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FORMULATION OF BRONCHODILATOR DRUGS-METHYLXANTHINES

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ABSTRACT

Bronchitis is infection and inflammation of the mucous lining of the trachea and bronchi. It can be in acute and chronic forms and generally shows the symptom as a sequel to upper respiratory infections such as cold or influenza. The condition occurs most vigorously in old ages persons, children and smokers of any age group. Asthma is common and distressing condition which is symbolized by recurrent attacks of spasm of the tubes of the lungs which shows as wheezing, coughing and sense of suffocation, suffers face breathing problem. Methylxanthines and their derivatives can play important role in the treatment of bronchitis as well as asthma. Methylxanthines are used for the preparation of group of drugs. These are playing very important for smoothing of bronchial muscles and stimulate central nervous system (CNS).The bronchodilator effects of such drugs are applied in the treatment in acute asthma. Such drugs are also used in the treatment of aponea and have diuretic effect. Oxpentifylline, a Xanthine derivative acts as vasodilator. Naturally occurring are caffeine, theophylline and theobromine. Their derivatives can be used in the improvement form for the treatment of asthma. Modifiedformsare Diprophy lline, Etamiphy lline Camsylate,Proxiphylline,HydroxytheophyllinandEtofylline They can be prepared and sold into the market as tradenamesviz.Aminophylline,AminophyllineHydrate,CholineTheophyllinae. Theobromine is also used in the treatment of angina pectoris and hyper tension. The basic nucleus is xanthine.It can be substituted by various groups for the preparation of more effective drugs. Now a day's air pollution is fast growing and Indian citizens are suffering from respiratory problems .More emphasis is required on bronchial drugs and treatment of bronchitis, asthma, emphysema and acute respiratory infection .Aminophyllineis found to be a better drug among others. It can be given orally as well as through injection both.

KEYWORDS: Bronchitis, infection, oxygen, Asthma, Nasal irritation

INTRODUCTION

Normally we breathe about fifteen times per minute, inhaling about half a liter of air each time. During exercise, when cells are hungry for oxygen, rate and depth of respiration increases and the lungs take in ten times of the oxygen supplied during rest. Breathing itself is an intricate process. The lungs hang loosely in the chest, each in separate compartment with the heart in between. If the respiratory system is to operate at full efficiency, it is essential to breathe through the nose rather than the mouth. Asthma can arise at any age but it is commonly found in children and adolescents. The complication increases with time of rough. In asthmatics patient having a sudden a group of cold symptoms like nasal congestion. Nasal irritation and bout of sneezing, indicating that the nasal mucous membrane is having swollen and secretory in response to some psychological or environmental trigger. Attacks of asthma may last for only few minutes, or may continue for hours or even days, leaving the sufferer in a stage of physical, mental and emotional exhaustion

Bronchitis is infection and inflammation of the mucous lining of the trachea and bronchi. It can be in acute and chronic forms and generally shows the symptom as a sequel to upper respiratory infections such as cold or influenza. The condition occurs most vigorously in old ages persons, children and smokers of any age group. Asthma is common and distressing condition which is symbolized by recurrent attacks of spasm of the tubes of the lungs which shows as wheezing, coughing and sense of suffocation, suffers face breathing problem. **Methylxanthines and their derivatives can play important role in the treatment of bronchitis as well as asthma.** Bronchodilators are medications that relax the bronchial muscles. Relaxing these muscles makes the air ways larger, allowing air to pass through the lungs easier. This helps people with COPD breathe better. Many different kinds of bronchodilators are available in the markets. They can be grouped according to how long they work (called short- and long-acting drugs) or the way in which they enlarge or dilate the airways (beta-agonists, anticholinergics or theophyllines). While all bronchodilators increase the diameter the airways, they work in different ways to do so. It is therefore possible to combine bronchodilators in order to achieve maximal benefit. Many people with COPD experience constant breathing difficulty. Bronchodilators therefore need to be taken regularly to keep breathing under control, this is called maintenance medication. Conversely, reliever medications are used for temporary breathless.

