



## A REVIEW ON BROMHEXINE HYDROCHLORIDE AND THE DIFFERENT ANALYTICAL METHODS USED FOR ITS DETERMINATION

**KELVIN BUCKTOWAR**

*Department of Pharmaceutics, T. John College of Pharmacy, Gottigere, Bannerghatta Road, Bangalore, Karnataka, India*

### ABSTRACT

Bromhexine hydrochloride is a mucolytic agent (expectorant) used in the treatment of respiratory disorders associated with viscid or excessive mucus. The active ingredient Bromhexine hydrochloride is an expectorant which works by loosening mucus in the chest, making it easier to cough up secretions. It is also used to treat productive, chesty coughs. It is chemically named 2-amino-3,5-dibromobenzyl (cyclohexyl) methylamine hydrochloride. According to IUPAC it is 2,4-dibromo-6-[[cyclohexyl (methyl) amino] methyl] aniline; hydrochloride. Bromhexine hydrochloride is a synthetic substance obtained as a synthetic analog of vasicine, a substance found in plants called *Adhoda vasica*. The mechanism of action is based on phlegm degradation, thereby easing coughs. The different analytical methods used to quantify the drug as a single active pharmaceutical ingredient includes flow injection analysis with ion selective electrodes, inductively coupled plasma mass spectrometry, electrokinetic chromatography, electrochemical oxidation at the glassy carbon electrode, liquid chromatography, liquid gas chromatography, GC with mass detection, and Voltammetry. The drug has also been quantified in its combined formulations using HPLC, direct and derivative UV spectrophotometry.

**KEYWORDS:** *Bromhexine hydrochloride, mucolytic, respiratory, expectorant, analysis*



Corresponding Author



**KELVIN BUCKTOWAR**

Department of Pharmaceutics, T. John College of Pharmacy, Gottigere, Bannerghatta Road, Bangalore, Karnataka, India

Received on: 17-06-2017

Revised and Accepted on: 21-08-2017

DOI: <http://dx.doi.org/10.22376/ijpbs.2017.8.4.p43-49>

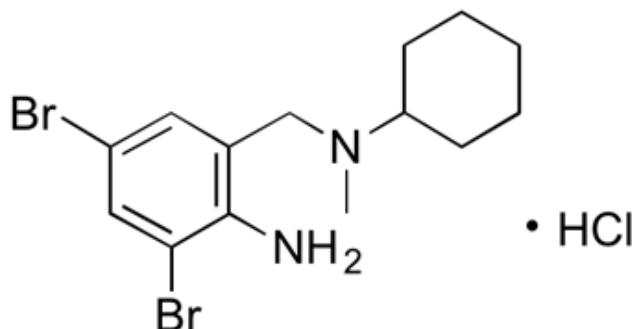


[Creative commons version 4.0](https://creativecommons.org/licenses/by-nc-sa/4.0/)

## INTRODUCTION

Bromhexine hydrochloride is a mucolytic agent rendering the sputum less viscous thereby facilitating easy expulsion of it from the respiratory tract.<sup>1</sup>The drug is official in IP and BP.

## STRUCTURAL FORMULA<sup>2</sup>



Molecular formula : <sup>2</sup> C<sub>14</sub>H<sub>20</sub>Br<sub>2</sub>N<sub>2</sub>.HCl  
 Molecular weight : 412.594 g/mol  
 Monoisotopic mass: 409.976 g/mol  
 Exact mass : 411.974 g/mol  
 IUPAC name : 2,4-dibromo-6-[[cyclohexyl(methyl)amino]methyl]aniline;hydrochloride  
 Chemical name : 2-amino-3,5-dibromobenzyl(cyclohexyl)methylamine hydrochloride

## SYNONYMS

1. Benzenemethanamine, 2-amino-3,5-dibromo-N-cyclohexyl-N-methyl-, monohydrochloride
2. Toluene-a,2-diamine,3,5-dibromo-Na-cyclohexyl-Na-methyl-,monohydrochloride
3. 2-Amino-3,5-dibromo-N-cyclohexyl-N-methylbenzylamine monohydrochloride
4. Bromhexine chloride
5. Bromhexine monohydrochloride
6. Cyclohexylmethyl(2-amino-3,5-dibromobenzyl)ammonium chloride
7. N-Cyclohexyl-N-methyl-(2-amino-3,5-dibromobenzyl)ammonium chloride
8. N-Cyclohexyl-N-methyl-N-(2-amino-3,5-dibromobenzyl)ammonium chloride
9. Na-Cyclohexyl-Na-methyl-3,5-dibromotoluene-a,2-diaminehydrochloride

Category : Mucolytics

Dose : 8-16 mg (Tablets)

Description: White crystalline powder

## SOLUBILITY

Slightly soluble in alcohol and methylene chloride,

Sparingly soluble in water.

