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Validated UV spectroscopic method for estimation of Salbutamol from tablet formulations

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Abstract

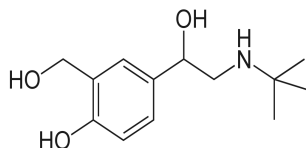
A simple, sensitive and specific UV spectrophotometric method was developed for the estimation of Salbutamol in tablet dosage form. The optimum conditions for the analysis of the drug were established. The wavelength maxima (λ_{max}) for Salbutamol were found to be 276 nm. The linearity for this method was found to be in the range of 10-120 μ g/ml. The method showed high sensitivity with reproducibility in results. The lower limit of detection and the limit of quantification were found to be 4.234 and 12.702 respectively. The calibration curve was drawn by plotting graph between absorbance and concentration. Coefficient of correlation was higher than 0.99. The regression of the curve was $Y = 0.002x + 0.0821$. Precision of the method was found to be 1.625 ± 0.324 against the label claim of 4mg. The percentage recovery was found to be 98.56 ± 0.238 . The sample solution was stable up to 12 hours. The proposed method may be suitably applied for the analysis of Salbutamol in tablet pharmaceutical formulation for routine analysis.

Key words: Salbutamol, UV Spectroscopy, Tablet dosage form.

INTRODUCTION

Salbutamol, *RS*-[4-[2-(*tert*-butylamino)-1-hydroxyethyl]-2-(hydroxymethyl)phenol] is a short-acting β_2 -adrenergic receptor agonist used for the relief of Broncho-spasm in conditions such as asthma and chronic obstructive pulmonary disease[1,2,3]. Salbutamol is still commonly delivered as a racemic mixture (+,-). Salbutamol, even though S-Salbutamol is known to have a detrimental effect on asthma sufferers (in fact the exact opposite effect of the R Isomer[4]. Selective β_2 -adrenoceptor stimulant that causes the relaxation of the smooth muscles through the

increase of the intracellular cyclic adenosine monophosphate (cAMP) due to this, bronchial and uterine muscles get relaxed, the peripheral vessels are dilated and heart rate increases[5]. Activation of the β -2 adreno-receptors opens ATPase channels and drives potassium from the extra cellular to the intracellular space[6]. This both decreases extracellular Hyperkalaemia and increases intracellular potassium, so decreasing the chance of arrhythmias[7]. Salbutamol also has certain anti-inflammatory properties whose clinical significance is not determined[8].



Chemical Structure of Salbutamol

In previous studies, the Simultaneous Determination of Salbutamol Sulphate and Bromhexine Hydrochloride in Tablets were done by Reverse Phase Liquid Chromatography and Immunoaffinity-chromatography[9,10]. HPLC-Fluorometric detection is also reported for estimation of Salbutamol from plasma samples[11]. Chiral HPLC assay and derivative spectroscopic method are also reported for Analysis of Salbutamol and Related Impurities[12-13]. But for routine analysis, no simple and accurate method is available for determination of Salbutamol in tablet dosage form. The aim of present work is to find out a simple, sensitive, specific, spectrophotometric method and its validation for estimation of Salbutamol from pharmaceutical formulation.

MATERIAL AND METHOD

Instruments

UV-Visible double beam spectrophotometer (UV-1800, SHIMADZU Co, Japan) with 1cm matched quartz cells, Micropipette of Variable volume 10-1000 μ L (Gene Pete Co.) and Digital balance (Citizen Co.) were used.

Materials

Salbutamol was procured as gift sample from JC. Industries Ltd, Maharashtra. The obtained Salbutamol was having 99.99% w/w assay value and was used without further purification. Methanol, Potassium dihydrogen phosphate, Hydrochloric acid, Sodium hydroxides were purchased from CDH (P) Ltd. New Delhi. All chemicals and reagents used were of analytical grade. The Salbutamol tablets were purchased from local market of Moradabad.

Preparation of Standard Stock Solution

The standard stock solution was prepared by dissolving Salbutamol in 0.1N HCl to make final concentration of 200 μ g/ml. Different aliquots were taken from stock solution and diluted with 0.1N HCl separately to prepare series of concentrations from 10-120 μ g/ml. The λ_{max} was found by UV spectrum of Salbutamol in 0.1NHCl, in the range of 200-400 nm and it was found to be 276 nm. Absorbance was measured at 276 nm against 0.1N HCl as blank. The calibration curve was prepared by plotting absorbance versus concentration (μ g/ml) of Salbutamol.

