Spectrofluorimetric estimation of salbutamol sulphate in different dosage forms by formation of inclusion complex with β-cyclodextrin

Abstract

A simple, precise, reproducible and accurate spectrofluorimetric method for estimation of Salbutamol sulphate (SAL) in bulk drug and various dosage forms has been developed. This method is based on formation of inclusion complex of SAL in β-cyclodextrin (BCD) which gives fluorescence at excitation wavelength of 279.6 nm and emission wavelength of 609.8 nm in water. Formation of inclusion complex of drug with BCD enhances fluorescence intensity of drug leads to increased sensitivity. The developed method was validated according to ICH guidelines with respect to accuracy, precision, linearity, limit of detection, limit of quantification. Linearity was observed in the range of 4-20 μg/ml with correlation coefficient of 0.9982. The simplicity of the method permitted rapid analysis suitable for routine control. The developed method was successfully applied for the estimation of SAL in different marketed dosage forms like tablets, syrup and aerosol.

Key words: Salbutamol sulphate, β-cyclodextrin, Spectrofluorometry, Method validation Pharmaceutical formulations

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INTRODUCTION

Salbutamol Sulphate (SAL) is chemically (RS)-1-(4-hydroxy-3-hydroxy methyl phenyl)-2-(tert-butyl amino) ethanol sulphate. It is β_2-adrenoceptor agonist very widely used as bronchodilator in the treatment of asthma and seasonal allergies.[1] SAL is official in IP, BP and USP[2-4] and the official method for quantification of SAL bulk drug is non-aqueous titration, while for syrup and injection dosage form, colorimetric method is employed. Electrochemical techniques,[5-7] chromatographic methods,[8-10] spectrophotometric methods[11-15] and automated methods such as flow injection analysis[16,17] are also reported for detection of SAL in bulk drug and pharmaceutical formulation. The reported chromatographic methods for estimation of SAL are time consuming while official electrochemical and colorimetric methods are less selective and sensitive. Literature survey revealed that different analytical methods are available for estimation of SAL from different marketed formulations. Hence the aim of the research work is to develop a single analytical method applicable for estimation of SAL in various marketed formulations. The present research article describes the development and validation of spectrofluorimetric method for SAL using β-cyclodextrin (BCD) as an inclusion complex. The developed method was validated and was extended for the estimation of SAL in different pharmaceutical formulations.

EXPERIMENTAL

Materials and chemicals

Pure sample of SAL and BCD was gifted from Barouq Pharmaceuticals Ltd.

(Anand, India) and Roquette Ltd. (Mumbai, India), respectively. The pharmaceutical formulations of SAL like tablets, syrup and aerosol (all with brand name ASTHALIN, Cipla Pharmaceuticals Ltd. India) were purchased from local market. Sulphuric acid (98%), ethanol, diethyl ether and dimethylsulphoxide (DMSO) were used of analytical grade. Distilled water was used throughout the study.

Instrument

Spectrofluorimetric measurements were carried out using Spectrofluorometer FP 6500 with 1 cm quartz cell (JASCO Corporation, Japan).

Analytical methodology for estimation of SAL in Pharmaceutical Formulations

Standard preparation

SAL (20 mg) was accurately weighed and transferred into 200 ml volumetric flask and diluted up to mark with water. An aliquot (1 ml) was further diluted with water in 10 ml volumetric flask, to obtain final concentration 10 μg/ml.

BCD (50 mg) was weighed accurately and transfer into 50 ml volumetric flask and diluted up to mark with water to obtain concentration 1 mg/ml.

Preparation of inclusion complex

Accurately weighed 20 mg of SAL was dissolved in 5 ml of DMSO. BCD solution (1 mg/ml) was added with continuous agitation to prepare different ratios of SAL: BCD in different proportion from 1: 0.5 to 1: 2.0, it was then diluted with water to obtain concentration of 100 μg/ml SAL in BCD inclusion complex. An aliquot (1ml) was further diluted with water in 10 ml volumetric flask to obtain final concentration 10 μg/ml.

Spectrofluorometric determination

For selection of excitation and emission wavelength of inclusion complex, excitation spectra was scanned between 220-400 nm, while emission spectra was scanned between 400-700 nm. The wavelengths selected for analysis was 279.6 nm as excitation wavelength and 609.8 nm as emission wavelength. Fluorescence intensity of standard and sample solutions determined at selected excitation and emission wavelength.

Sample preparation

Tablet dosage form

Twenty tablets were weighed and crushed. Tablet powder equivalent to 20 mg of SAL was accurately weighed and transferred to volumetric flask; 10 ml water was added into crushed powder and was sonicated for 20 minutes. Above solution was filtered using whatman filter paper 41. Filtrate was collected in crucible and was allowed to evaporate in vacuum dryer until the constant weight was obtained. Collected dry powder was dissolved in 5 ml DMSO and mixed with BCD solution (1 mg/ml, 24 ml) with continuous agitation and kept aside for 20 min and diluted up to 250 ml with water. An aliquot was further diluted with water to obtain final concentration 9.6 μg/ml.

Syrup dosage form

Ten ml of syrup containing 4 mg of SAL was accurately pipetted out and mixed with 25 ml 0.05 M H_2SO_4. Aqueous solution was extracted twice with 50 ml diethyl ether. Aqueous extract was collected in 250 ml volumetric flask. Ether extract was washed with 10 ml water. All aqueous extract was collected together and passed through charcoal to remove coloring matter. DMSO (5 ml) was added in aqueous solution and then BCD solution (1mg/ml, 4.8 ml) was added with continuous agitation and kept aside for 20 min. Volume was adjusted upto the mark with water in 250 ml volumetric flask. An aliquot was further diluted with water to obtain final concentration 9.6 μg/ml.

Aerosol dosage form

For assay of SAL from aerosol dosage form (200 μg/dose), pressurized container removed from the actuator. All the labels and markings present on the container were removed with a suitable solvent. Container was placed in the plastic bag and cooled at least -20 ^{0}C for 24 hrs in deep freezer. Small hole was carefully pierced on the shoulder of the container. Propellant was allowed to evaporate (about 3 hrs) and then top was removed. The top and valve of the open container were washed with little ethanol. All the component of the container put in ethanol (about 20 ml) and sonicated for 15 minutes. Combined alcoholic extract was evaporated into vacuum dryer to obtained constant weight. Collected dry powder was dissolved in 5 ml DMSO and further treated same as given under tablet dosage form to prepare inclusion complex and further diluted to prepare final concentration 9.6 μg/ml.

Sample solutions of all pharmaceutical formulations of SAL were analysed as described under spectrofluorometric determination.

Method validation

The developed method was validated in terms of linearity, limit of detection (LOD), limit of quantification (LOQ), precision and accuracy.