Melting point : 240-244 °C

Boiling point : 441.5 °C at 760 mmHg

Flash point : 220.8 °C

## PHARMACOLOGICAL ACTION

Bromhexine hydrochloride is a mucolytic expectorant which exhibits its action by increasing bronchial secretions and reducing their viscosity. In addition, it produces an increase in immunoglobulin levels in airway secretions. This agent was recently recommended as a new therapy for pathological states, such as alcoholic chronic pancreatitis where there is an increased viscosity of the pancreatic juice. Bromhexine

hydrochloride may be administered in combination with antimicrobial agents in the treatment of respiratory infections, due to its capacity to disrupt the mucopolysaccharides of bronchial secretion and as a result in enhancing the bronchial penetration of antimicrobial drugs.<sup>3</sup>

## PHARMACOKINETICS

On oral administration, Bromhexine hydrochloride is rapidly absorbed from the gastrointestinal tract and undergoes extensive first-pass metabolism in the liver. Its oral bioavailability is stated to be only about 20%. It is widely distributed to body tissues and is highly bound to plasma proteins. About 85-90% of a dose is excreted in the urine mainly as metabolites. It has a terminal elimination half life of up to about 6-8 hours. Bromhexine crosses the blood brain barrier and small amounts cross the placenta.<sup>4</sup>

## MECHANISM OF ACTION

It is secretolytic, increasing the production of serous mucus in the respiratory tract and makes the phlegm thinner and less viscous. This contributes to a secretomotoric effect by helping the cilia transport the phlegm out of the lungs. Bromhexine hydrochloride thins and loosens mucus to help clear stubborn chest congestion. For this reason it is often added to cough syrups.<sup>5</sup>

## USES

Bromhexine Hydrochloride is used in conditions where breathing is difficult because there are a lot of secretions (also referred to as mucus) in your air passages.<sup>6</sup> Such conditions include

- common cold
- flu
- infections of the respiratory tract
- Relieves chesty coughs and breathing difficulties due to excess mucus in cold, flu and respiratory tract infections

## USES OF BROMHEXINE HYDROCHLORIDE DURING PREGNANCY AND BREASTFEEDING

Bromhexine hydrochloride should be used during pregnancy only if the benefit to the mother outweighs

the risk to the foetus. Animal studies have shown adverse effects of Bromhexine inhaler, syrup and tablets on the unborn baby. It should not be used during the first three months of pregnancy unless recommended by a doctor. Bromhexine hydrochloride passes into breast milk. Avoid breastfeeding while using this medicine.<sup>7</sup>

### CONTRAINDICATIONS

- Galactose Intolerance: Do not take Bromhexine hydrochloride if you have galactose intolerance. Bromhexine hydrochloride tablets contain lactose as expensive.
- Antibiotics: Bromhexine hydrochloride may increase the amount of antibiotic penetration. Antibiotics are medicines used to treat infections.
- Pregnancy: The use of Bromhexine hydrochloride tablets during the first trimester is not recommended.
- Breastfeeding mothers: It is not recommended that Bromhexine hydrochloride tablets to be taken by women who are breastfeeding.
- Stevens-Johnson Syndrome: There have been very rare reports of severe skin reactions of Stevens Johnson Syndrome. Stevens-Johnson Syndrome (SJS) is a type of severe skin reaction. Together with toxic epidermal necrolysis (TEN) it forms a spectrum of disease, with SJS is less severe. Early symptoms include fever and flu-like symptoms. A few days later the skin begins to blister and peel forming painful raw areas.
- Lyell's syndrome: There have been very rare reports of severe skin reactions of Lyell's syndrome. Lyell's syndrome, or toxic epidermal necrolysis is a rare, potentially life-threatening mucocutaneous disease, usually provoked by the administration of a drug and characterised by acute necrosis of the epidermis.<sup>8</sup>

