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# Simple Titrimetric Method for the Estimation of Salbutamol Sulphate (SBS) in Pharmaceutical Formulations

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## Abstract

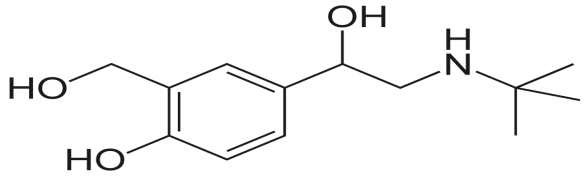
*A titrimetric method which is simple, sensitive and rapid is described for the assay of salbutamol sulphate (SBS) in bulk drug and in tablet dosage forms using N-bromosuccinimide (NBS) as reagents. In titrimetry, aqueous solution of salbutamol sulphate is treated with a measured excess of NBS in acetic acid medium and after the oxidation of SBS is complete, the unreacted oxidant is determined iodometrically.In this method the amount of NBS reacting corresponds to the amount of SBS content. Titrimetric method is applicable over 1.74 x $10^{-4}$ – 8.68 x $10^{-4}$ mol/L range and the reaction stoichiometry is found to be 1:6 (SBS: NBS). Intraday and inter-day precision and accuracy for the developed method was evaluated. The method was successfully applied to the assay of SBS in tablet and capsule formulations and the results were statistically compared with those of a reference method. The accuracy and reliability of the methods were further ascertained by recovery experiments via the standard-addition technique.*

**Keywords:** Salbutamol sulphate, assay, titrimetry, N-bromosuccinamide.

## Introduction

Salbutamol, *RS*-[4-[2-(*tert*-butylamino)-1-hydroxyethyl]-2-(hydroxymethyl) phen-ol] is a short acting β2-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].

Salbutamol sulphate (SBS) whose structure is given in figure 1 is a selective β-2-agonist antiasthmatic. Its primary action is to stimulate adenyl cyclase which catalyzes the formation of cyclic adenosin monophosphate. The drug is official in *European Pharmacopoeia*[5], which describes a potentiometric titration in non-aqueous medium, *British Pharmacoeia*[6] and *Indian Pharmacopoeia*[7]. Some different methods of analysis have been reported for the determination of SBS, including HPLC[8-10] and UV-spectrophotometry[11,12], but most of them require extensive sample preparation prior to the measurement step, some are less sensitive and some other are relatively complicated in terms of assay procedure or equipment required for analysis.




SBS in pharmaceuticals has been assayed by visible spectrophotometric methods based on reactions such as redox[13,14], reduction followed by chelation[15], oxidative coupling[16,17], diazotization and coupling[18-19], nitrosation[20], nitration[21], nitration followed by Meisenheiner complex formation[22] and charge-transfer complex formation[23]. However, many of these procedures suffer from some disadvantage, such as poor sensitivity, heating or extraction step, critical working conditions or the use of organic solvents, and are hence unsatisfactory for routine analysis. The only visual titrimetric method[24] reported employs NBS as the oxidimetric titrant in the presence of potassium bromide and using methyl red as indicator. However, the method is applicable over a macro scale. Recently, Issa *et al*.[25] have reported a conductometric titration method using phosphotungstic and phosphomolybdic acids as titrants. Even these procedures are time consuming and less sensitive.

Different methods for the estimation of SBS in tablets, capsules and syrups employ N-bromosuccinimide[26], bromate–bromide solution[27] as an oxidizing agents, rhodamine-B and methylene blue dyes[26,27] as reagents for spectrophotometric analysis.Diazotised o-nitroaniline (DONA)[28] and diazotised p-nitroaniline (DPNA)[29] as a for colour formation, Continuous and Stop flow methods[30] and, Spectroflourometric Estimations[31].

This paper describes simple and rapid method for estimation of SBS in tablets using N-bromosuccinimide as an oxidizing agent. The proposed method has the advantage of being rapid and simple and is free from interferences from common tablet and capsule excipients. The results obtained were closely comparable to those of a reported method, and recovery tests were also found to be satisfactory.

## Material and Methods

All chemicals used were of analytical reagent grade and solutions were made in distilled water. Formulation i. e. Asthalin tablets, (Cipla India Ltd.) each containing 2/4 mg containing SBS were purchased from local commercial sources and used in the estimation.

NBS solution (0.01 mol/L) was prepared by dissolving N-bromosuccinimide (MERCK –Merck Limited, Mumbai, India) in water with the aid of heat and standardized[22]. The solution was kept in an amber coloured bottle stored in a refrigerator and used for titrimetry.

Sodium thiosulphate solution (0.01 mol /L, Loba Chem. Industries, India) was prepared in water and standardized. Potassium iodide (10%) and starch (1%) were prepared in the usual way.

