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THE SIMULTANEOUS ESTIMATION OF SALBUTAMOL SULPHATE AND AMBROXOL HYDROCHLORIDE IN ORAL LIQUID DOSAGE FORM

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ABSTRACT

Salbutamol is a bronchodilator and Ambroxol hydrochloride is a mucolytic. Combination of these drugs is used in the formulation of cough syrups. In the literature, there is no method reported for the simultaneous estimation of the drugs in oral liquid dosage form. Hence, the present work is aimed to develop reverse phase HPLC method for the simultaneous determination of Salbutamol sulfate (SAL), and Ambroxol hydrochloride (AMB) in oral liquid dosage form and validation of the developed method. The chromatographic separation of the drugs was achieved with the mobile phase system sodium dihydrogen phosphate buffer pH 3.0: acetonitrile: methanol in the ratio of 65:10:25 with the flow rate of 1 mL/min and injection volume 10 µL. An Inertsil C8-3 (250 × 4.6 mm, 5 µm) column was used, and the detection wavelength was 276 nm. This system produced sharp peaks with good resolution, minimum tailing and satisfactory retention times of SAL and AMB were found to be 3.157and 11.883 min respectively indicating the suitability of the system. The developed method was validated for various parameters accuracy, precision, linearity, robustness, and specificity as per ICH guidelines.

KEYWORD: Salbutamol, Ambroxol, Oral liquid dosage form, RP-HPLC.

INTRODUCTION

Salbutamol sulphate and ambroxol hydrochloride are commonly used drugs in the management of respiratory disorders, particularly those involving bronchoconstriction and

excessive mucus production. These drugs are often combined in oral liquid dosage forms to provide synergistic therapeutic effects by improving airflow and facilitating mucus clearance.

Salbutamol sulphate is a selective β_2-adrenergic receptor agonist and belongs to the class of bronchodilators. It is widely used in the treatment of conditions such as bronchial asthma, chronic obstructive pulmonary disease (COPD), and other obstructive airway diseases. The primary mechanism of action of salbutamol involves stimulation of β_2-receptors in the bronchial smooth muscle, leading to relaxation of the muscles and dilation of the airways. This results in rapid relief from bronchospasm, reducing symptoms like wheezing, shortness of breath, and chest tightness. Salbutamol has a quick onset of action, usually within minutes, making it an effective rescue medication for acute asthma attacks. It can be administered through various routes, including inhalation, oral tablets, and syrups. However, common side effects may include tremors, palpitations, headache, and nervousness due to its systemic β-adrenergic effects.

Ambroxol hydrochloride, on the other hand, is a mucolytic and expectorant agent used to manage respiratory conditions associated with thick and viscous mucus. It acts by depolymerizing mucopolysaccharides present in mucus, thereby reducing its viscosity and making it easier to expel from the respiratory tract. Additionally, ambroxol stimulates the production of pulmonary surfactant, which reduces mucus adhesion to the bronchial walls and improves mucociliary clearance. This helps in clearing the airways and enhancing breathing efficiency. Ambroxol is commonly prescribed in conditions such as bronchitis, asthma with productive cough, and other respiratory tract infections. It is available in various dosage forms, including syrups, tablets, and inhalation solutions. The drug is generally well tolerated, with mild side effects such as gastrointestinal discomfort, nausea, and dry mouth.

The combination of salbutamol sulphate and ambroxol hydrochloride is particularly beneficial in patients suffering from respiratory disorders with both bronchospasm and mucus hypersecretion. While salbutamol opens up the airways by relaxing bronchial muscles, ambroxol facilitates the removal of mucus, thereby providing comprehensive relief. This dual action improves respiratory function and patient comfort. Such combinations are widely used in clinical practice for effective symptomatic management.

Salbutamol Sulphate

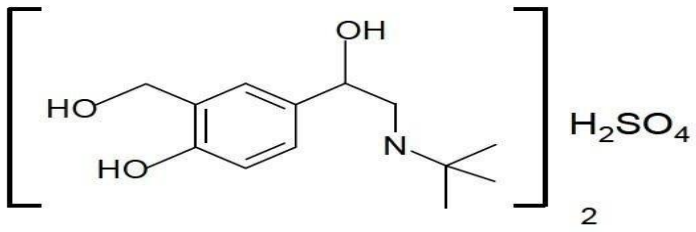


Fig 1.1: Molecular Structure of Salbutamol Sulphate.

