

A REVIEW ON METHOD DEVELOPMENT ON ESTIMATION OF ACEBROPHYLLINE AND DOXOXYLLINE

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Article Received on
20 April 2019,

Revised on 10 May 2019,
Accepted on 31 May 2019

DOI: 10.20959/wjpr20197-15196

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ABSTRACT

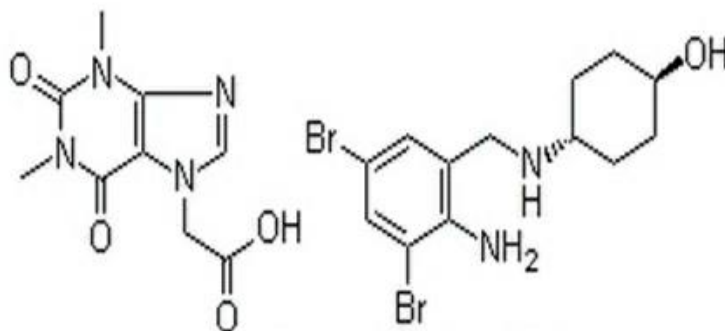
Asthma is a common long term inflammatory disease of the airway of the lungs it is characterized by a various recurring symptoms, reversible air flow obstruction and bronchospasm. Acebrophylline and doxofylline act as anti- asthmatic drug. A simple selective and precise HPLC method of analysis of acebrophylline and doxofylline both in bulk and in their combine formulation has been developed. Various analytical method have been reported for the estimation of these drugs in their individual forms as well as their combined dosage form.

KEYWORDS: Acebrophylline, Doxofylline, RP-HPLC (high performance liquid chromatography), column, mobile phase.

INTRODUCTION

Acebrophylline(ACEBRO) is an antiinflammatory and airway mucus regulator. It contains ambroxol and theophylline-7-acetic acid that facilitates the bio synthesis of pulmonary surfactant while later rises blood levels of ambroxol, by stimulating surfactant production. Chemically ACEBRO is (1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purine_7yl) acetic acid-4{[(2-amino-3,5-dibromophenyl)methyl]amino} cyclohexanol. It is a salt obtained by the reaction of equimolar amounts of theophylline-7-acetic acid and ambroxol. Theophylline-7-acetate promote the relaxation of brochial muscles.

Doxofylline(DOXO) is xanthine derivative, chemically it is 7-(1,3-dioxolan-2-methyl)-3,7-dihydro-1,3-dimethyl-1H-purine-2,6-dione. It is used in the treatment of asthma.

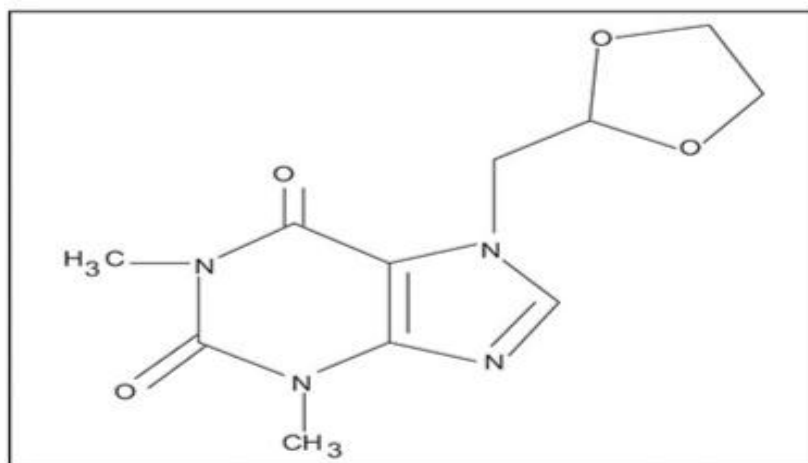
INTRODUCTION OF DRUG PROFILE**Acebrophylline****Structure of Acebrophylline**

IUPAC name: (1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purine_7yl) acetic acid-4{[(2-amino-3,5-dibromophenyl)methyl]amino} cyclohexanol

Molecular formula: $C_{22}H_{28}Br_2N_6O_5$

Molecular mass: 616.311 gm/mol

Solubility: Methanol

Doxofylline**Structure of Doxofylline.**

Molecular weight: 266.25 gm/mol

Solubility: sparingly soluble: Aqueous Buffer

Soluble: Ethanol.