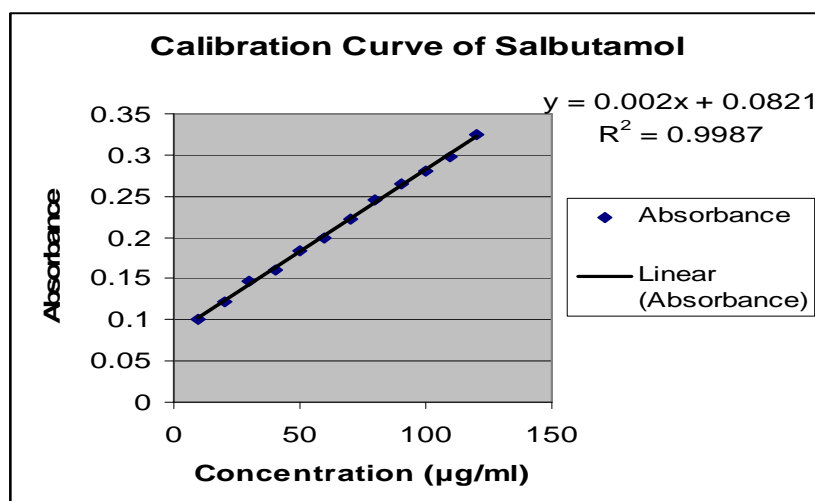


Fig 1. Calibration curve of Salbutamol

Application of the Proposed Procedure for the Determination in Tablets

The proposed method was applied in order to determine the Salbutamol in tablets formulation. The marketed tablet formulation of Salbutamol was used for this. Twenty five tablets were weighed and average weight was calculated, crushed to fine powder. The powder equivalent to 100 mg of Salbutamol was transferred in 100 ml volumetric flask and dissolved in 0.1NHCl by shaking. The volume was made up to mark to get final concentration of 1mg/ml. Frequent shaking given and volume was made up to 100ml mark with 0.1N HCL. The solution was then filtered through Whatman filter paper #41. This filtrate was diluted suitably with 0.1N HCL to get the solution of 100µg/ml concentration.

The working solution of drug (100µg/ml) was prepared from standard stock solution in 0.1NHCl. The absorbance of this solution was measured and amount of Salbutamol was calculated from the calibration curve. The readings were taken in triplicate.

Method Validation

As per the ICH guidelines, accuracy, precision, LOD, LOQ and linearity of the calibration curve were determined [14-16]. For linear response measurement, the least squares method was applied. The statistical analysis was calculated by ANOVA. Amounts of 60 and 80µg/ml of Salbutamol standard solution were added into pre analysed 60 and 80µg/ml samples and absorbance were measured and the recovery was calculated.

RESULTS AND DISCUSSION

The development of spectrophotometry methods for the determination of drugs has increased considerable in recent years because of their importance in pharmaceutical analysis. Due to greater solubility in HCL, it was selected for further study. The values of standard deviation and coefficient of variation were satisfactorily low. The percentage recovery range of 99% to 101% was indicating the accuracy of method. From the proposed method, it was found that Salbutamol obeys linearity within the concentration range of 10-120 µg/ml. It was found that the % RSD is less than 2, which indicates that the method is highly reproducible.

Table 1: Analytical validation parameters:

| Parameter | Result |
|--------------------------------------|--|
| Absorption maxima(nm) | 276 |
| Linearity Range ($\mu\text{g/ml}$) | 10-120 |
| Standard Regression Equation | $Y = 0.002x + 0.0821$ |
| Correlation Coefficient (r^2) | 0.9987 |
| Accuracy (% recovery \pm SD) | 98.56 ± 0.238 |
| Precision (%) | 1.625 ± 0.324 (Intraday) 1.279 ± 0.215 (Interday) |
| LOD ($\mu\text{g/ml}$) | 4.234 |
| LOQ ($\mu\text{g/ml}$) | 12.702 |
| %Drug found in tablet formulation | 99.53 |

The analytical and necessary validation parameters for the UV spectrophotometric determination of Salbutamol from tablet formulation are presented in Table 1

Table 3: Results of recovery and precision

| Ingredient | Amount of drug from formulation | % Addition | Amount added ($\mu\text{g/ml}$) | Amount recovered ($\mu\text{g/ml}$) | % Recovery | Precision (Intra day)* | Precision (Inter day)* |
|------------|---------------------------------|------------|-----------------------------------|---------------------------------------|------------|------------------------|------------------------|
| Salbutamol | 60 | 100 | 60 | 59.16 | 98.56 | 1.62 | 1.27 |
| | 80 | 100 | 80 | 78.54 | 98.18 | 0.78 | 0.51 |

Standard addition method was used to assess the accuracy. For evaluating precision, the selected concentration (60 and 80 $\mu\text{g/ml}$) were prepared in 0.1N HCL and analyzed to determine the intra-day and inter day variability.

The intra-day and inter day precision were determined and presented as the RSD %. The precision and accuracy of the analysis are given in Tables 1, indicates high precision and accuracy.

Table 4: Determinations of active ingredients in tablets

| Sample | Label Claimed | Amount Found mg /Tab. | % Labeled Claim * |
|------------|---------------|-----------------------|-------------------|
| Salbutamol | 4mg | 3.9812 ± 0.126 | 99.53 |

The proposed methods can be applied for quantitative assay of Salbutamol in tablet dosage form. The method was applied on commercially available brand of Salbutamol and results showed that the drug content of this formulation was in accordance with the labeled claim 4mg.

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