IUPAC Name :4-[2-(tert-butylamino)-1-hydroxyethyl]-2-(hydroxymethyl)phenol;sulfuric acid

Molecular formula: C_{13} H_{21} NO_3 · ½H_2SO_4

Molecular weight: 337.39 g/mol

Pharmacokinetic Data

Bioavailability: 50%

Protein binding: 10%

Metabolism: Hepatic

Excretion: 80% Renal, 20% Faecel

Ambroxol Hydrochloride

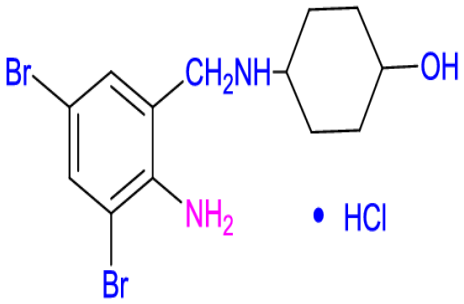


Fig 1.2: Molecular Structure of Ambroxol Hydrochloride.

IUPAC Name:- 4-[(2-amino-3,5-dibromophenyl)methylamino] cyclohexan-1-ol;hydrochloride

Molecular formula: C_{13} H_{19} Br_2ClN_2O

Molecular weight: 378.10 g/mol

Pharmacokinetic Data

Bioavailability: 70-80%

Protein binding: 90%

Metabolism: Hepatic

Excretion: 90% Renal, 10% Faecel

REVIEW OF LITERATURE:

1. Kumar et al., 2021 developed a simple RP-HPLC method for simultaneous estimation of salbutamol sulphate and ambroxol hydrochloride in oral liquid dosage form. The separation was achieved using a C18 column with a suitable mobile phase of buffer and organic solvent. The method showed good linearity, precision, and accuracy as per ICH guidelines. Recovery studies confirmed reliability with values close to 100%. The developed method was rapid and suitable for routine quality control analysis. It demonstrated robustness under small variations in analytical conditions and proved effective for pharmaceutical formulations.

2. SriKalyani et al., 2013 developed an RP-HPLC PDA method for simultaneous estimation of salbutamol and ambroxol. A Phenomenex C18 column and ammonium acetate-acetonitrile mobile phase were used. Detection was carried out at 227 nm. The method showed high specificity and resolution with acceptable retention times. Validation parameters such as linearity, precision, accuracy, and robustness were within acceptable limits. The method proved efficient for bulk drugs and formulations. It is particularly useful in pharmaceutical industries for routine analysis and stability studies due to its reproducibility and sensitivity.

EXPERIMENTAL

CHEMICALS AND REAGENTS

Table: 1- List of Chemicals and reagents.

S.NO.	NAME	MANUFACTURER	GRADE
1.	Salbutamol Sulphate and Ambroxol Hydrochloride working standard	Janaxa Pharmaceuticals	-
2.	Salbutamol Sulphate and Ambroxol Hydrochloride	Janaxa Pharmaceuticals	-
3.	Dummy pellets 16 # 20	Jackson	-
4.	Disodium hydrogen orthophosphate	Merck	GR
5.	Ortho phosphoric acid	Merck	GR
6.	Acetontrile	Merck	HPLC
7.	0.45 µm Nylon filter	Axivia	S0761009

EQUIPMENT/INSTRUMENT DETAILS

Table: 2- List of Equipment/Instrument details.

S.NO.	INSTRUMENT NAME	MODEL
1.	HPLC system	Agilent 1220 Infinity LC(G4288C)
2.	Analytical balance	Shimadzu
3.	pH Meter	Thermo electron corporation orion 2 star
4.	Sonicator	Ultrasonic cleaner power sonic 420

All remaining chemicals are of the highest grade available commercially unless otherwise specified.

METHOD DEVELOPMENT

Chromatographic Conditions (Optimized)

Parameter	Condition
Column	C18 column (250 mm × 4.6 mm, 5 µm)
Mobile Phase	0.02 M KH_2PO_4buffer : Methanol (70:30 v/v)
pH	3.0 (adjusted with OPA)
Flow Rate	1.0 mL/min
Detection Wavelength	246 nm
Injection Volume	20 µL
Column Temperature	30°C
Run Time	10–12 min

Preparation of Solutions

(A) Preparation of Mobile Phase

1. Prepare 0.02 M phosphate buffer.
2. Adjust pH to 3.0 using orthophosphoric acid.
3. Mix buffer and methanol in 70:30 ratio.
4. Filter through 0.45 µm membrane.
5. Sonicate to degas.

(B) Preparation of Standard Stock Solution

1. Accurately weigh:

- Salbutamol Sulphate (10 mg)
- Ambroxol Hydrochloride (10 mg)

2. Transfer to 100 mL volumetric flask.
3. Add mobile phase.
4. Sonicate for 10 minutes.

5. Make volume up to mark.

Further dilute to obtain working concentrations.