IUPAC name: 7-(1,3-dioxolan-2-methyl)-3,7-dihydro-1,3-dimethyl-1H-purine-2,6-dione 2-(7-teofillinmetil)-1,3 diossolano.

Molecular formula: $C_{11}H_{14}N_4O_4$

MECHANISM OF ACTION**Acebrophylline**

It acts as a bronchodilator effect due to inhibition of the intracellular phosphodiesterases followed by an increase of adenosine monophosphate cyclic levels, which promote the relaxation of bronchial muscles. Ambroxol act as a mucolytic agent by increases the mucociliary clearance by stimulating cilia motility. Acebrophylline inhibit the synthesis and release of leukotrienes and tumoir necrosis factors and reduce inflammation.

Doxofylline

One of the mechanisms of action of is thought to arise from the inhibition of phosphodiesterase activity thus increasing the levels of cAMP and promoting smooth muscle relaxation. The interaction of doxofylline with beta-2 adrenoceptors was demonstrated by a study using nonlinear chromatography, frontal analysis and molecular docking. Serine 169 and serine 173 residues in the receptor are thought to be critical binding sites for doxofylline where hydrogen bonds are formed. Via mediating the actions of beta-2 adrenoceptors, doxofylline induces blood vessel relaxation and airway smooth muscle relaxation.

Reported Methods of Acebrophylline and Doxofylline

SR. No.	Drug	Method	Brief introduction	Ref. no.
1	Acebrophylline and acetylcysteine(<i>Tablet</i>).	RP-HPLC	Mobile phase :buffer solution and acetonitril (90:10) Column: hypersil BDS, C18 Flow rate: 1ml/min Wavelength: 260nm	[1]
2	Acebrophylline (<i>capsule</i>)	UV spectrophotometer	Wavelength (λ_{max}): 274nm Linearity range: 2-20 μ g/ml Regration : 0.9994	[2]
3	Acebrophylline, montelukast, and levocetirizine dihydrochloride(<i>tablet</i>)	HPLC	Column: Macherey-Nagel C18 pH: 3.5 mobile phase: ammonium acetate buffer and methanol(15:85) flow rate: 0.6ml/min Wavelength: 230nm	[3]
4	Acebrophylline	HPTLC	Mobile phase: toluene and methanol 5:5v/v Wavelength: 248nm Linear range: 500-2500ng/band	[4]
5	Doxofylline (<i>Tablet</i>)	RP-LC method	Mobile phase: water: methanol: ethyl acetate (80:10:10% v/v/v) Flow rate:1.0ml/min Column :supelco C18 DB Wavelength: 277nm	[5]

6	Acebrophylline and doxofylline (Tablet)	HPTLC	Mobile phase:Toluene:methanol:glacial acetic acid(6:2:2v/v/v) TLC: aluminum sheets, silica gel 60F 254. Rf value :0.29 (ACEBRO), 0.64(DOXO) Linear range: 100-600(ACEBRO), 400-2400ng/spot(DOXO)	[6]
7	Doxofylline and terbutaline sulfate	RP-HPLC	Mobile phase: methanol and acetonitrile (80:20) Column: Hypersil BDS C18. Flow rate:1.0 ml/min. Retention time :2.869min(DOXO), 3.942 min(Terbutaline sulfate)	[7]
8	Doxofylline and terbutaline sulphate.	Spectrophotometric method.	Wavelength: 277nm and 279 nm. Concentration range:10-50 and 20-60 µg/ml. Solubility: chloroform(DOXO), water(terbutaline sulphate)	[8]
9	Doxofylline and terbutaline sulphate.	RP-HPLC	Mobile phase: ammonium acetate : Acetonitrile (85:15% v/v) Flow rate:1.0 ml/min. Column: zorbax-SB phenyl Wavelength : 274nm.	[9]
10	Doxofylline and terbutaline sulphate	HPLC	Mobile phase: Methanol : Aq. Phosphate buffer(90:10v/v) Flow rate: 1 ml/min. Wavelength : 282nm. Retention time: 2.925(Doxofylline), 4.233(Terbutaline sulphate)	[10]

CONCLUSION

Acebrophylline and Doxofylline play an important role in asthma. These drugs are available in the market in tablet dosage form. Many methods have been reported for the estimation of these drugs. This method can simply and suitably take up for regular quality control analysis of acebrophylline and doxofylline in pure and its pharmaceutical dosage forms. So there is a need to develop a suitable accurate and validated method for their simultaneous estimation in combined dosage form.

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