Taj Pharmaceuticals Ltd.

Theophylline

CAS No. [58-55-9]

IUPAC Name: 1,3-dimethyl-7H-purine-2,6-dione | CAS Registry Number: 58-55-9
Synonyms: theophylline, Elixophyllin, Theophyllin, Theolair, Theocin, Nuelin, Synophylate, Bronkodyl, Aerolate, Theovent, Respbid, Theobid, Uniphyl, 1,3-Dimethylxanthine, Pseudotheophylline, aminophylline, Slo-phyllin, Elixophylline, Liquophylline, Armophylline

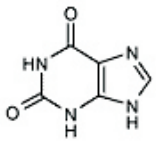
Molecular Formula: C7H8N4O2
Molecular Weight: 180.164020 [g/mol]
Chemical Name : Theophylline
CAS # : [58-55-9]
End Use : Bronchodilator
H-Bond Donor: 1 H-Bond Acceptor: 4

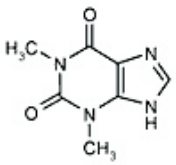
A methyl xanthine derivative from tea with diuretic, smooth muscle relaxant, bronchial dilation, cardiac and central nervous system stimulant activities. Theophylline inhibits the 3',5'-CYCLIC NUCLEOTIDE PHOSPHODIESTERASE that degrades CYCLIC AMP thus potentiates the actions of agents that act through ADENYLATE CYCLASE and cyclic AM

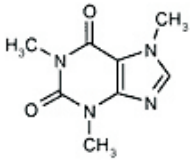
DRUG CLASS AND MECHANISM: Theophylline belongs to a class of medications called bronchodilators, used in treating asthma and other airway diseases. Asthma is a breathing problem involving narrowing of the airways. Airways are breathing passages that allow air to move in and out of the lungs. Airways can be narrowed due to accumulation of mucus, spasm of the muscles that surround these airways, or swelling of the lining of the airways. Airway narrowing leads to symptoms of shortness of breath, wheezing, cough and congestion. The narrowed airways can open either spontaneously or from medications. Medications that open airways are called bronchodilators. Theophylline opens airways by relaxing the smooth muscles in the walls of the airways. Theophylline can also be helpful in patients with emphysema and chronic bronchitis when their symptoms are partially related to reversible airway narrowing. Theophylline also strengthens right heart function and diaphragm movement.

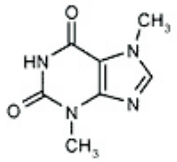
The main actions of theophylline involve:

- relaxing bronchial smooth muscle
- increasing heart muscle contractility and efficiency: positive inotropic
- increasing heart rate: positive chronotropic
- increasing blood pressure
- increasing renal blood flow
- some anti-inflammatory effects
- central nervous system stimulatory effect mainly on the medullary respiratory center.


Xanthine
(dioxypurine)


Theophylline
(1,2-dimethylxanthine)


Caffeine
(1,3,7-trimethylxanthine)


Theobromine
(3,7-dimethylxanthine)

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Theophylline

CAS Number 58-55-9

History

Theophylline was first extracted from tea leaves and chemically identified around 1888 by the German biologist Albrecht Kossel.Just seven years after its discovery, a chemical synthesis starting with 1,3-dimethyluric acid was described by Emil Fischer and Lorenz Ach. The Traube synthesis, an alternative method to synthesize Theophylline has been introduced in 1900 by another German scientist, Wilhelm Traube. Theophylline's first clinical use came in 1902 as diuretic.It took additional 20 years until its first description in asthma treatment.

Pharmacokinetics

Absorption

Bioavailability is 100%. However, taking the drug late in the evening may slow the absorption process, without affecting the bioavailability. Taking the drug after a meal high in fat content will also slow down the absorption process, without affecting the bioavailability.

Distribution

Theophylline is distributed in the extracellular fluid, in the placenta, in the mother's milk and in the central nervous system. The volume of distribution is 0.5 L/kg. The protein binding is 40%. The volume of distribution may increase in neonates and those suffering from cirrhosis or malnutrition, whereas the volume of distribution may decrease in those suffering from obesity.

Metabolism

Theophylline is metabolized extensively in the liver (up to 70%). It undergoes N-demethylation via cytochrome P450 1A2. It is metabolized by parallel first order and Michaelis-Menten pathways. Metabolism may become saturated (non-linear), even within the therapeutic range. Small dose increases may result in disproportionately large increases in serum concentration. Methylation in Theophylline is also important in the infant population. Smokers and people with hepatic (liver) impairment metabolize it differently.

Elimination

Theophylline is excreted unchanged in the urine (up to 10%). Clearance of the drug is increased in these conditions: children 1 to 12, teenagers 12 to 16, adult smokers, elderly smokers, cystic fibrosis, hyperthyroidism. Clearance of the drug is decreased in these conditions: elderly, acute congestive heart failure, cirrhosis, hypothyroidism and febrile viral illness.

The elimination half-life varies: 30 hours for premature neonates, 24 hours for neonates, 3.5 hours for children ages 1 to 9, 8 hours for adult non-smokers, 5 hours for adult smokers, 24 hours for those with hepatic impairment, 12 hours for those with congestive heart failure NYHA class I-II, 24 hours for those with congestive heart failure NYHA class III-IV, 12 hours for the elderly.

Indications

The main therapeutic uses of theophylline are aimed at:

- chronic obstructive pulmonary disease (COPD)
- asthma
- infant apnea

Uses Under Investigation

A clinical study reported in 2008 that theophylline was helpful in improving the sense of smell in study subjects with anosmia.

Side-effects

The use of theophylline is complicated by the fact that it interacts with various drugs, chiefly cimetidine and phenytoin, and that it has a narrow therapeutic index, so its use must be monitored to avoid toxicity. It can also cause nausea, diarrhea, increase in heart rate, arrhythmias, and CNS excitation (headaches, insomnia, irritability, dizziness and lightheadedness). Its toxicity is increased by erythromycin, cimetidine, and fluoroquinolones, such as "cipro" (ciprofloxacin). It can reach toxic levels when taken with fatty meals, an effect called dose dumping.

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or by contacting the sponsor, Taj Pharmaceuticals Limited., at:
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This leaflet was prepared by
Taj Pharmaceuticals Limited,
Mumbai (India).
MPSTJ278
Last revised: 29 August 2009