(C) Preparation of Sample Solution

1. Weigh 20 ml.
2. Calculate average weight.
3. Weigh quantity equivalent to label claim.
4. Transfer to 100 mL volumetric flask.
5. Add mobile phase.
6. Sonicate for 20 minutes.
7. Filter through 0.45 µm filter.
8. Dilute appropriately.

Method Development Strategy

Step 1: Wavelength Selection

- Scan individual drugs in UV (200–400 nm).
- Select common wavelength (246 nm gives good absorbance for all three).

Step 2: Mobile Phase Optimization

- Trials with:
- Water: Methanol
- Buffer: Methanol
- Buffer: Acetonitrile
- Best peak shape obtained with phosphate buffer (pH 3.0) and methanol.

Step 3: pH Optimization

- Tested pH 2.5–4.5.
- Best resolution and symmetry at pH 3.0.

Step 4: Flow Rate Optimization

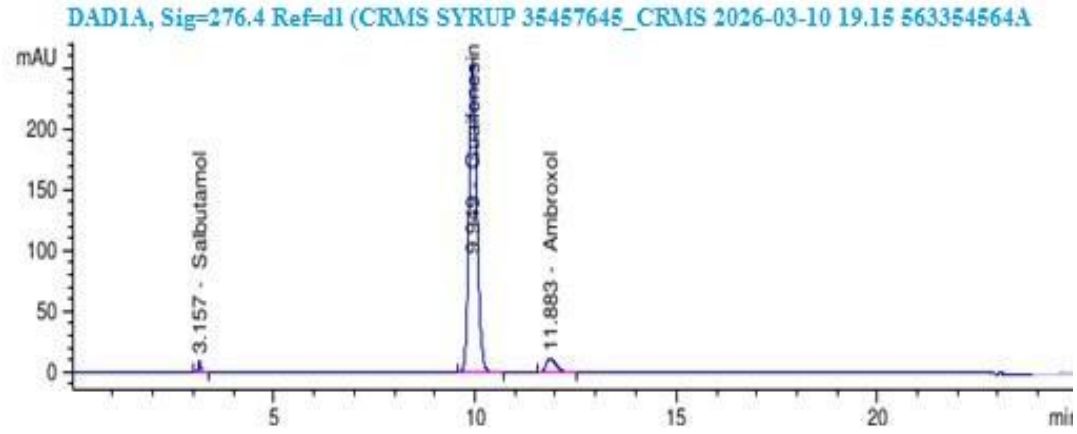
- 0.8–1.2 mL/min tested.
- 1.0 mL/min gave proper separation and acceptable retention time.

System Suitability Parameters

Before analysis, evaluate:

- Retention time

- Theoretical plates (N > 2000)
- Tailing factor (< 2)
- Resolution (> 2 between peaks)
- %RSD of peak area (< 2%)



Standard chromatogram for Salbutamol Sulphate and Ambroxol Hydrochloride

Table: Linearity data of Salbutamol Sulphate.

S.No.	Concentration (µg/mL)	Peak area	
1	5.00	1784.443	Slope =3706 C.C = 0.99 (≈1.0)
2	7.05	2676.681	
3	10	3520.368	
4	12.5	4422.826	
5	15	5267.516	

Table: Linearity data of Ambroxol Hydrochloride.

S.No.	Concentration (µg/mL)	Peak area	
1	75	110.443	Slope =1434 C.C = 0.99 (≈1.0)
2	112.5	166.149	
3	150	220.646	
4	187.5	272.420	
5	225	326.137	

Table: Regression characteristics of the linearity plot of Salbutamol Sulphate and Abroxol Hydrochloride.

Parameters	Salbutamol Sulphate	Ambroxol Hydrochloride
Correlation Coefficient	0.99 (≈1.0)	0.99 (≈1.0)
Regression Equation	y = 3.706x	y = 1.434x

Theoretical plates	4124	5888
Tailing	1.622	1.180

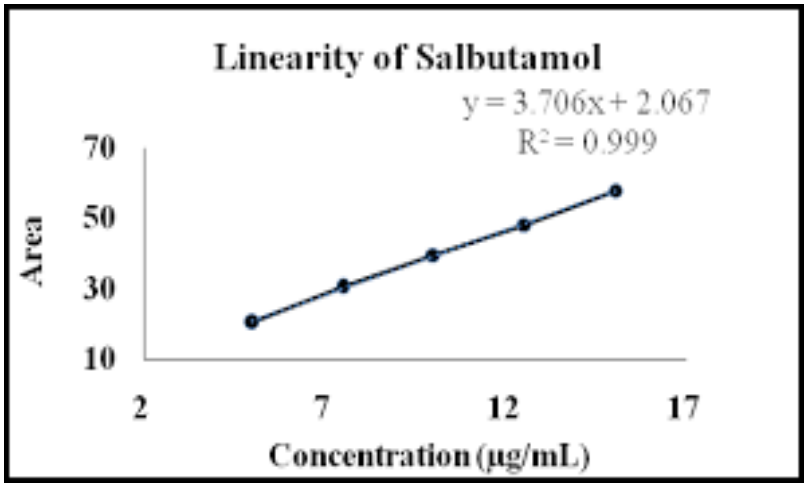


Fig.: Linearity Curve for Salbutamol Sulphate.