### SIDE EFFECTS

- Nausea
- Diarrhoea
- Vomiting
- Stomach Pain
- Mild stomach problems
- Headache
- Dizziness
- Sweating
- Temporary rise in some liver enzyme levels
- Skin rashes, including pinkish, itchy swellings (also called hives)
- Difficulty in breathing
- Swelling of the face, lips, mouth, tongue, or throat, which may cause difficulty swallowing or breathing

### LABEL INDICATIONS

The required label indication is 'Helps clear chest congestion'

### SIDE EFFECTS

Gastrointestinal side effects may occur occasionally with Bromhexine hydrochloride and a transient rise in serum aminotransferase values has been reported.

### PRECAUTIONS

Bromhexine hydrochloride should be avoided in patients allergic to this medicine.<sup>9</sup>

### SPECIFICATIONS

Several animal studies of Bromhexine Hydrochloride that has been carried out and their respective specifications are as follows (Table 1)

Table 1  
Specifications of Bromhexine Hydrochloride

| Organism | Test Type | Route           | Reported Dose (Normalized Dose) | Effect  |
|----------|-----------|-----------------|---------------------------------|---|
| Mouse    | LD50      | Intraperitoneal | 2210mg/kg <sup>10</sup>         | Cardiac: other changes  |
| Mouse    | LD50      | Intravenous     | 44mg/kg                         | Behavioural: tremor   |
| Mouse    | LD50      | Oral            | 3gm/kg <sup>11</sup>            | Behavioural: tremor   |
| Mouse    | LD50      | Subcutaneous    | > 14gm/kg <sup>12</sup>         | Behavioural: tremor   |
| Rabbit   | LD50      | Oral            | 10gm/kg <sup>13</sup>           | Cardiac: other changes<br>Lungs, thorax or respiration: respiratory depression                  |
| Rat      | LD50      | Intraperitoneal | 1680mg/kg <sup>14</sup>         | Sense organs and special senses: lacrimation: eye<br>Behavioural: tremor<br>Behavioural: ataxia |
| Rat      | LD50      | Oral            | 6g/kg <sup>15</sup>             | Sense organs and special senses: lacrimation: eye<br>Behavioural: tremor<br>Behavioural: ataxia |
| Rat      | LD50      | Subcutaneous    | > 14g/kg                        |   |

### DOSAGE

Bromhexine Hydrochloride is available in various formulations such as tablets, inhalation, syrup. The various required dosages along with their respective doses are as shown (Table 2)

**Table 2**  
**Dosages of Bromhexine Hydrochloride**

|   |   |
|---|---|
| <b>Bromhexine 2 mg / ml syrup</b> <sup>16</sup> |   |
| Patients above the age of 14                    | 4-8 ml every 8 hours ( <i>three times a day</i> )           |
| Children aged 6-14 years                        | 4 ml every 8 hours ( <i>three times a day</i> )             |
| Children aged 2-6 years                         | 2.5 ml every 8 hours ( <i>three times a day</i> )           |
| <b>Bromhexine 4 mg / 5 ml syrup</b>             |   |
| Patients above the age of 14                    | 10ml-20ml three times a day ( <i>every 8 hours</i> )        |
| Children aged 6 -14 years                       | 10 ml three times a day ( <i>every 8 hours</i> )            |
| Children aged 2 - 6 years                       | 5 ml three times a day ( <i>every 8 hours</i> )             |
| <b>Bromhexine inhalation</b>                    |   |
| Adults  | 4 ml every 12 hours ( <i>twice a day</i> )                  |
| Patients above the age of 14                    | 2 ml to every 12 hours ( <i>twice a day</i> )               |
| Children aged 6-14 years                        | 1 ml every 12 hours ( <i>twice a day</i> )                  |
| Children aged 2-6 years                         | 10 drops, every 12 hours ( <i>twice a day</i> )             |
| <b>Bromhexine tablets</b>                       |   |
| Patients above the age of 14                    | 8-16 mg, three times a day ( <i>every 8 hours</i> )         |
| Children aged 6 - 14 years                      | Bromhexine 8 mg, three times a day ( <i>every 8 hours</i> ) |

