A Review on Acebrophylline Lozenges for bronchial Asthma: A Novel Approach

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Abstract : Asthma is chronic inflammatory disease of the airways that causes airway hyper responsiveness, mucosal edema, and mucus production. World-wide approximately 300 million people have asthma. Acebrophylline is a bronchodilator with mucosecretolytic and anti-inflammatory activity. Acebrophylline inhibits intracellular phosphodiesterase and facilitates brochial muscles relexation by increasing cAMP levels Acebrophylline is good highly effective within the treatment of the Bronchial Asthama. Lozenges are solid preparations that contain one or more medicaments, usually during a flavoured, sweetened base, and are intended to dissolve or disintegrate slowly within the mouth or these are medicated candy intended to be dissolved slowly within the mouth.

Keyword: Asthma, Acebrophylline , Lozenges Drug Delivery, Heating and congealing method.

❖ INTRODUCTION

1.1 INTRODUCTION TO ASTHMA[1-2]

- Asthma is defined as a chronic inflammatory disease of the airways that causes airway hyper responsiveness, mucosal edema, and mucus production. Asthma is characterized by chronic airway inflammation and increased airway hyper responsiveness resulting in symptoms of wheeze, cough, chest tightness and dyspnoea.

SYMPTOMS OF ASTHMA

- Within the condition of Asthma Symptoms like,
  wheeze, cough, chest tightness, Mood Changes, Change in facial appearance, Itchy-watery or glassy eyes

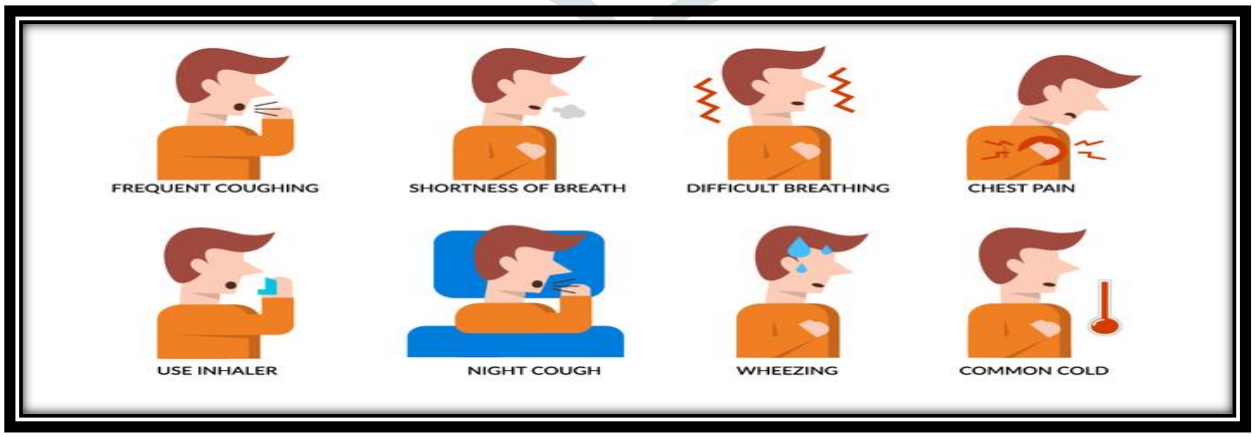


Figure No.1 Symptoms of Asthma

CAUSES:

There are several factors liable for asthma attacks and there for triggers vary from person to person.

The main factors include:-

- Respiratory infections caused by cold.
- Airborne substances like dust mites, pet dander, etc.
- Environmental factors like pollution, smoke, dust, pollen, etc.
- Smoking during pregnancy and after delivery are under greater risk.
- Genetic factors including case history of asthma or allergies to dust and pollens.

DIAGNOSIS:[3-4]

The diagnosis of asthma concern a radical medical record , physical examination, and objective estimate of lung function (spirometry preferred) to verify the diagnosis Broncho provocation challenge testing and estimate for markers of airway inflammation can also be helpful for diagnosing the disease**.**

Diagnosis of asthma supported medical record, physical examination and objective measurements

1.Medical history:
Assess for traditional symptoms of asthma:

- Wheezing
- Breathlessness
- Chest tightness
- Cough (with our without sputum)

Assess for symptom patterns implicational of asthma:

- Recurrent/episodic
- Occur/worsen within the dark or early in the morning
- Occur/worsen upon hazard to allergens (e.g., animal dander, pollen, dust mites) or aggravations (e.g., exercise, cold air, tobacco smoking, infections)
- Respond to appropriate asthma therapy
- Assess for family or personal history of atopic disease (particularly allergic rhinitis)

2.Physical Examination:

- Examine for wheezing on auscultation
- Examine upper tract and skin for signs of other atopic conditions