Chronic obstructive lung disease (COPD) describes a group of lung conditions (diseases) that make it difficult to empty the air out of the lungs. This difficulty can lead to shortness of breath (also called breathlessness) or the feeling of being tired. COPD is a word that can be used to describe a person with chronic bronchitis, emphysema or a combination of these. COPD is a different condition from asthma, but it can be difficult to distinguish between COPD and chronic asthma. Two people may have COPD, but one may have more symptoms of chronic bronchitis while another may have more symptoms of emphysema. It is helpful to understand the difference between the two conditions, as COPD means a person may have some chronic bronchitis as well as emphysema. **COPD is often caused by smoking**, but in a few cases it's caused by inhaling toxins in the environment. The damage to the lungs and airways is permanent. There is no cure for COPD, but there are medications that can help you breathe easier by opening the airways and reducing the inflammation.

TYPES OF BRONCHODILATORS

The three main groups of bronchodilators are beta-agonists, anticholinergics and theophyllines. Bronchodilators are important in treating the symptoms of COPD, such as breathlessness, cough and sputum production. People with COPD are generally prescribed at least one bronchodilator; however, sometimes two or three medications are needed to control symptoms. Bronchodilators can also be used to "relieve" worsening symptoms. Reliever drugs are usually short acting and, therefore, are not the best way to control day-to-day symptoms. In order to give you regular control or to maintain your breathing, these short-acting bronchodilators would have to be taken frequently, day and night, 24 hours a day. This is not very practical for most people. It is unusual to find two people with COPD on the same program of medication. Some need bronchodilators from only one group, while some need bronchodilators from all three groups. For example, a person may need a beta-agonist as well as an anticholinergic and a theophylline drug. The number of different bronchodilators people with COPD need depends on how well their symptoms are controlled.

Short-Acting Bronchodilators:-

Albuterol, Levalbuterol (Xopenex), and ipratropium (Atrovent) are all short-acting bronchodilators. They come in the form of an inhaler or as a liquid that you can add to a nebulizer to inhale.

The side effects are few, but some people will experience dry mouth, blurred vision, or a cough.

Other side effects include tremors (shaking), as well as the feeling that the heart is racing or beating faster than normal. If you have a heart condition, you should tell your doctor before taking these medications.

Corticosteroids:-

For someone with COPD the airways can be inflamed, which makes it more difficult to breathe. Corticosteroids are a type of medication that reduce inflammation in the body, making air flow easier to the lungs. There are several corticosteroids. Some are prescribed with bronchodilators because these two medications can work together to make breathing more effective. Fluticasone (Flovent), budesonide (Pulmicort), and prednisolone are the ones doctors commonly prescribe for COPD.

- Fluticasone comes as an inhaler that you use once or twice daily. Some people report headaches, sore throat, a change in their voice, and allergic reactions.
- Budesonide comes as a powder, liquid, or in an inhaler. Some people who have used this

medication get colds or an infection in the mouth (thrush).

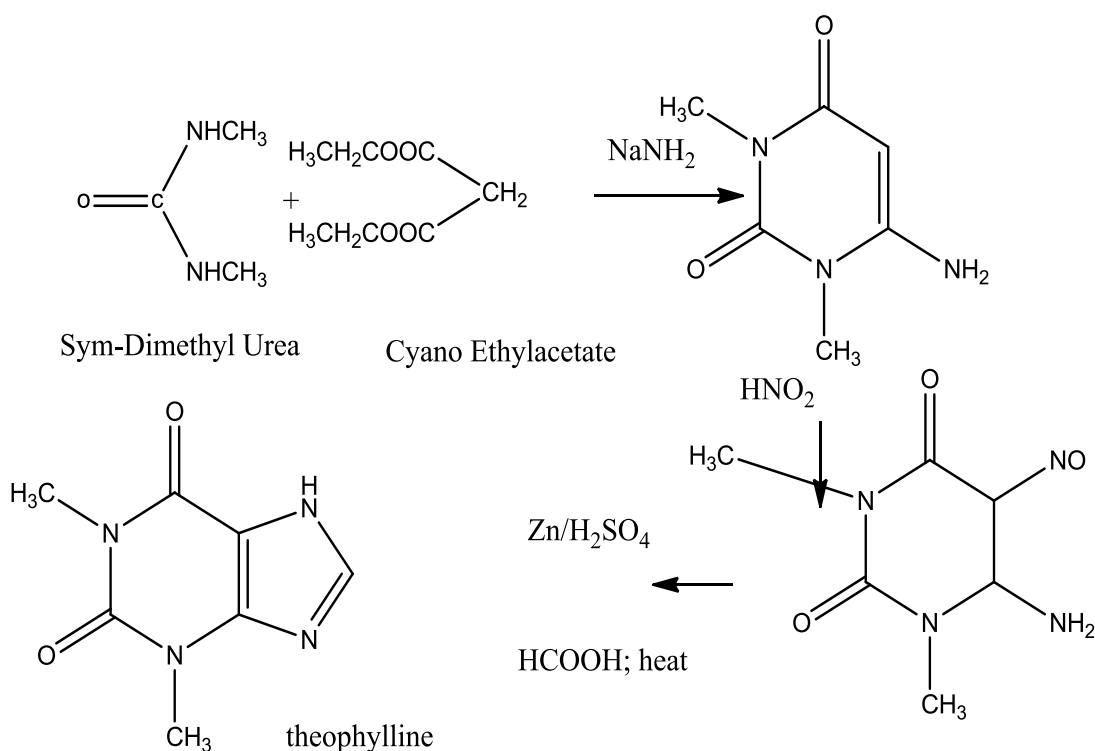
- Prednisolone comes as a pill, liquid, or as a shot and is usually given for emergency rescue.

