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Review on Analytical Method for Quantitative Determination of Etophylline and Theophylline in bulk and in different dosage forms

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ABSTRACT:

Theophylline is used to treat lung disease and COPD (Bronchitis, emphysema). Etophylline is derivative of Theophylline, used as anti-asthmatic agent. It is adenosine antagonist that relaxes muscles of bronchi. They are under the class of drug Xanthine. These medicines need to be used regularly for relief of asthmatic symptoms. Various analytical methods are reported for estimation and stability of Theophylline and Etophylline in bulk and in different Formulation. A comprehensive Literature review is prepared for Theophylline and Etophylline.

KEY WORDS: Theophylline, Etophylline, RP-HPLC, SpectroPhotometric.

1. INTRODUCTION: 1.1 ETOPHYLLINE^[1,2,3]

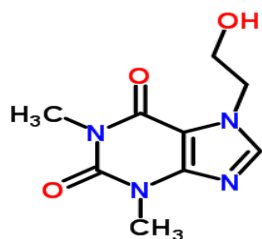
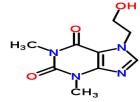


Figure1.1 Chemical Structure of Etophylline

Etophylline is chemical derivative of Theophylline, belongs to class Xanthines. It is indicated in Asthama, Chronic obstructive pulmonary disease, chronic bronchitis and emphysema.

Table 1.1: Drug Profile of Etophylline

Sr. No.	Parameters	Description
1	Category	Bronchodilator Agent
2	Structure ^[2]	
3	Chemical Formula	C ₉ H ₁₂ N ₄ O ₃
4	IUPAC Name	7-(2-Hydroxyethyl) 1,3-dimethyl purine-2,6-dione
5	Molecular Weight	224.22 gm/mol
6	Characteristic	White Crystalline powder or crystals.
7	Solubility	Freely soluble in water and soluble in methanol. Moderately soluble in Ethanol, Sparingly soluble in chloroform, Practically insoluble in ether.
8	Log P	1.24

9	Melting Range	160-165°C
10	Storage	Store at 2 to 8°C
11	CAS No.	519379
12	Indication	Chronic obstructive bronchoneumopathy, Asthama

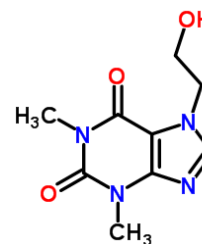


Table 2.1 Drug Profile

1.2 OFFICIAL METHODS FOR ETOPHYLLINE

Etophylline is official in European Pharmacopeia. Official methods are described below.

Official Methods for Estimation of Etophylline

In European Pharmacopeia 6.0 published by EDQMH, the detection of Etophylline is by HPTLC method where mobile phase Ammonia, Ethanol and Chloroform (1:10:90, v/v/v); plate HF 254, Wavelength 254 nm.

The Second Method found in European Pharmacopeia 6.0 Potentiometric method where **Titrant** 0.1M Perchloric acid is while **Titrate** 0.2 gm Etophylline in 50 ml Acetic anhydride.

1.3 REPORTED METHOD FOR ETOPHYLLINE

Various Analytical methods are reported for Etophylline in bulk and in pharmaceutical formulation.

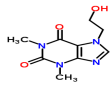
The Derivative Spectrophotometric method solution methanol wavelength 273nm.

The HPTLC method is having mobile phase of Acetone, Methanol and Formic acid (9:3:0.01, v/v/v); Plate F275, having wavelength 275nm.

The HPLC method was having mobile phase, Column is Waters Spherisorbs of dimensions (250 mm x 4.6 mm, 5µ); Mobile phase is 0.02 M Ammonium Acetate buffer (Methanol: Acetonitrile[70:30]) pH4.5 adjusted flow rate is 1ml/min of wavelength 275nm.

2. THEOPHYLLINE: [2,4,6,7]

2.1 Theophylline is used to treat respiratory disease like chronic obstructive pulmonary disease (COPD) and Asthama, chemically it is 1,3-dimethylxanthine. It is naturally found in Tea and Cocoa, as the drugs belongs to xanthine family are naturally found. A small amount of Theophylline is produced in liver by metabolizing Caffeine.

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➤ Theophylline is official in The United States Pharmacopeial Convention (USP 32- NF 27) and European pharmacopeia (Ph Eur 6.0).