Objective Measurements:

- Perform spirometry (preferred) to verify the diagnosis
- Diagnostic criteria: FEV_1 ↑ (after bronchodilator): ≥ 12% and ≥ 200 mL Consider PEF as an alternate if spirometry is unavailable
- Diagnostic criteria: PEF ↑ (after bronchodilator): ≥ 20% and 60 L/min
  Diurnal variation: >20%
- The spirometry (or PEF) may be normal, but manifestation are present consider:
- Challenge testing (e.g. Methacholine, histamine, mannitol excise)

Allergy testing

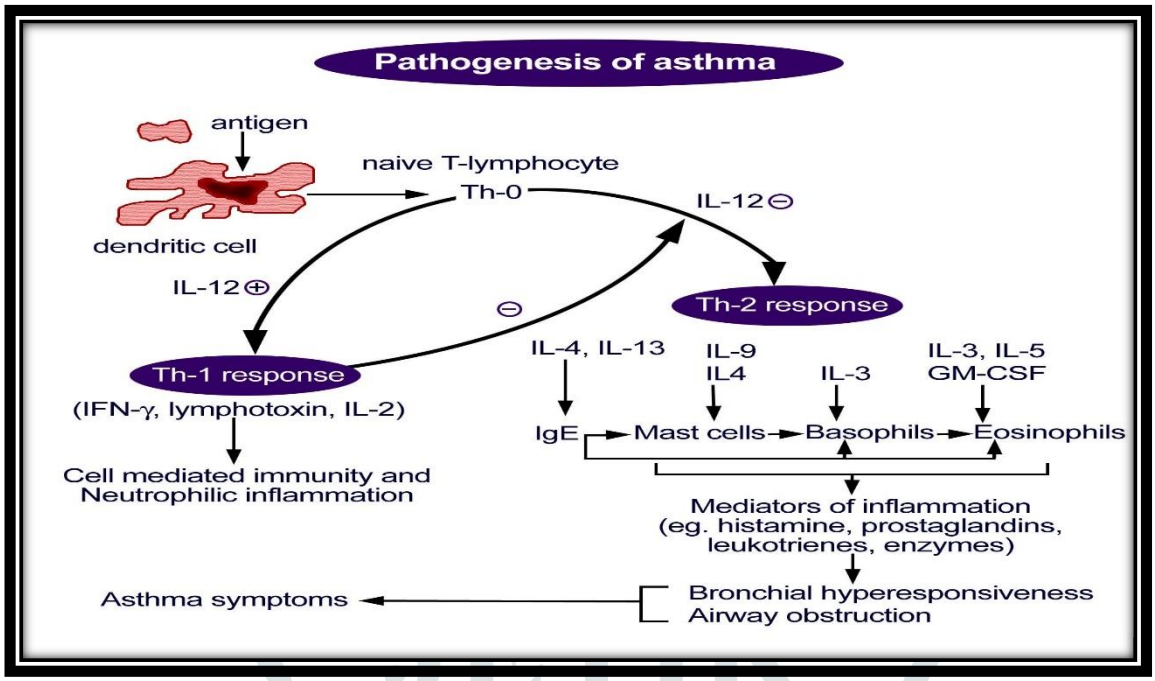
- Perform skin tests to estimate allergic status and analyse possible triggers

EPIDEMIOLOGY: [5]

- In many countries the popularity of asthma is increasing
- 255,000 asthma deaths in 2005.
- Over 80% of asthma casualty in low and lower-middle income countries
- World-wide approximately 300 million people have asthma and this is often expected to rise to 400 million 2025.
- Asthma being commoner in additional developed countries
- Currently, 8.4% of persons within in the US have asthma as compared with 4.3% of the population worldwide, and both numbers are on the increase.
- The typical annual asthma prevalence is higher in children (9.5%) than adults (7.7%). The prevalence of asthma is higher in black persons than white persons, and therefore the ethnicity most affected is that the Puerto Rican population.
- Asthma prevalence increases with each successive lower poverty line group.

- There are interesting relationships between asthma and certain otolaryngologist diseases.

PATHOPHYSIOLOGY: [6]



Figures No.2: pathophysiology of Asthma

Available Management:

1. Non-Pharmacological
2. Pharmacological

NON–PHARMACOLOGICAL MANAGEMENT:

- Patient and family education to know the disease, and to foster self-confidence and fitness
- Avoid smoking
- Avoid "identified cause" where possible
- Control of extrinsic factors which cause allergy like pets, moulds and certain foodstuffs, particularly in childhood
- Avoid beta-blockers, aspirin and NSAIDs.

