INTRODUCTION
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Asthma is a condition marked by repetitive, sudden, episodic attacks of shortness of breath, wheezing and coughing, which can be relieved with adequate medications. It is caused by chronic airway inflammation and is characterized by edema of airways; excessive muscus secretions, impairment of muscolliary clearance and increased reactivity of respiratory smooth muscles. Inflammation leads to airway hyper responsiveness which can lead to further airflow obstruction.

Asthma and allergic rhinitis have well documented relationship. Studies have shown that the prevalence of allergic rhinitis was four to six times greater in individuals with asthma than in the general population, 57% of asthmatic patients have associated rhinitis.¹

Guidelines for the diagnosis and management of asthma have been published since 1990. The recommendations for the treatment of asthma were organized around four components of effective asthma management.²

- Use of objective measures of lung function to assess the severity of asthma and to monitor the course of therapy.
- Environmental control measures.
- Comprehensive pharmacological therapy for long term management.
- Patient education.

Several medications are available to treat the twin causes of asthma symptoms i.e. chronic inflammation and constriction of bronchi, the airways in lungs.

They fall in two categories: Antinflammatory agents and Bronchodilators. However, if asthma is more persistent or severe,
long term relief can be achieved with a combination of medications.(2)

The national Asthma Education and Preventive Program (NAEPP) in conjunction with the National heart, long and blood institute (NHLBI) has found that adding a long acting inhaled bronchodilator to the prescribed inhaled corticosteroids (ICS) works better than just the ICS itself, in most cases the two medications are taken separately using two different inhalers. However, combinations delivered through a single inhaler have recently come in the market, allowing for shorter treatment and decreasing the need for multiple inhalers(3).

Amongst all antiasthmatic agents, theophylline has many recognized benefits in the treatment of asthma. These include bronchodilator and responsiveness to exercise induce Asthma. This methyl xanthine, as a long term control medication is available as a tablet, capsule or syrup. Common brands of theophylline include TheoDur® Sio-Bid®, Uniphyl® UniDur®, Aminophyline(4).

The allergic rhinitis and some other allergic conditions such as sneezing, itchy and watery eyes and runny nose can be prevented by H1 receptor antagonists / antihistamines(5). These are designed to dock at H1 receptors on cells but blocking histamine from doing so. These agents have been investigated as an asthma treatment for more than 50 years including classical Antihistamines like CPM (present in Triaminic®, Pedicare®, Coricidin®, Tripolidine maleate (Actifed®), Brompheniramine maleate, diphenhydramine and clemastine. Most of these agents are absorbed quickly and are advantageous for treatment of sudden, brief allergic reactions(6,7).

Despite all favourable features theophylline falls out of favour with many clinicians who manage asthmatic patients, since effect of theophylline is related to concentration at the receptor site, which rapidly attains equilibrium with serum. Fluctuations are observed in
serum concentrations over a dosing interval associated with fluctuations in efficacy. As the serum concentrations decline from therapeutic to subtherapeutic levels at the end of dosing interval, patients with labile airways are likely to have increased symptoms\(^{(8)}\). Since the frequency and severity of toxicity increases of serum concentrations beyond 20 mcg/ml, maximum potential benefit with minimum risk of toxicity is most likely when the serum concentration is maintained within the 10-20 mcg/ml therapeutic range. Fluctuations in serum concentrations at "steady state" is the function of rate of absorption, dosing interval and the clearance of the drug. In the individual patient, the shortest convenient dosing interval is 8 hrs, such that patient need not to wake up at night. Rapid release dosage forms administered at eight hour intervals to patients with rapid elimination will result in unacceptably large fluctuations, the patient remaining under medicated.

Such fluctuations can be reduced by decreasing the rate of elimination, shortening dosing interval or slowing the rate of absorption. Of these, three alternatives, slowing the rate of absorption is the best practical solution\(^{(9)}\).

The need for cost effective asthma therapy is driven by the high prevalence of asthma as well as the high cost of both medical care and lost productivity through illness. Limited healthcare resources demand proven therapies that maintain sustained disease control. Optimal disease control is the essence of effectiveness, but this in turn is dependent on correct drug selection and appropriate drug delivery\(^{10}\). Asthma patients can be treated safely and effectively with the inhalation devices currently available. The devices of choice are pressurized metered dose inhalers with spacers and some dry powder inhalers.\(^{11}\) Pulmonary delivery of glucocorticoids and cyclosporine solutions, liposomes and microemulsions is also reported which are in the form of liquid aerosol systems.\(^{12}\)
Traditional oral delivery is also a popular route for antiasthmatics i.e. controlled release tablets, which provide controlled plasma level of drugs. In this study principle of bimodal drug release is utilized. Bimodal drug release is characterized by an initial rapid release, followed by a period of constant release.\(^{(13)}\) Bimodal drug release systems produce rapid drug release during initial phase to provide quick onset of action and to compensate for relatively slow absorption in the stomach and large intestine. It can provide more uniform delivery of drug into the systemic circulation and also provide therapeutic blood levels similar to those produced by administration of two similar does over an extended period of time.\(^{(14)}\)

Theophylline is available in variety of extended release dosage forms. The different controlled release formulations of theophylline available are matrix tablets, multiparticulate/ pellets, barrier coated reservoir system liquid oral preparations containing microcapsules, syrup, microporous capsule, microspheres and even prodrug and transdermal patches.\(^{(30-42)}\)

Considering the need for successful innovative drug delivery system for bimodal release of combination of Theophylline and CPM (CPM), an attempt is made to develop a bilayer matrix tablet formulation. The tablet formulation consists of one immediate release layer. (Layer A), containing doses of Theophylline and CPM required for quick onset of action and one controlled release matrix layer (Layer B), which releases the dose of Theophylline over the period of 12 hours. Different combinations of hydrophilic polymers are evaluated for getting controlled release profile of drug from Layer B. The drug release profiles are compared by applying suitable mathematical models.