## BRAND NAMES

Bromhexine Hydrochloride is available is different brand names as shown in Table 3

**Table 3**  
**Brand Names of Bromhexine Hydrochloride**

| Constituents                     | Brand Name          | Dosage Forms  | Company                           |
|----------------------------------|---------------------|---------------|-----------------------------------|
| Bromhexine Hydrochloride 4mg/5ml | Bromhexine Sopharma | Syrup         | Sopharma PLC                      |
| Bromhexine Hydrochloride 4mg/5ml | Bronchotussine      | Syrup         | Adelco Chromatourgia              |
| Bromhexine Hydrochloride 4mg/5ml | Bisolvon            | Oral solution | Boehringer Ingelheim              |
| Bromhexine Hydrochloride 4mg/5ml | Bisolvon            | Oral solution | Ecosse Ltd                        |
| Bromhexine Hydrochloride 4mg/5ml | Bisolvon            | Oral solution | NeoFarma                          |
| Bromhexine Hydrochloride BP 8mg  | Flecoxin 8 Tablets  | Tablet        | Remedica Ltd.                     |
| Bromhexine                       | Theosal PD          | Syrup         | Monichem Healthcare Pvt Ltd       |
| Bromhexine                       | Bromex              | Syrup         | Hygeia Pharmaceuticals            |
| Bromhexine 4mg                   | Bromex              | Syrup         | Cipla Ltd                         |
| Bromhexine Hydrochloride 8mg     | Bromex              | Tablet        | Cipla Ltd                         |
| Bromhexine                       | Mucospel            | Syrup         | S R Pharmaceuticals               |
| Bromhexine                       | Brohex              | Syrup         | Biochem Pharmaceutical Industries |
| Bromhexine                       | Ventex PD           | Syrup         | Cure Quick Pharmaceuticals        |
| Bromhexine Hydrochloride 8mg     | Bromhexine tablet   | Tablet        | Ipca Laboratories Ltd             |
| Bromhexine 4mg                   | Bromhexine elixir   | Syrup         | Ipca Laboratories Ltd             |
| Bromhexine                       | Bisolvon            | Oral solution | Zydus Cadila                      |
| Bromhexine Hydrochloride 8mg     | Bisolvon            | Tablet        | Zydus Cadila                      |
| Bromhexine 4mg                   | Pelkof              | Syrup         | PAX HEALTHCARE                    |

## ANALYTICAL METHODS

Various analytical methods are present to determine Bromhexine hydrochloride. These methods are Compendial Methods (Table 4), Chromatographic Methods (Table 5), UV Spectroscopic Methods (Table 6)

## COMPENDIAL METHODS

**Table 4**  
**Compendial Methods for the analysis of Bromhexine Hydrochloride**

| PHARMACOPOEIA | METHOD   |
|---------------|--|
| IP            | <b>Potentiometry</b><br>Weigh accurately about 0.3g, dissolve in 70 ml of ethanol(95%), add 1 ml of 0.1M hydrochloric acid and titrate with 0.1 M sodium hydroxide,<br>Determine the end point potentiometrically. Record the volume added between the two inflections. <sup>17</sup><br>1 ml of 0.1 M sodium hydroxide is equivalent to 0.04126 g of<br>$C_{14}H_{21}Br_2ClN_2$ |
| BP            | <b>Potentiometric Titration</b><br>Dissolve 0.300 g in 70 ml of ethanol(95%) and add 1 ml of 0.1 M hydrochloric acid. Carry out a potentiometric titration using 0.1M sodium hydroxide. Read the volume added between the two points of inflexion. <sup>18</sup><br>1 ml of 0.1 M sodium hydroxide is equivalent to 41.26 mg of<br>$C_{14}H_{21}Br_2ClN_2$                       |
| EP            | <b>Potentiometric Titration</b><br>Dissolve 0.300 g in 70 ml of ethanol (95%) and add 1 ml of 0.1 M hydrochloric acid. Carry out a potentiometric titration using 0.1M sodium hydroxide. Read the volume between the 2 points of inflexion. <sup>19</sup><br>1 ml of 0.1 M sodium hydroxide is equivalent to 41.26 mg of<br>$C_{14}H_{21}Br_2ClN_2$                              |