PHARMACOLOGICAL MANAGEMENT: [7]

Table no.:1. Management of Asthma

Bronchaditrators	3,Stlmpnthomimetics: Salbutamol, Terbutaline, Bambuterol, Salmeterol, Formoterol, Ephedrine.
Methylxentine :	Theophylline (Anhydrous), Choline Theophylline, Hydroxyethyl Theophylline, Theophylline Ethanoate Of Piper Zine, Doxophylline, Acebrophylline.
Anticholinergics:	Ipratropium Bromide, Tiotropium Bromide.

Leucotriene Antginist:	Montelukast, Zahrlukast.
Corticosteroids	Glucocorticoids
Systemic:	Hydrocortisone, Prednisolone et al.
Inhalation:	Beclomethasone Di Propionate, Budesonide, Fluticasone Propionate, Flunisoiide, Ciclesonide.
Anti-Lge Antibody :	• Omalizumab

INTRODUCTION TO LOZENGES: [8-9-10]

- Lozenges are solid preparations that contain one or more medicaments, usually during a flavoured, sweetened base, and are intended to dissolve or disintegrate slowly within the mouth or these are medicated candy intended to be dissolved slowly within the mouth to lubricate and sooth the irritated tissues of throat Development of lozenges dates back to 20th century and is remain in commercial production.
- Lozenges are one among the widely used dosage forms.
- The advantages the medicated lozenges is that they increase the retention time of the dosage form in mouth which increases bioavailability, reduces gastric irritation and bypasses first pass metabolism.
- This dosage form are often adopted for local also as systemic therapy and a good range of active Ingredient are often incorporated in them lozenges or troches are experiencing a renewed popularity as a way of delivering many various drug products.

Figure no.:3: lozenges

INGREDIENTS UTILIZED IN THE FORMULATION OF LOZENGES: [11-12]

1. Candy Base: Base are liable for structure of lozenges Base possesses the very desirable physical property of controlling the crystallization of concentrated sugar solutions and maintaining freshness of the finished product through its humectant properties
    - Sucrose
    - Dextrose

- Mannitol
- Lactose
- Fructose

2. pH adjuster: It's use the maintain the pH within the formulation.
    - Citric acid
    - Acetic acid
    - Carboxylic acid
3. Polymer: Polymer are liable for releasing Patten of drug and supply the hardness of the lozenges.
    - Carboxyl methyl cellulose
    - Micro crystalline cellulose
    - Carbopol
    - HPMC K 30
4. Flavour: It liable for the test masking of the actual drug.
    - Ginger oil
    - Rose oil
    - Pippermnt oil
    - Lemon grass oil

METHOD OF PREPARATION: [13]

Heating congealing method:

