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Review Article

Analytical Techniques for the Assay of Tulobuterol - A Review

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Abstract

Tulobuterol is a potent bronchodilator and chemically it is 1-(o-chloro phenyl)-2-tert-butyl amino ethanol alpha-((tert-butyl amino) methyl)-o-chloro benzyl alcohol. In comparison to other analogues Tulobuterol has a long acting effect. Various analytical techniques such as gas chromatography, high performance liquid chromatography, spectrophotometry, liquid chromatography-mass spectrometry etc. so far developed for the quantification of Tulobuterol in pharmaceutical formulations were reviewed and the significant parameters were highlighted.

Keywords: Tulobuterol; Syrup; BREMAX

Introduction

Tulobuterol ($C_{12}H_{18}ClNO$) is a bronchodilator and it is chemically known as 1-(o-chloro phenyl)-2-tert-butylaminoethanol alpha-((tert-butyl amino) methyl)-o-chloro benzyl alcohol. The molecular weight is 227.73 grams/mole and the pKa values are found to be 9.55 and 13.9. Tulobuterol (Figure 1) relaxes the airway muscles and makes breathing easier [1,2] and it is administered by oral, inhalation and as transdermal patch. Tulobuterol is available with brand name BREMAX as tablet (Labelled claim: 1 mg and 2 mg) and also as syrup from Abbott Laboratories (India).

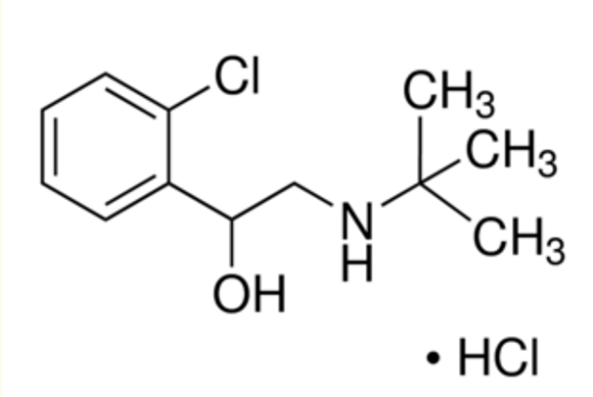

Figure 1: Chemical structure of Tulobuterol.

Ravindra Reddy., *et al*. developed a new UV spectrophotometric method in methanol [3] and an extractive spectrophotometric method using bromo cresol green reagent [4] for the assay of Tulobuterol in API and its pharmaceutical dosage forms where the λ_{max} was reported at 212 nm and 624 nm respectively. A wide range of linearity (25 - 125 µg/ml) was observed while using methanol whereas a narrow range was reported while performing the visible spectrophotometry using bromo cresol green reagent (0.1 - 0.8 µg/ml).

Kavita Parui and Snehalatha Boddu [5] developed a liquid chromatographic method for the determination of Tulobuterol in transdermal drug delivery system in which a mixture of acetonitrile and 0.02M Potassium dihydrogen phosphate buffer (60:40) was used as mobile phase after adjusting the pH to 3.0 with Ortho phosphoric acid and the linearity was observed as 25 - 75 µg/ml. LIU Zhimei., *et al.* [6] determined Tulobuterol in Tulobuterol transdermal patch by HPLC using a mixture of methanol and sodium heptane sulfonate solution as mobile phase (55:45) in which the aqueous phase was prepared by using pH 4.0 acetic acid and sodium acetate buffer solution and a very narrow linearity was observed as 0.005 - 0.1 µg/ml.

Longmei Cheng., *et al.* quantified Tulobuterol in human plasma [7] by liquid chromatography-tandem quadrupole mass spectrometry (LC-MS/MS) in presence of an internal standard Tulobuterol-d9 using 0.1% formic acid: acetonitrile (30:70) as mobile phase in which the linearity was very narrow i.e. 0.00001-0.005 µg/ml. Xiao Han., *et al.* [8] developed a liquid chromatography–tandem mass spectrometry method (LC-MS/MS) for the determination of Tulobuterol in rat plasma in presence of an internal standard, Clenbuterol using 0.1% formic acid: water: methanol as mobile phase and the method was applied for the pharmacokinetic study of Tulobuterol patches. The linearity in this method was narrow and is found to be 0.0005 - 0.1 µg/ml. Fengguo Xu., *et al.* and XU Feng-Guo., *et al.* developed a high-performance liquid chromatography-mass spectrometry (LC-MS) for the determination of Tulobuterol using a mixture of methanol: 10 mM ammonium acetate (pH 4.0) in presence of an internal standard, Clenbuterol HCl [9] and a mixture of methanol: 0.01 M ammonium acetate (70:30) without internal standard [10] respectively but with the same linearity range 0.0005-0.04 µg/ml in rabbit's plasma.

Kugako Matsumura., *et al.* quantified Tulobuterol and its metabolites in human urine by mass fragmentography using chemical ionisation (Ammonia) and helium as carrier gas [11] and also in human serum by electron-capture gas-liquid chromatography using nitrogen as carrier gas in presence of an internal standard l, l-Bis- (4-fluorophenyl)-2,2 dichloro ethane [12]. Thienpont LM., *et al*. measured Tulobuterol by capillary gas chromatography (GC/MS) in human plasma [13] using helium as carrier gas in presence of an internal standard, Des chloro Tulobuterol.

The analytical methods or instrumental techniques used by different authors for the quantification of Tulobuterol in pharmaceutical formulations such as tablets, transdermal patches as well as biological samples such as human plasma, human serum, human urine, rat plasma, rabbit plasma were briefly summarised in table 1.

Reagent/Mobile phase (v/v)	Linearity (µg/ml)	Comment	Ref
Spectrophotometry			
Methanol	25-125	λ_{max}: 212 nm	[3]
Bromo Cresol Green	0.1-0.8	λ_{max}: 624 nm	[4]
Liquid chromatography			
Acetonitrile: 0.02M Potassium dihydrogen phosphate buffer (60:40) pH adjusted to 3.0 with Ortho phosphoric acid	25-75	HPLC	[5]
Methanol: Sodium heptane sulfonate solution (Prepared by pH 4.0 acetic acid-sodium acetate buffer solution) (55:45)	0.005-0.1	HPLC (Transdermal patch)	[6]
Liquid chromatography-Mass spectroscopy			
0.1% Formic acid: Acetonitrile (30:70) Tulobuterol-d9 (Internal standard)	0.00001-0.005	LC-MS/MS Human plasma	[7]

0.1% Formic acid: Water: Methanol Clenbuterol (Internal standard)	0.0005-0.1	LC-MS/MS Rat plasma	[8]
Methanol: 10 mM Ammonium acetate (pH 4.0) Clenbuterol HCl (Internal standard)	0.0005-0.04	LC-ESI-MS Rabbit's plasma	[9]
Methanol: 0.01 M Ammonium acetate (70:30)	0.0005-0.04	LC-MS Rabbit's plasma	[10]
Gas chromatography			
Chemical Ionisation: Ammonia Carrier gas: Helium	0.005-0.3	GC-MS Human urine	[11]
Carrier gas: Nitrogen l, l-Bis- (4-fluorophenyl)-2,2 dichloro ethane (Internal standard)	-	Electron capture GLC Human serum	[12]
Carrier gas: Helium Des chloro Tulobuterol (Internal standard)	0-0.0061	Capillary GC/MS Human plasma	[13]

Table 1: Review of analytical techniques.

Conclusion

The present review helps the readers to understand the existing analytical techniques developed so far for the estimation of the bronchodilator Tulobuterol and gives an overall idea about the limitations and advantages of these methods.

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