A 10-mL aliquot of pure drug solution containing 2.0–4.0 mg of SBS was accurately measured and transferred into a 100-mL titration flask. The solution was acidified by adding 5 mL of 5 mol/L acetic acid followed by the addition of 10 mL of 0.01 mol/L NBS. The content was mixed well and the flask was kept aside for 15 min under occasional swirling. Then, 5 mL of 10% potassium iodide was added to the flask and the liberated iodine was titrated with 0.01 mol/L sodium thiosulphate to a starch end point. A blank titration was run under the same conditions.

Fifty to 100 tablets were accurately weighed and powdered. An amount of tablet powder equivalent to 100 mg of SBS was accurately weighed into a 100 mL calibrated flask, 60 mL of water was added and shaken for 20 min. Then, the volume was diluted to the mark with water, the content was mixed well and filtered using a Whatman No. 42 filter paper. The first 10 mL portion of the filtrate was discarded and a convenient aliquot of the subsequent portion was analyzed by titrimetry as described earlier.

**Recovery experiment** – To a fixed and known amount of drug in the tablet/capsule powder (pre-analysed), pure SBS was added at three different levels, and the total was found by the proposed methods, from which the percent recovery of pure drug added was calculated.

## Results and Discussion

The propabable mechanism for the reaction is shown by Basavaiah et al,[24] (scheme 1),

The reaction stoichiometry that was used for all calculations was found to be 1:6. The relation between the amount of the drug and titration end point was examined. Quantitative results were obtained in an acetic acid medium and a 1.0 mol/L acetic acid concentration was found optimal although the reaction stoichiometry was unaffected in the range 0.2–2.0 mol/L acetic acid. The oxidation reaction was found to be complete and quantitative in 15 min. A 10 mL aliquot of 0.01 mol/L NBS (0.1 mmol) solution was found adequate for quantitative oxidation of SBS in the range determined 0.1–0.4 mg/mL.

The proposed methods were applied to the analysis of SBS in tablets and capsules and the results were statistically compared with those obtained by Ray and Bandopadhyay reported method[9], which consisted of measuring the absorbance of blue chromogen at 670 nm after treating tablet extract with Folin-Ciocalteau reagent in alkaline medium.

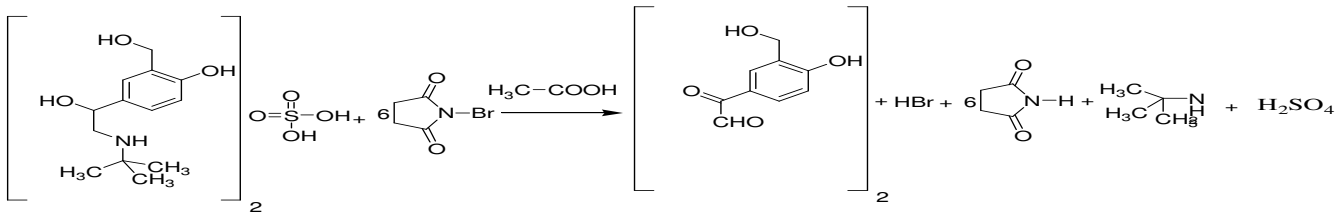



**Table-1**
**Assay of formulations by the proposed method**

| Formulation | Nominal amount of SBS (mg) | Literature method[9] | Proposed method |
|---|---|---|---|
| Asthaline | 2 | 98.7 ± 0.9 | 97.3 ± 2 |
| | 4 | 99.1 ± 0.8 | 99.3 ± 1.2 |

**Table-2**
**Recovery studya**

| Method | SBS in Formulation | SBS Added | Total SBS Found | SBS recovered (%) |
|---|---|---|---|---|
| Titrimetry | 0.15 | 0.10 | 0.27 | 97.5 ± 1.6 |
| | 0.15 | 0.20 | 0.38 | 99.2 ± 2.1 |
| | 0.15 | 0.30 | 0.40 | 99.5 ± 1.3 |

From the recovery experiment, it was found that the percent recovery of the pure drug added to tablet powder ranged from 97.5 to 104.5, as shown in table II, and The recovery of SBS in selectivity testing was found to be 101.5 ± 2.

The proposed methods are simple, rapid and reliable compared to most existing methods. In contrast to the direct titration method (16) reported earlier, the proposed method is more sensitive with a determinable range of 0.1–0.5 mg mL–1 (1.74 x $10^{-4}$ – 8.68 x $10^{-4}$mol L–1) and can be applied to a single tablet or capsule so that tablet to tablet or capsule. The methods are accurate to –3.0 to +2.3% when applied to the determination of SBS in formulations.

## Conclusion

In conclusion, the results of the estimation demonstrate that the proposed titration method can be used to determine the content uniformity of tablets and capsules. Besides the simplicity of the procedure, the relative cheapness of apparatus demonstrates their advantageous characteristics in addition to their high accuracy and precision.

Applicability of this method to the determination of salbutamol in urine and blood samples after appropriate sample pretreatment will be the topic of our further research.

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