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A REVIEW ON CHROMATOGRAPHIC METHODS FOR THE SIMULTANEOUS ESTIMATION OF BROMHEXINE HYDROCHLORIDE AND SALBUTAMOL SULPHATE

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ABSTRACT

Salbutamol Sulphate and bromhexine hydrochloride as components of a multi-ingredient formulation is useful in asthma therapy. This article reviews the Chromatographic methods for simultaneous determination of bromhexine and salbutamol in pharmaceutical samples. The most commonly adopted methods for the determination of bromhexine and salbutamol are RP- HPLC. Recent preferences in the simultaneous estimation of bromhexine and salbutamol proves primacy of RP- HPLC and confirms a general trend of moving towards more sensitive methods having higher resolution potential, consuming small quantities of samples and reagents and requiring less time for analysis.

KEYWORDS

Salbutamol sulphate, Bromhexine hydrochloride, RP-HPLC and HPLC.

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INTRODUCTON

Bromhexine hydrochloride is chemically 2-Amino-3, 5-dibromo-N-cyclohexyl-N-methylbenzylamine hydrochloride is a mucolytic agent used in the treatment of respiratory disorders associated with viscid or excessive mucus[1]. It helps to relieve respiratory difficulties by dissolving various chemical bonds within secretions, which in turn can lower the viscosity by altering the mucin containing components[2]. It works through decreasing the amount of respiratory tract fluid and reducing its viscosity by activating enzymes that hydrolyze mycopolysaccharides. Bromhexine is used for respiratory infections, such as cold and influenza[3].

Bromhexine has been determined quantitatively by different methods such as Spectrophotometry, HPLC, Colorimetry, TLC, Flow injection spectrophotometry and Electrophoresis[4]. The drug is official in IP and BP.

Salbutamol is chemically 2-(hydroxymethyl) 4-[1-hydroxy- 2-(tert-butylamino) ethyl] phenol. It is a short-acting β2-adrenergic receptor agonist used for the relief of bronchospasm in conditions such as asthma and COPD. It is usually given by the inhaled route for direct effect on bronchial smooth muscle. Selective β2-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. Binding of albuterol to beta (2)-receptors in the lungs results in relaxation of bronchial smooth muscle[5]. Activation of the β-2 adreno-receptors opens ATPase channels and drives potassium from the extra cellular to the intracellular space. This both decreases extracellular hyperkalaemia and increases intracellular potassium, so decreasing the chance of arrhythmia[6]. Salbutamol Sulphate in pharmaceuticals has been assayed using visible spectrophotometric methods based on reactions such as redox, reducing and then chelating, oxidative coupling, diazotization and coupling, nitrosation, nitration followed by Meisenheiner complex formation and charge-transfer complex formation. A number of analytical methods exist for the determination of Salbutamol in biological fluids, including reversed phase high- performance liquid chromatography equipped with ultraviolet, fluorescent detection, electrophoresis, amperometry, thin layer chromatography, cation exchange, direct conductivity, gamma radiation and liquid chromatography mass spectrometric detection[7]. Both the drugs are official in I.P. and B.P. Literature survey reveals that there are some spectrophotometric methods for the individual determination of Salbutamol and bromhexine and HPLC methods for the simultaneous determination of Salbutamol and Bromhexine. But there is no HPTLC method available for the simultaneous determination of Salbutamol and Bromhexine[8].

Chromatographic Methods

This review gives an account on the different Chromatographic methods for the simultaneous estimation of bromhexine and salbutamol from different journals.

Chromatography is a versatile method of separating many different kind of chemical mixtures. HPLC is a chromatographic system that can separate a mixture of mixes and is utilized as a part of natural chemistry and scientific science to distinguish measure and refine the individual segments of the mixture[9]. It depends on pumps to pass a pressurized liquid dissolvable containing the example mixture through a segment loaded with a strong adsorbent material. Reversed phase HPLC (RP-HPLC) has a non-polar stationary phase and a watery, tolerably polar mobile phase. One basic stationary phase is silica which has been surface-adjusted with RMe_2SiCl. Salbutamol sulphate and bromhexine hydrochloride have been simultaneously determined by HPLC methods.

Summary of chromatographic methods for the Simultaneous estimation of Bromhexine Hydrochloride and Salbutamol Sulphate is given in Table No.1.

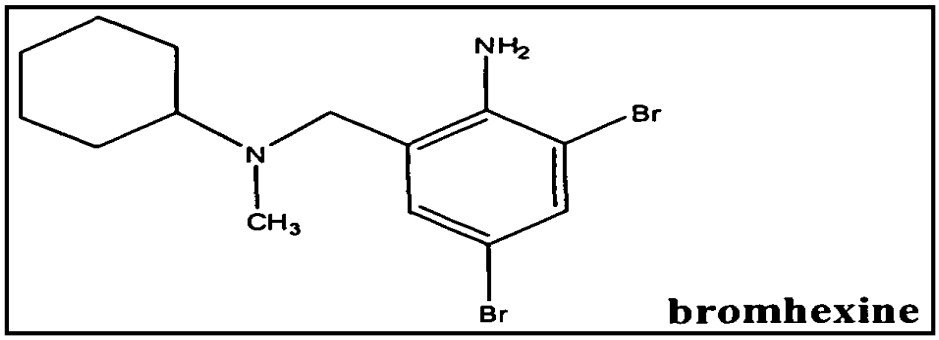
Various HPLC methods are reported for the determination of the Bromhexine Hydrochloride and Salbutamol Sulphate or combination with other drugs in various marketed formulation. The stationary phase commonly used is C_{18} column and mobile phase is commonly used is acetonitrile and phosphate buffer and methanol, its proportion varies with condition of method and range of pH is 3 to 4. The commonly used wavelength for detection is in the range of 220-270 nm. The flow rate is mostly 1ml/min. All this method are found to be accurate, linear and precise. In the first method the resolution between the two peaks was 1.85. The obtained results confirmed that the method is highly suitable for its intended purpose of separation of salbutamol sulphate and bromhexine hydrochloride and its simultaneous determination in tablet formulations. In the second method the reproducibility, repeatability and accuracy of the proposed method