2.2 Official Methods of Theophylline [8,12,17,18,19,20,21,22]

1. The RP-HPLC method was found in USP 32-NF-27 for theophylline having mobile phase 0.05 M Sodium Acetate trihydrate+0.01% Glacial Acetic Acid: Acetonitrile (30:70) having Colum packing of L1 with the dimensions of (300 mm x 4.0mm, 5µ), flow rate 1ml/min. Wavelength 280nm.
2. In European Pharmacopeia 6.0 RP-HPLC method has been described having mobile phase Acetonitrile :10mM Sodium Acetate pH was adjusted with Glacial Acetic Acid, Column packing L1(250

mmx4.00mm,7 μ), flowrate of 2ml/min and wavelength was 272

2.3 Reported Method of Theophylline

1. The different journals has reported articles on theophylline, one of them is by Derivative Spectrophotometric Method where wavelength was 244nm and the range of 4-12 μ g/ml.
2. The other reported method is RP-HPLC where mobile phase was found to be of 10mM Ammonium Acetate buffer, Acetonitrile and Methanol where pH 6.0 was adjusted and the ratio was found to be (90:5:5,v/v/v) , flow rate is 1ml/min of wavelength 272nm, column of Purosphere C18 was selected having dimensions of (250 mmx 4mm, 5 μ m)
3. The other reported method is Ion-Pair Liquid Chromatography where selection of mobile phase of Acetic Acid(1%) and methanol along with buffer 3mM Sodium-1-Octane Sulphonate as ion pairing agent was used Column of Spherisorb C18 (250 mm x 4.6 mm, 10 μ m) having flow rate of 1ml/ min and wavelength was selected as 277nm.
4. HPLC method was found to be approaching having mobile phase of Acetonitrile and Water in the ratio of (25:75,v/v) column of Inertsil C18 (250mm x 4.6mm, 5 μ m)was used having flow rate of 1ml/min and wavelength of 275nm.
5. One of the UV Spectrometry method was found where selection of wavelength can be done. The author selected wavelength of 271nm.
6. One of the UV Spectrometry method was referred for solvent selection of methanol and water with the ratio of (1:1). Where wavelength hereby was selected as 273nm.
7. HPLC method was convincing having mobile phase as Acetonitrile and 50mM Sodium Acetate Buffer having ratio of (15:85,v/v) where pH was adjusted to pH 6.0 with dilute Hydrochloric Acid, Column of Hi-Q-Sil C18 (250mmx4.6mm, 5 μ m) dimensions where selected and the flow rate was found to be 1ml/min wavelength of 270nm.
8. The other HPTLC method having mobile phase of Chloroform and Acetone (1:1,v/v) and plate of F254 was selected for the detection.
9. The mobile phase of the HPLC method was found to be methanol and 10mM Tetrabutyl Ammonium Hydrogen Sulphate with the ratio of (50:50,v/v), where column of Phenomenax was selected of dimensions (250mm x 4.6mm,5 μ m), flow rate of 1ml/min and wavelength was selected 274nm.

10. Here the reported method the mobile phase and column has been changed but the analytical technique remains the same, now the mobile phase consist of Acetonitrile and Phosphate buffer with the ratio of (65:35,v/v) where pH 4.2 was adjusted with Triethylene Amine, Column Zorbax ODS was selected the dimensions categorized as (250mm x 4.6mm, 5 μ m) having wavelength of 210nm and flow rate 1.5ml/min for the detection.

2.4 Reported method for Theophylline and Etophylline in combination

- There are number of methods reported for the both drugs individually but in combination there is limitation.
- Least number of methods found where HPLC and UV Spectroscopy is the main.
- The HPLC methods consist of different mobile phase and column.
- Through the study of these articles selection of wavelength can be easy and accurate.
- Not only wavelength can also give brief idea of mobile phase also.
- From the detailed study of literature it has been found that the combination having developed analytical method is least and mostly found in Parenteral dosage form and Tablet dosage form.
- Syrup can be considered to be the newly developed dosage form and can be moved forward for the analytical development.

CONCLUSION:

The present review depicts the reported spectrophotometric and chromatographic methods which had developed and validated for the estimation of Etophylline and Theophylline. According to the literature review it has been concluded that the different spectrophotometric and chromatographic methods are available for the estimation of Etophylline and Theophylline in the bulk drug as well as in combination in different dosage form. These all methods are accurate, precise, reproducible, and robust. Most of the methods are of RP- HPLC and of UV Spectrophotometry as these methods provides best available reliability, repetability, analysis time and sensetivity.

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