**CHROMATOGRAPHIC METHODS**

**Table 5**  
**Chromatographic Methods for the analysis of Bromhexine Hydrochloride**

| Title   | Method                           | Mobile phase  | Stationary phase   | Wavelength (nm) |
|---|----------------------------------|---|--|-----------------|
| Bromhexine hydrochloride film content on High Performance Liquid Chromatography <sup>20</sup>                                     | HPLC                             | Acetonitrile 0.05 mol·L <sup>-1</sup> :Phosphate buffer (containing 0.2% triethylamine)(30:70)    | An Altima C18 Column (4.6 mm × 150 mm, 5 μm)                             | 249 nm          |
| Molecularly imprinted solid phase extraction for the selective determination of bromhexine in human serum and urine <sup>21</sup> | Solid phase Extraction with HPLC | 3 × 1 ml Methanol/Acetic Acid (10/1 v/v)  | Octadecylsilica column (55 mm × 4 mm, 3 μm particles)                    | 270 nm          |
| Estimation Of Bromhexine and Terbutaline In Bulk And Tablet Dosage Forms <sup>22</sup>  | HPLC                             | Phosphate buffer (0.05 M, pH 3): Acetonitrile (70:30 v/v)   | ODS C8 column (length 250 mm and internal diameter 4.6 mm)               | 270 nm          |
| Simultaneous Estimation of Amoxicillin Trihydrate and Bromhexine hydrochloride from Oily Suspension <sup>23</sup>                 | RP-HPLC                          | Methanol and Glacial Acetic Acid (50:50 v/v)  | ODS C18 (250 X 4.5mm ID)   | 254 nm          |
| Simultaneous determination of Terbutaline and Bromhexine in Combined Pharmaceutical Dosage Form <sup>24</sup>                     | RP-HPLC                          | Methanol: Acetonitrile: Ortho-Phosphoric acid in the ratio of 80:10:10 (v/v/v)                    | Inertsil ODS C-18 column 5μm column having 250 x 4.6mm internal diameter | 270 nm          |
| Simultaneous Determination of Bromhexine HCl and Baicalin in Chinese Compound Medicine <sup>25</sup>                              | RP-ion pair HPLC                 | Water/Acetonitrile/Phosphoric acid/Triethylamine (78/22/0.1/0.1 v/v/v/v)                          | C18 Column (250 x 4.6mm internal diameter, 5 μm)                         | 225 nm          |
| Simultaneous Determination of Salbutamol Sulphate and Bromhexine Hydrochloride in Tablets <sup>26</sup>                           | RP-HPLC                          | Acetonitrile, Methanol and Phosphate buffer, pH 4 in the ratio 60:20:20 v/v.                      | SS Wakosil-II C-18 column  | 224 nm          |
| TLC Densitometric Determination of Bromhexine Hydrochloride in Pharmaceuticals  | TLC Densitometric Method         | n-Butanol–Glacial Acetic Acid–Water (26:7.5:7.5)  | Pre-coated silica gel plates   | 325 nm          |
| Determination of Bromhexine Hydrochloride in Human Plasma   | HPTLC                            | a mixture of n-Butyl acetate: Methanol : GAA: Water(HPL grade) in the ratio of 5:2.5:2.5:1v/v/v/v | TLC plates precoated with silica gel 60 F254                             | 246             |

**UV SPECTROSCOPIC METHODS**

**Table 6**  
**UV Spectroscopic Methods for the analysis of Bromhexine Hydrochloride**

| Sl/No | Title   | Method                                    |
|-------|---|---|
| 1     | Bioequivalence study of bromhexine by liquid chromatography–electrospray ionization-mass spectrometry after oral administration of bromhexine hydrochloride tablets <sup>27</sup> | LC-MS                                     |
| 2     | Determination of Pseudoephedrine Hydrochloride and Bromhexine Hydrochloride in Pharmaceuticals <sup>28</sup>  | Gas Liquid Chromatography & Ion Pair HPLC |
| 3     | Simultaneous Determination of Bromhexine and Amoxicillin in Pharmaceutical Formulations <sup>29</sup>   | Capillary Electrophoresis                 |
| 4     | Bromhexine hydrochloride with morin as chemiluminescent reagent <sup>30</sup>   | Chemiluminescence                         |