Methylxanthines:-

Some people have severe difficulty with COPD and the regular or first-line treatments alone don't seem to help. When this happens, some doctors will prescribe theophylline, which works as an anti-inflammatory and relaxes the muscles in the airway, to take along with a bronchodilator. **Theophylline** comes as a pill or a liquid that you take on a daily basis, and combined with other medications, it can help you breathe easier. Some people have had side effects when they have used theophylline. Some people report feeling queasy or vomiting. People who take theophylline have also had tremors and trouble sleeping.

Chemical Preparation of Theophylline:-

It is prepared by following synthesis using sym Dimethyl Urea and ethylcyanoacetate scheme is given below



Long-Acting Bronchodilators:-

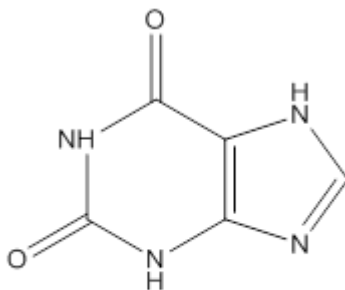
Long-acting bronchodilators are medications that are used to treat COPD over a longer period of time. They are usually taken once or twice daily over an extended period, and they come as inhalers or nebulizers. The long-acting bronchodilators are:

- tiotropium (Spiriva)
- salmeterol (Serevent)
- formoterol (Foradil, Perforomist)
- arformoterol (Brovana)

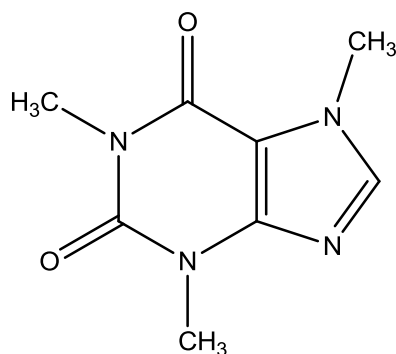
- indacaterol (Arcapta)
- aclidinium (Tudorza)

Because these are used to gradually help with breathing, they are not effective in an emergency or as rescue medication. There are some side effects that can happen when you use these medications eg. Dizziness etc. Other more serious side effects that people have experienced include allergic reactions (rashes), blurred vision, and a rapid heart rate.

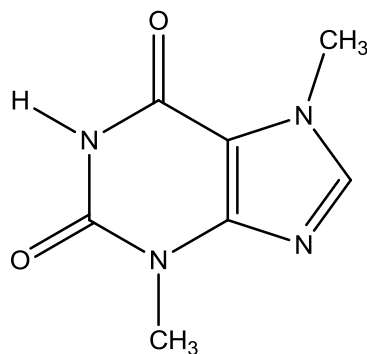
DRUGS HAVING CLOSELY RELATED STRUCTURES OF METHYL XANTHINE