were found to be satisfactory which is evidenced by low values of standard deviation and percent relative standard deviation (0.226 and 0.66 for BH and SS respectively). Thin Layer Chromatographic method was found to be simple, rapid, economical, selective and reliable. It is helpful without the use of much complex instruments and therefore useful for routine analysis of ternary mixture of salbutamol sulphate, bromhexine hydrochloride and etofylline. The fourth method was found to be the method satisfied the International Committee on Harmonization acceptance criteria for linearity, sensitivity, precision, accuracy, and robustness.

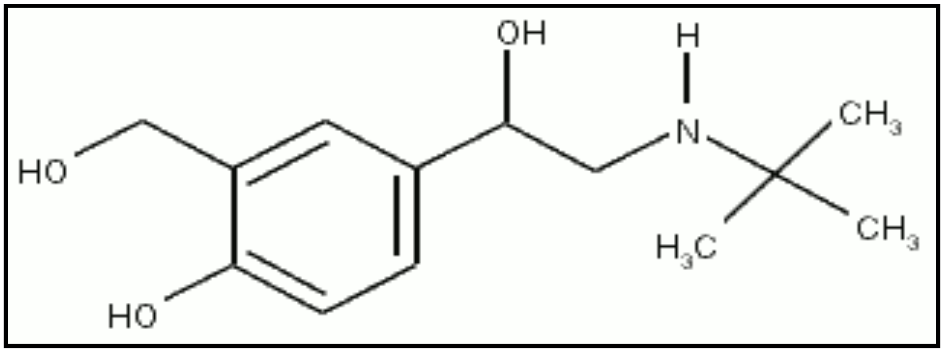
The developed liquid chromatographic method was applied for the analysis of nine commercial samples. The fifth method shows good sensitivity for all analytes with excellent separation and optimum resolution between the two analytes. In the sixth method methanol- water mobile phase and hibar HPLC column have been used with good resolution between analyte is obtained.

Table No.1: Chromatographic methods for the simultaneous estimation of salbutamol sulphate and Bromhexin hydrochloride

S.No	Title	Method	Mobile Phase	Stationary Phase	Wavelength (nm)
1	Simultaneous determination of bromhexine and salbutamol in tablets by reverse phase HPLC method[10]	RP-HPLC	Acetonitrile: Methanol: Phosphate buffer (60:20:20) v/v	SS Wakosil-II C_{18}	224nm
2	Simultaneous determination of bromhexine hydrochloride and salbutamol sulphate in pharmaceutical dosage by reverse phase HPLC method[11]	RP-HPLC	Acetonitrile: Methanol (65:35%v/v)	Zorbax Eclipse C_{18}	225 nm
3	Thin layer Chromatography method for the determination of Ternary Mixture containing Salbutamol sulphate, Bromhexine hydrochloride and Etofylline[12]	TLC	Methanol: n-Hexane (2:1)	TLC plates precoated with silica gel 60	254nm
4	A Versatile HPLC Method for the Simultaneous Determination of Bromhexine, Guaifenesin, Ambroxol, Salbutamol/Terbutaline, Pseudoephedrine, Triprolidine, and Chlorpheniramine Maleate in Cough–Cold Syrups[13]	HPLC	Acetonitrile: Sodium hexane sulfonate: Ammonium acetate: Water (35:4:10:51)	NX C_{18}	254 nm
5	Development and Validation of HPLC method for the Simultaneous estimation of Salbutamol sulphate and Ipratropium Inhalation Dosage form[14]	HPLC	Phosphate buffer: Methanol (40:60v/v)	Symmetry C_{18}	226nm
6	A New Rp-Hplc Method Development For Simultaneous Estimation of Salbutamol Sulphate, Theophylline And Furosemide[15].	RP- HPLC	Methanol: Water (50:50v/v)	Hibar 250*4.6mm HPLC column	274 nm



Bromhexine HCl



Salbutamol

CONCLUSION

Presented systematic review discusses about various HPLC methods for the simultaneous determination of bromhexine and salbutamol in pharmaceutical samples. New trends and advances for simultaneous estimation of bromhexine and salbutamol are based on using high-pressure liquid chromatography which is widely available, flexible and method could be automated; there are different column filling, different solvents with different polarity as mobile phases and different detection modes. The faster time, high sensitivity; specificity and better separation efficiency enable RP- HPLC are to be used frequently for the determination of Bromhexine Hydrochloride and salbutamol in comparison with the other methods like HPLC and TLC. The RP-HPLC strategy is precise, exact, particular, reproducible and delicate. The system has a few focal points, including fast investigation, a straight forward portable stage, basic specimen planning, and enhanced affectability. This makes the strategy suitable for routine examination in quality-control labs.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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