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Review Article

Medicated Lozenges: An Updated Review

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ABSTRACT

Lozenges are palatable solid unit dosage form administered in oral cavity. Lozenges have been in use since 20th century and are still in commercial production. The lozenges are solid medicated, flavored and sweetened base dosage forms intended to be sucked and hold in the mouth/pharynx. The benefits of the medicated lozenges is they increase the retention time of the dosage form in oral cavity which increases bioavailability, reduces gastric irritation and bypasses first pass metabolism. Different types of lozenges available in market are caramel based medicated lozenges, compressed tablet lozenges, hard lozenges and soft lozenges and their methods of preparation along with ingredients used in their preparation are discussed. Lozenges have bright future as a novel method of delivering drugs for local action and systemic effect in the oral cavity. The present review covers more or less all aspects associated with lozenges and also throws light on the application of lozenges. It includes various researches till date, formulation and evaluation parameters, packaging and applications of lozenges.

Keywords: Lozenges, Troches, Local and Systemic delivery, Pastilles, Excipients.

INTRODUCTION

Oral drug delivery is the most flavored route for the administration of various medications and tablets are the most widely accepted dosage form. Solid dosage forms are popular because of the ease of administration, accurate dosage, self-medication, pain avoidance, and most importantly patient compliance. Among the major problems faced by many patients with conventional tablet dosage form is difficulty in swallowing. The word "Lozenge" is derived from French word "**Losenge**", which means a diamond shaped geometry having four equal sides. Lozenges are solid preparations that contain only medicaments, usually in a flavored, sweetened base, that are intended to dissolve or disintegrate slowly in the mouth.

They can be prepared by molding (gelatin or fused sucrose and sorbitol base) or by compression of sugar based tablets. Molded lozenges are sometimes referred to as **pastilles**, whereas

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compressed lozenges may be referred to as **troches**. Medicated lozenges are designed to increase retention of dosage form in oral cavity which increases bioavailability,reduces gastric irritation and bypasses first pass metabolism.

Drugs often incorporated into lozenges include analgesics, anesthetics, antimicrobials, antiseptics, antitussives, aromatics, astringents, corticosteroids, decongestants and demulcents. Sore throats, sores and other irritations in mouth and pharynx are common ailments that can cause pain. Most of the lozenges formulations are available as over the counter products where there is no need of prescription from a registered medical practitioner while some are prescribed by the medical practitioners.

Definition: Lozenges are various-shaped, solid dosage forms usually containing a medicinal agent and a flavoring substance, intended to be dissolved slowly in the oral cavity (mouth or pharynx) for localized or systemic effect. They are also called troches or pastilles.

Figure 1: Image of lozenges

ADVANTAGES OF LOZENGES

1. Ease of administration to pediatrics and geriatrics.
2. Production cost is less and better patient compliance.
3. Prolonged drug action.
4. Avoid first pass metabolism.
5. Local and systemic effect through oral cavity.
6. Easy to prepare, with minimum amount of equipment and time.
7. Suitable for patients having difficulty in swallowing (dysphagia).
8. Provides flavor and pleasant taste in mouth.

DISADVANTAGES OF LOZENGES

1. Possible draining of drug into the stomach.
2. Non ubiquitous distribution of drug in saliva for local therapy.
3. Accidental swallowing of entire dosage form.
4. Heat stable drugs are suitable.
5. Children having above 6 years of age can use lozenges safely.
6. Drugs having minimum bitter taste are suitable.
7. Hard lozenges become grainy.

TYPES OF LOZENGES

Lozenges are classified into various classes based on various methods like:

A) According to the site of action
   a) Local effects E.g. antiseptics, decongestants.
   b) Systemic effects E.g. vitamins, nicotine

B) According to texture and composition
   a) Chewy or caramel based medicated lozenge
   b) Compressed tablet lozenges
   c) Soft lozenges
   d) Hard candy lozenges
   e) Centre filled hard lozenges

C) 1) Antifungal lozenges
   2) Nicotine lozenges
   3) Zinc lozenges
   4) Throat lozenges
   5) Morning sickness lozenges
   6) Erectile dysfunction lozenges

TYPES OF LOZENGES AND THEIR MANUFACTURING

a) Chewy or caramel based medicated lozenges

These are the dosage form in which medicament is incorporated into a caramel base which is chewed instead of being dissolved in mouth. They are often highly fruit flavored and may have a slightly acidic taste to cover the acrid taste of glycerin. These are specially used for pediatric patients and are a useful means for administering medication for gastrointestinal absorption and systemic use. One of the more popular lozenges for pediatric use is the chewable lozenge or "gummy- type" candy lozenge.

Ingredients:

Candy base: It is made up of mixture of sugar and corn syrup in ratio of **50:50** to **75:25** sugars to corn syrup.

Humectants: They are used to improve chew and mouth feel properties and include glycerin, propylene glycol and sorbitol.

Whipping agents: They are used to incorporate air in toffee- based confections to obtain the desired degree of soft chew. Examples of whipping agents are milk protein, egg albumin, gelatin, xanthan gum, starch, pectin and carrageenan.

Lubricant: It includes vegetable oils and fats to avoid the sticking of candy to the teeth while chewing.

Medicament: 35-40 % of medicament is incorporated in lozenges.

Seeding crystals: Seeding crystals includes addition of fine powdered sugar at 3-10 % to warm candy mass to speed up the crystallization.

Flavors: E.g. Ginger, clove, mint etc.