## CONCLUSION

Bromhexine hydrochloride is a widely used mucolytic agent worldwide. It is a highly efficient drug and pharmacologically proven to render the sputum less viscous thereby facilitating its easy expulsion from the respiratory tract. Bromhexine hydrochloride has been discussed in all its aspects in this review. HPLC-HPTLC-UV methods were found to be the most widely used. Furthermore the analytical methods mentioned are time

saving, simple and do not require elaborate treatments associated with chromatographic methods. Without any doubt, there will be new types of Bromhexine hydrochloride formulations and also newer techniques for its analysis.

## CONFLICT OF INTEREST

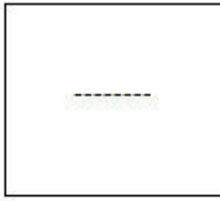
Conflict of interest declared none

## REFERENCES

1. Harikumar S, Sharma A. Development and evaluation of bromhexine hydrochloride floating microparticulates. *Asian J Pharm.* 2012;6(1):38.
2. Indian Pharmacopoeia 2007. Government of India, Ministry of Health and Family welfare. Controller of publications. New Delhi. 2007;(2) p 812
3. Jacoby C. Bromhexine Hydrochloride. 2011 Oct; 1–4. Available from: <http://www.healthguidance.org/entry/14925/1/Bromhexine-Hydrochloride.html>
4. Tsujimoto T, Tsuruzono T, Hoppo K, Matsumura Y, Yamao J, Fukui H. Effect of bromhexine hydrochloride therapy for alcoholic chronic pancreatitis. *Alcohol Clin Exp Res* 2005 Dec 1;29(s3).
5. Gubbi S, Jarag R. Liquisolid technique for enhancement of dissolution properties of bromhexine hydrochloride. *Res J Pharm Technol.* 2009;2(2):382–6.
6. Takeda H, Abe Ym Misawa M, Yanaura S, Kuroiwa Y. The role of vagal reflex in mechanism of secretagogic action of bromhexine. *jpn J Pharmacol.* 1984 Aug; 35(4) 445-50.
7. Pharmaceutical Society of Singapore, Reviewed by the Health Sciences Authority. Updated 29 June 2011. [http://www.hsa.gov.sg/content/dam/.../Updates/.../PIL\\_Ambroxol\\_29-6-2011.pdf](http://www.hsa.gov.sg/content/dam/.../Updates/.../PIL_Ambroxol_29-6-2011.pdf)
8. Jadhav NR, Paradkar AR, Shah GN. Adsorption studies of bromhexine hydrochloride on talc. *Res J Pharm Technol.* 2013;6(11):1247–50.
9. *Drugs in Japan* 1982; (6): p 737
10. Azodi-Deilami S, Abdouss M, Javanbakht M. The syntheses and characterization of molecularly imprinted polymers for the controlled release of bromhexine. *Appl Biochem Biotechnol.* 2011;164(2):133–47.
11. *Archives Internationales de Pharmacodynamie et de Therapie.* 1966; (163): p 284.
12. Prasuna Sundari P, Vijaya Shanthi V. A Review: Analytical Methods for Determination of Itraconazole in Pharmaceutical and Biological samples. 2013;1(1):21–4.
13. Cruz Oliva D, Torres Vélez K, Revilla Vázquez AL. Simultaneous determination of bromhexine and amoxicillin in pharmaceutical formulations by capillary electrophoresis. *Journal of the Mexican Chemical Society.* 2011 Jun;55(2):79-83.
14. Saritha P, Singh TC, Gyanakumari C. Spectrophotometric Determination of Isoxsuprine in Pure and Pharmaceutical Forms. *IOSR J Appl Chem.* 2015;8:2278–5736.
15. Rao SV, Rao IN, Reddy T, Sastry CS. Assay of bromhexine hydrochloride in pharmaceutical formulations by extraction spectrophotometry. *Indian J Chem Technol.* 2005;12(2):170–4.
16. John J Borg., Review of Ambroxol and Bromhexine containing medicines started. *Awtorita Dwar II-Medicini.* 2014;12(5):1-2
17. Jain V, Sharma MC. Validated RP-HPLC method for determining the levels of bromhexine HCl, chlorpheniramine maleate, dextromethorphan HBr and guaiphenesin in their pharmaceutical dosage forms. *J Taibah Univ Sci.* 2016 Jan 31;10(1):38–45.
18. Javanbakht M, Namjumanesh MH, Akbari-Adergani B. Molecularly imprinted solid-phase extraction for the selective determination of bromhexine in human serum and urine with high performance liquid chromatography. *Talanta.* 2009 Nov 15;80(1):133–8.
19. Kumar A, Nanda S. A validated high performance liquid chromatographic method for estimation of bromhexine and terbutaline in bulk and tablet dosage forms. *Pharm Methods* 2011 Oct 1;2(4):218-22.
20. LIU S, ZHAO L, LIU X, ZHOU F, JIANG S. Simultaneous Determination of Bromhexine HCl and Baicalin in Chinese Compound Medicine by a Reversed-Phase Ion-Pair HPLC. *J Food Drug Anal.* 2004 Dec 1;12(4):306-10.
21. Dharmesh M, Avinash N, Mehul K, Ketan D and Shital F. Development and validation of spectrophotometric method for simultaneous estimation of bromhexine hydrochloride and phenylephrine hydrochloride in their combined pharmaceutical dosage form by simultaneous equation method, *Inventi Rapid: Pharm Analysis & Quality Assurance.* 2013;1(1):21–4.
22. Zhang W, Feng F, Wang Y. Bioequivalence study of bromhexine by liquid chromatography–electrospray ionization–mass spectrometry after oral administration of bromhexine hydrochloride tablets. *J Pharm Biomed Anal.* 2008 Dec 1;48(4):1206-10.
23. Rao EV, Rao GR, Raghuveer S, Khadgpathi P. Gas-liquid chromatographic and ion-pair high-performance liquid chromatographic determination of pseudoephedrine hydrochloride and bromhexine hydrochloride in pharmaceuticals. *Analyst.* 1987;112(6):871-4.

