	0.001	0.001	0.001
% RSD	0.27	-0.53	0.73

**Mean of five replicates*

Table 3 Intraday and Inter day precision data for levosalbutamol

S. no	*Order*	*Concentration*	*Intra day*		*Inter day Precision*	
			Mean Absorbance	*%RSD*	*Mean Absorbance*	*%RSD*
1		20	0.19	0.798	0.192	0.539
2	*Zero*	30	0.27	0.210	0.274	0.21
3		50	0.46	0.498	0.465	0.66
4		5	0.09	1.13	0.088	1.5
5	*First*	10	0.14	0.800	0.144	0.877
6		15	0.22	0.536	0.215	0.723
7		40	0.146	1.044	0.147	1.03
8	*Second*	50	0.28	0.361	0.280	0.552
9		60	0.38	0.154	0.3774	0.273

3.3 Accuracy

The mean % recoveries for levosalbutamol zero, first and second order were found to be 99.9, 99.87 and 100.17, respectively (Table 4). The % recovery of added drugs is well within the limits of 98-102%. It indicates the accuracy of this method.

Table 4 Recovery study for levosalbutamol

Parameters	*Zero order*			*First order*			*Second order*		
Accuracy	*80%*	*100%*	*120%*	*80%*	*100%*	*120%*	*80%*	*100%*	*120%*
Amount present (µg/ml)	20	20	20	10	10	10	40	40	40
Amount Added (µg/ml)	16	20	24	8	10	12	32	40	48
Amount recovered***** **(**µg/ml)	35.75	39.7	44.5	17.87	19.98	22.1	72.1	80.12	88.21
% Recovery	99.31	99.25	101.14	99.28	99.9	100.45	100.14	100.15	100.24
% Mean Recovery		99.9			99.87			100.17	

3.4 Analysis of market formulations

The assay result obtained by using the proposed method for the analysis of marketed formulations containing levosalbutamol. The results showed in table 5 and 6. The average content of levosalbutamol was found to be 98-100% in acceptance limit. This indicates that present method can be successfully used for the estimation of levosalbutamol.

Table 5 Assay of levosalbutamol (tablet 2mg)

Parameters	*Zero order*	*First order*	*Second order*
Label Claim (mg/tablet)	2	2	2
Amount Estimated (mg/tablet)*	2.01	1.994	1.990
Percentage Label Claim (%)	100.5	99.70	99.54

Mean of three reading

Table 6 Assay of levosalbutamol (rota caps 100mcg)

Parameters	*Zero order*	*First order*	*Second order*
Label Claim (mcg/cap)	100	100	100
Amount Estimated (mcg/cap)*	100.53	100.2	99.86
Percentage Label Claim (%)	100.53	100.2	99.86

Mean of three reading

4. Conclusion

Proposed study describes method for the estimation of Levosalbutamol sulphate. The method was validated and found to be simple, sensitive, accurate and precise as per ICH guidelines .The proposed method in routine quality control laboratories for determination of Levosalbutamol sulphate.

Acknowledgement

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