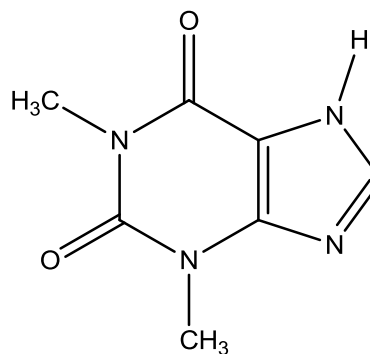
Xanthine



Caffeine



Theobromine



Theophylline

Theophylline and Theobromine, are almost similar in their structure. They have closely related structures of **METHYL XANTHINE**. Caffeine is a stimulant, it is found in vegetation with theophylline and theobromine in **TEA LEAVES of tea plant its botanical name is *Thea Sinensis*** and it is also found in well coffee plant its scientific name is ***Coffea Arabica***. **Caffeine and** theobromine are also present in seeds Cacao plant i.e. ***Theobroma cacao***.

Theophylline is white crystalline powder, smell less slightly soluble in water, its absorption is very fast when it is orally taken. Its absorption becomes slow in presence of food, metabolises in liver to give 1,3-

dimethyl uric acid, 1-methyl uric acid and 3-methylxanthine. These metabolites are passed away through urine. Theophylline gives relief to bronchitis, asthma, emphysema, relax bronchial muscles, soothing throat and acute respiratory infections. Hence it is used in expectorant. Its application in drug is very important because most of the people are suffering dust allergy due to the presence of very high Air Pollution.

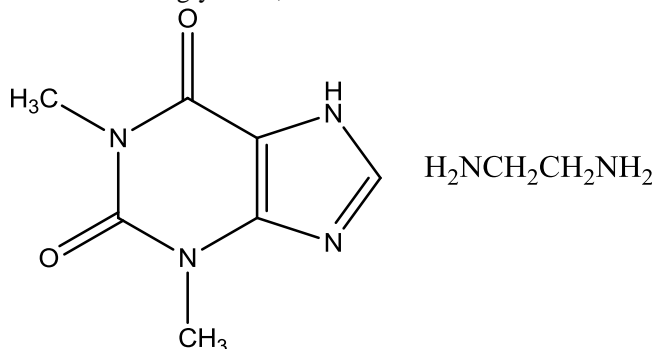
Medically its doses are prescribed as 16mg per kg body weight daily or approx 400 mg daily. Medical

names are **LASMA; NUELIN; PRO-VENT; SLO-PHYLLINAND UNIPHYLLINE .**

CholineTheophyllinate:-

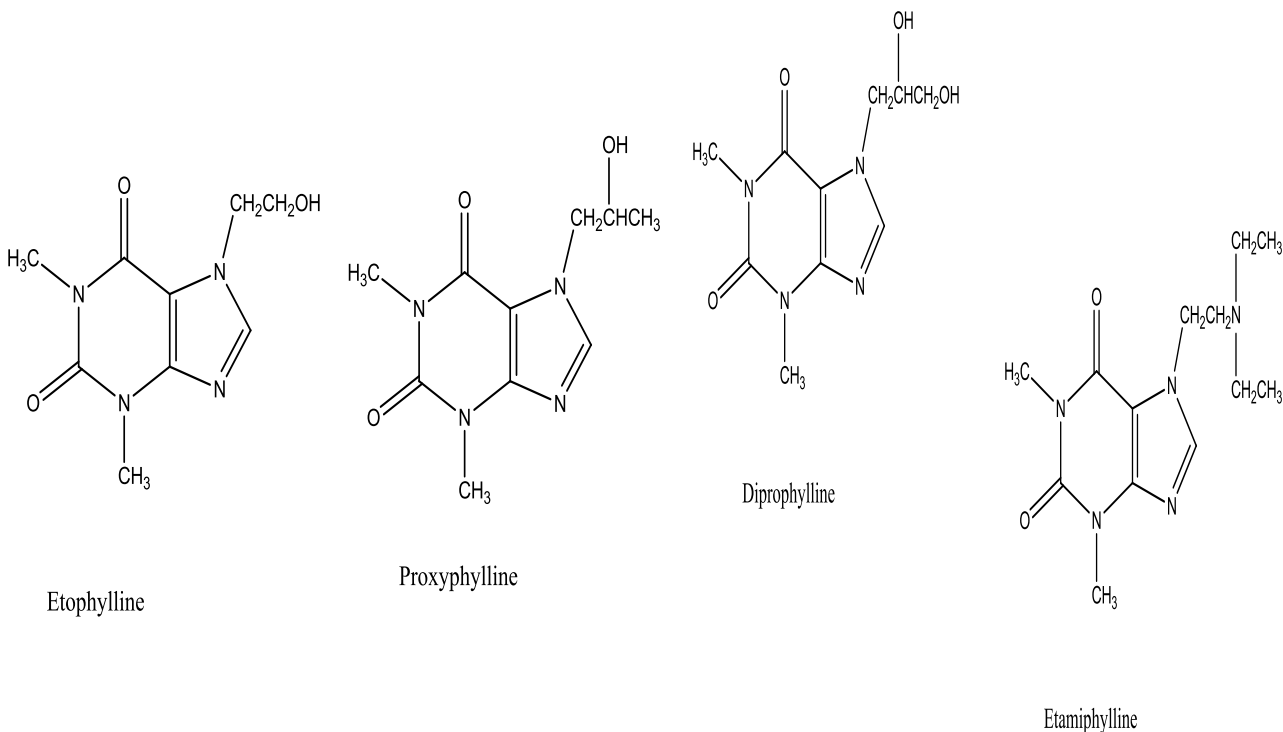
It is oxtriphylline. Medical names are Sabidal, Choledyl. It forms true water soluble salts of theophylline. It can be used as Theophylline sodium glycinate; Theophylline calcium glycinate;