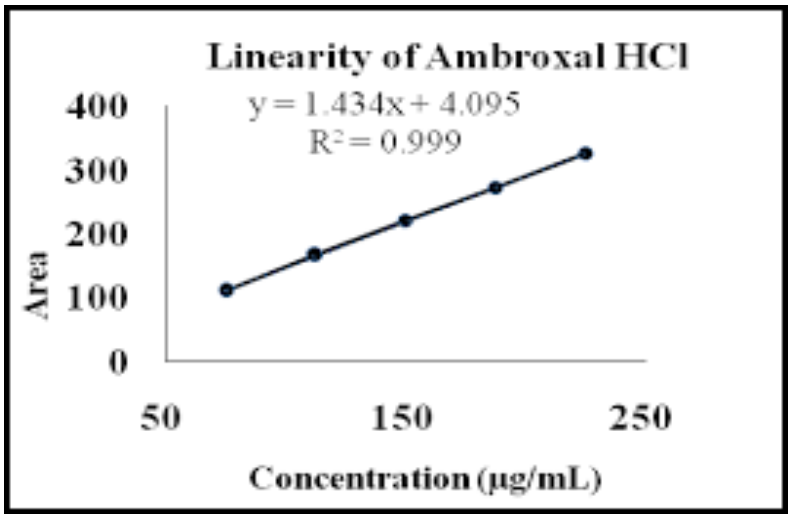


Fig.: Linearity Curve for Abroxol Hydrochloride.

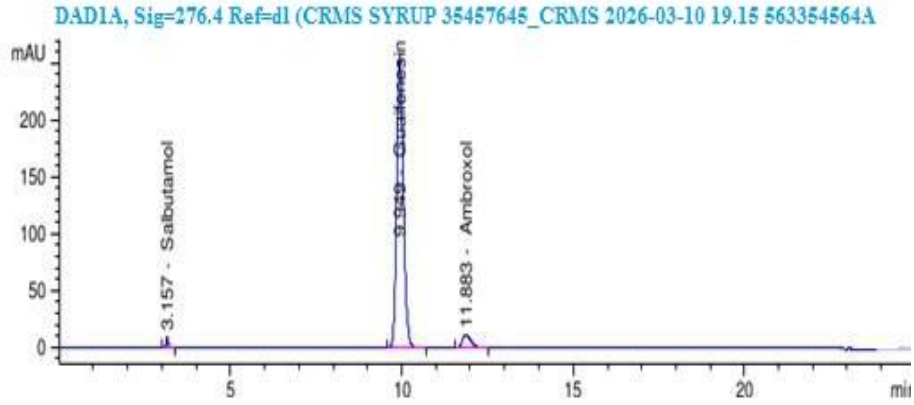


Fig.: Overlay chromatogram of Linearity for Salbutamol Sulphate and Abroxol Hydrochloride.

Table: Ruggedness of Salbutamol Sulphate

Injection No.	Peak Area
1	1742362
2	1740123
3	1739472
4	1720912
5	1701634
6	1692345
7	1681204
Mean	1716864.5714
SD	23370.9432
%RSD	0.62878

Table: Ruggedness of Abroxol Hydrochloride.

Injection No.	Peak Area
1	1197213
2	1196234
3	1183723
4	1173210
5	1163846
6	1153012
7	1140371
Mean	1172515.571
SD	19955.0915
%RSD	0.32328

CONCLUSION

Analytical Method Development and Validation for the Determination of Salbutamol Sulphate and Abroxol Hydrochloride in Tablet Dosage Form Using Rp HPLC Method was done. First it is discussed about drug of Salbutamol Sulphate and Abroxol Hydrochloride, second the materials and methods used in this work, the method development and the methodology of the validation parameters using HPLC, then third the results of system suitability, specificity, linearity, accuracy, precision, repeatability, intermediate precision and robustness.

The application of this method in routine analysis can be justified since easy sample preparation steps are involved and simple reagents, solvents were used experimentally. The method was validated as per ICH guidelines which demonstrated that the procedure is suitable for the intended purpose as it is linear, accurate, precise, rugged, robust, suitable and specific. It shows that the developed HPLC method could be conveniently adopted for the

routine quality control analysis of Salbutamol Sulphate and Abroxol Hydrochloride form its pharmaceutical formulation and bulk drug.

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