A REVIEW ON METHOD DEVELOPMENT ON ESTIMATION OF ACEBROPHYLLINE AND DOXOFYLLINE

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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 reoccurring symptoms, reversible air flow obstruction and bronchospasm. Acebrophylline and doxofylline act as anti-asthamatic 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 antiinflamantory 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 asthama.
INTRODUCTION OF DRUG PROFILE

Acebrophylline

![Structure of Acebrophylline](image)

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_{2}N_{6}O_{5}
Molecular mass: 616.311gm/mol
Solubility: Methanol

Doxofylline

![Structure of Doxofylline](image)

Molecular weight: 266.25gm/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_{4}O_{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

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<tr>
<th>SR. No.</th>
<th>Drug</th>
<th>Method</th>
<th>Brief introduction</th>
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<td>Acebrophylline (capsule)</td>
<td>UV spectrophotometer</td>
<td>Wavelength (λmax): 274nm Linearity range: 2-20µg/ml Regration : 0.9994</td>
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<td>3</td>
<td>Acebrophylline, montalukast, and levocetrizine dihydrochloride (tablet)</td>
<td>HPLC</td>
<td>Column: Macherey-Nagel C18 pH: 3.5 mobile phase: ammonium acetate buffer and methanol(15:85) flow rate: 0.6ml/min Wavelength: 230nm</td>
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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), 400-2400 ng/spot (DOXO)

Doxofylline and terbutaline sulfate | RP-HPLC | Mobile phase: methanol and acetonitrile (80:20)
Column: Hypersil BDS C18.
Retention time: 2.869 min (DOXO), 3.942 min (Terbutaline sulfate)

Concentration range: 10-50 and 20-60 µg/ml.
Solubility: chloroform (DOXO), water (terbutaline sulphate)

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: 274 nm

Doxofylline and terbutaline sulphate | HPLC | Mobile phase: Methanol : Aq. Phosphate buffer (90:10v/v)
Flow rate: 1 ml/min.
Wavelength: 282 nm.
Retention time: 2.925 (Doxofylline), 4.233 (Terbutaline sulphate)

CONCLUSION
Acebrophylline and Doxofylline play and important role in the asthama. These drug are available in the market in tablet dosage form. Many method have been reported for the estimation of this drugs. This method can simply and suitably take up for regular quality control analysis of acebrophylline and doxofylline in pure and it’s pharmaceutical dosage forms. So there is need to develop a suitable accurate and validated method for their simultaneous estimation in combine dosage form.

REFERENCES