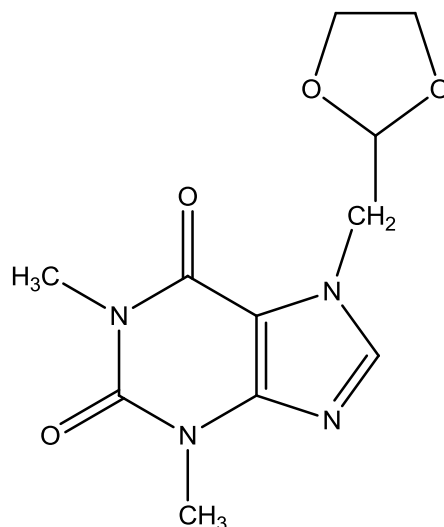
Theophylline sodium acetate; Theophylline calcium salicylate and Theophylline monoethanol amine. These salts are dissolved in human body fluid. It forms complex with ethylenediamine which is known as **Aminophylline**



Aminophylline

Modified Methylxanthines:-





Doxofylline

These drugs can be used as safe drug they can be easily prepared

Doxofylline is used in Asthma and in broncho spastic disorders.

CONCLUSION

Bronchitis would be rare if people took the right meal and their systems were not filled with mucus and poisonous waste matters, there is usually stomach trouble or constipation. **ASTHMA** may be fatal.

While looking a glimpse of researches done in the field of COPD DRUGS, it is evident that varieties of drugs are present in the market for its prevention. But when we talk about COPD drug which can go through the easy synthetic process, sharply targeted, low cost, and easily available and having least side effects, Aminophylline enters. More work in this area is being done with an aim to have more drugs in this category having above characteristics.

Recommendations:-

If a person is facing problem in breathing, he should rub the arms or feet hard in the direction of the heart.

1. Bronchitis sufferers should not take cold morning showers, a hot steamy bath should be in daily routine
2. Smoking should be given up as it directly irritates the bronchial mucosa.
3. Should not stay in stuffy, overheated and unventilated rooms. Avoid draughts and sitting on cold floors.
4. Coughing should not be suppressed, as it is nature' way of clearing the phlegm and

infective material from the bronchial tree. Removal of phlegm can be promoted by hot fermentations to the back and chest, then finishing with a cold formation.

5. Steam inhalations at night are very helpful and hot foot baths with a tablespoon of mustard in water.
6. Daily walking is most helpful and deep breathing should be done at intervals throughout the daily routine.
7. Anti-asthmatic drugs should not be discontinued suddenly without proper guidance, as this often allows asthma previously suppressed by drugs to 'bounce back'.
8. Physical fitness should be developed and excess weight removed, as it accentuates the respiratory difficulties of an asthmatic.
9. Swimming, Running and Jogging are excellent exercises for asthmatics.

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