24. Gupta AK, Kaskhedikar SG. Derivative spectrophotometric estimation of amoxicillin and bromhexine hydrochloride in tablets. *Asian J Chem.* 2003 Apr 1;15(2):977.
25. KP S, Sharma AK, Sahu LK. Simultaneous analysis of phenylpropanolamine, chlorpheniramine and bromhexine in syrups by derivative spectrophotometry. *Indian J Pharm Sci.* 2002;64(6):540.
26. Gangwal S, Trivedi P. Simultaneous determination of terbutaline sulphate, bromhexine hydrochloride and guaiphenesin in three-component tablet formulation by UV spectrophotometry. *Indian J Pharm Sci* 1999;61(2):128.
27. Song X, Wang X, Wang X, Ze D. Determination of aminophylline and bromhexine hydrochloride in dingchuan zhike tablets by UV spectrophotometry. *CHINA J Pharm Anal.* 1999;30:100-2.
28. J. Rose, *Advanced Physicochemical Experiments*, Pitman, 1<sup>st</sup> ed. London, UK, 1964. p. 54-68.
29. Likussar W, Boltz DF. Theory of continuous variations plots and a new method for spectrophotometric determination of extraction and formation constants. *Analytical Chemistry.* 1971 Aug 1;43(10):1265-72.
30. Ponnilaravasan I, Narendra CS, Asha P. Simultaneous estimation of ambroxol hydrochloride and loratadine in tablet dosage form by using UV spectrophotometric method. *Int J Pharma Bio Sci* 2011;2(2):338-44.

## Reviewers of this article



**Dr Ravi Shankar**

Pharmaceutics, UCSI University, Jalan Gading.



**Prof. Srawan Kumar G.Y**

Associate Professor, Nalanda Institute of Pharmaceutical Sciences, Sattenapalli, Guntur, Andrapradesh, India



**Prof. Dr. K. Suriaprabha**

Asst. Editor, International Journal of Pharma and Bio sciences.



**Prof. P. Muthuprasanna**

Managing Editor, International Journal of Pharma and Bio sciences.

**We sincerely thank the above reviewers for peer reviewing the manuscript**