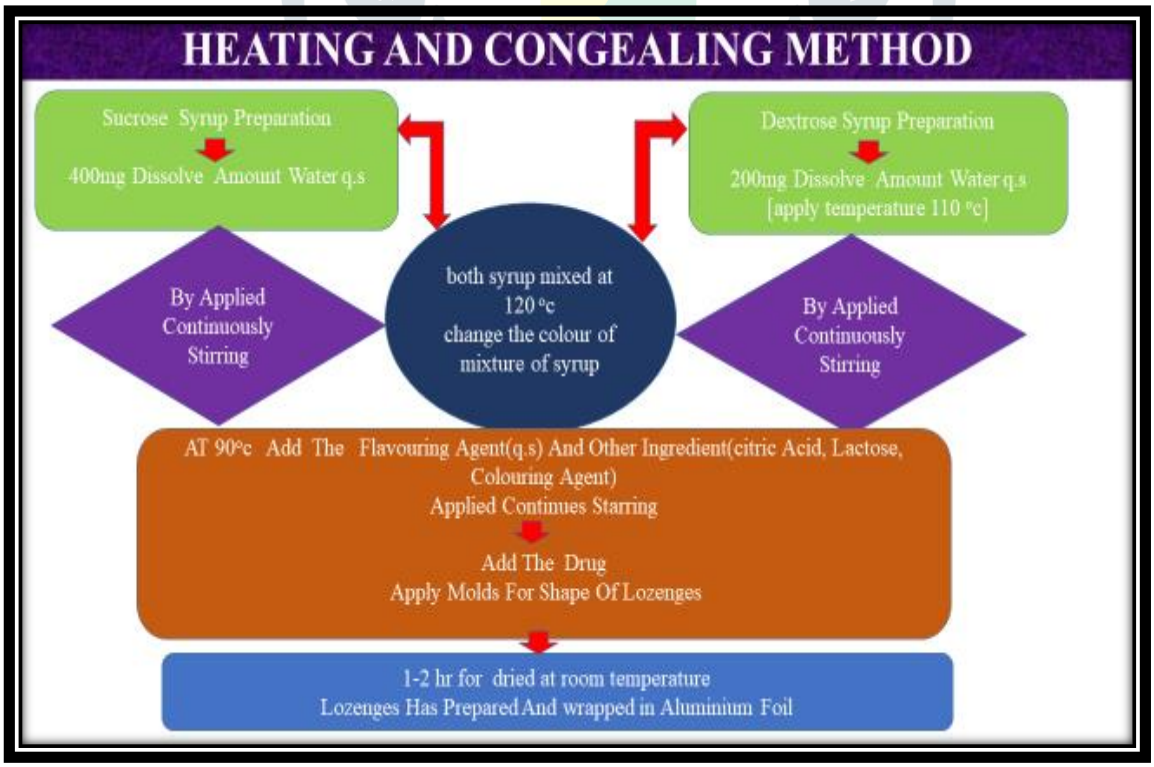


Figure No.4: Method of Preparation

EVALUATIONS PARAMETERS OF LOZENGES: [15-16-17-18-19]

- ✓ **Appearance:**

The samples were checked for any change in colour at monthly.

- ✓ **Thickness:**

The prepared Acebrophylline (Hard) candy lozenges were evaluated for Thickness (using Vernier Calipers)

- ✓ **Friability:**

The friability of the 20 lozenges from each batch was tested by a fribilator. speed of fribilator is 25 rpm and time is 4 min. The lozenges were then detested, reweighed and percentage weight loss was calculated by the equation,

% Friability = (initial Wt of lozenges - Wt. of lozenges after friability) × 100 / initial Wt of lozenges.

- ✓ **Hardness:**

To evaluate the diametrical crushing strength, 3 lozenges from each formulation were tested employing a MAC hardness tester. The mean ± SD values were calculated.

$$s = \sqrt{\frac{\sum(x - \bar{x})^2}{n - 1}}$$

- ✓ **Uniformity of weight (Average weight and Weight variation test):**

20 lozenges were selected and weighed collectively and individually on a balance. From the collective weight, average weight was calculated. Each lozenge weight was then compared with average weight to assure whether it had been within permissible limits or not. less than two of the individual weights deviated from the typical weight by quite 7.5% for 300 mg losenges and none by quite double that percentage.

$$\text{Average weight} = \frac{\text{weight of 20 lozenges}}{\text{W 20}}$$

$$\%\text{weight variation} = \frac{\text{average weight - weight of every tablet}}{\text{Average weight}} \times 100$$

- ✓ **Water Determination by Karl Fischer Titration:**

Four lozenges were powdered during a mortar and it had been taken as analyte. The Karl Fischer reagent was added from automated burette and therefore the endpoint decided Electrometrically. At the endpoint of the titration, a more than the reagent increased the flow of current which was measured in mill amperes. The air within the system kept dry with an appropriate desiccant and therefore the titration vessel was purged by means of a stream of dry

Nitrogen or current of dry air. .

- ✓ ***In vitro* mouth Dissolving Time** :

Mouth Dissolving Time decided by each batch formulation using USP disintegration apparatus, where lozenges were placed in each tube of the apparatus and time taken for the lozenges to dissolve completely in 100ml phosphate buffer of pH 6.8 at 37^0c. This test was wiped out triplicate. The typical dissolving time for lozenges was calculated and presented with variance.

- ✓ **Antimicrobial activity:**

This decide within in the agar diffusion medium employing Cup plate technique. Pure drug solution was used as standard. Drug extracted from formulations by help of methanol was used to make the test solution. The Quality(standard) solution and then make a formulations (test solution) which taken into separate cups bored into sterile agar previously seeded with organism (Candida albicans). After allowing diffusion of solutions for 2hrs, the plates were incubated for 48 hrs at 25 ºC. The zone of inhibition (ZOI) was compared thereupon of the quality. The optimized formulation was tested in triplicate.

✓ **Stability Studies**

To measure the drug and formulation stability, stability studies were done consisting with ICH and WHO guidelines. Optimized formulation Acebrophylline Lozenges were kept within the humidity chamber maintained at 40°C and 75% RH for 1 months. The sample were analysed for the physical changes and % drug content, in vitro release profile and other stability indicating parameters after 15 days and 1 month.

Conclusion:

Lozenges are oregano elliptically accepted formulations by the Asthma patients. Lozenges as medicated confections both for systemic and (local) native delivery of medicines are growing more popular. They're expected to accumulate more demand in pharmaceutical production as innovative dosage forms for potent drugs which seem to be a perfect dosage form. Lozenge provide easy administration, convenience to patient, large patient compliance and efficient treatment of low drug dosing, immediate onset of action, reduced dosage regimen and price effectiveness. New drug design during this area always benefit for the patient, physician and drug industries. This may offer better innovative dosage form. Lozenges enjoy a crucial position in pharmacy and can still remain at an equivalent in future.

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