Manufacturing Process:
The candy is cooked at 95-125°C and transferred to planetary / sigma blade mixer. Mass is allowed to cool to 120°C. This is followed by addition of whipping agent below 105°C. Then medicaments are added between 95-105°C. Colour is dispersed in humectants and added below 85°C followed by lubricant addition above 80°C. Chewable or caramel lozenges are formed in the form of long rope of suitable thickness cut to a desired size and then packed by using wrappers. This process is called as rope forming.

b) Compressed tablet lozenges
When the active ingredient is heat sensitive (thermolabile), it may prepared by compression. The granulation method is similar to that of any compressed tablet. These tablets differ from conventional tablets in terms of:

- Organoleptic property
- Non-disintegrating characteristics
- Slower dissolution profile

The lozenges is made using heavy compression equipment to give a tablet that is harder than usual, as it is desirable for the troche to dissolve slowly in mouth. Lozenges are usually flat faced with size of 5/8-3/4 inch, weight 1.5-4 kg, hardness 30-50 kg inch Sq. and erosion time ranges between 5-10 min.

Ingredients: Tablet base
Sugar: Dextrose, sucrose.
Sugar free vehicles:Sorbitol, mannitol, polyethylene glycol 6000 and 8000.
Other fillers: Calcium carbonate, di calcium phosphate, calcium sulphate, microcrystalline cellulose.
Binders: It helps to hold the particles of mass as discrete granules. Binders used for manufacturing of compressed tablet lozenges are acacia, corn syrup, sugar syrup, gelatin, polyvinyl pyrrolidone, tragacanth and methylcellulose.

Lubricants: These are used to improve flow of final troche mixture and include magnesium stearate, calcium stearate, stearic acid and PEG.

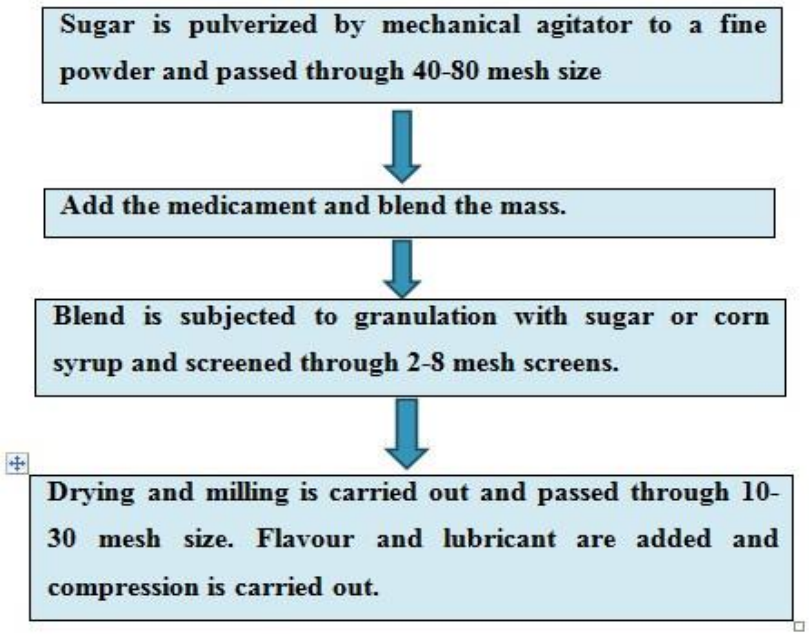
Colours: Water soluble and lakolene dyes.

Flavors: Zinger, clove, mint etc.

Manufacturing process
I. Direct Compression: - In this method all the ingredients are thoroughly mixed and directly compressed in to lozenges tablets.

II.Wet Granulation :- Sucrose is pulverized by mechanical combination to a fine powder then add binder solution and mass is formed and passed through sieve no.16 granules formed and dried then add lubricant, flavor prior to thecompression.

Direct compression process:



c) Soft lozenges

Soft lozenges have become popular because of the ease of preparation and applicability to a wide variety of drugs. Polyethylene glycol 1000 or 1450, chocolate or sugar, acacia base are used as base in the soft lozenges formulation and they gives soft texture to the lozenges. Some soft lozenges contain acacia and silica gel. One form of these soft lozenges is the pastille, which is defined as a soft variety of lozenge, usually transparent, consisting of a medication in a gelatin, glycerogelatin or acacia, sucrose base. Soft lozenges are similar to a historical form of medication that is making a comeback to the "confection".

Ingredients:

Base: Polyethylene glycol 1000, polyethylene glycol 1450, chocolate, sugar acacia base.
Suspending agent: silica gel

Manufacturing Process

These can be hand rolled and then cut into pieces or the warm mass is poured into the plastic mould. Mould cavity should be overfilled if PEG is used, as polyethylene glycol contracts as they cool. These not required in case of chocolate as it does not shrink.

c) Hard candy lozenges

Hard candy lozenges are consisting of sucrose, other sugar/carbohydrate in an amorphous or glassy state. Hard candy lozenges manufactured by cooking processes by dissolving desired quantity of sugar to prepare the candy base and other carbohydrates in one third amount of water in the candy cooker at temperature about 110°C. If corn syrup is used for the manufacturing of hard candy lozenges, the temperature should be kept in between 145-156°C. 2-4% medicaments are incorporated in hard candy lozenges. Moisture content should be between 0.5-1.5% and weight of hard candy lozenges lie between 1.5-4.5gm.They undergo slow and uniform dissolution over 5-10min. High temperature is required for the preparation of hard lozenges so heat sensitive ingredients are not suitable for this formulation.

Ingredients:

Base: This includes corn syrup, which is available on Baume basis. A 43° baume corn syrup is preferred in hard candy lozenges. Sugar base, candy base are also used.

Sweeteners: It involves sucrose, dextrose, maltose, lactose

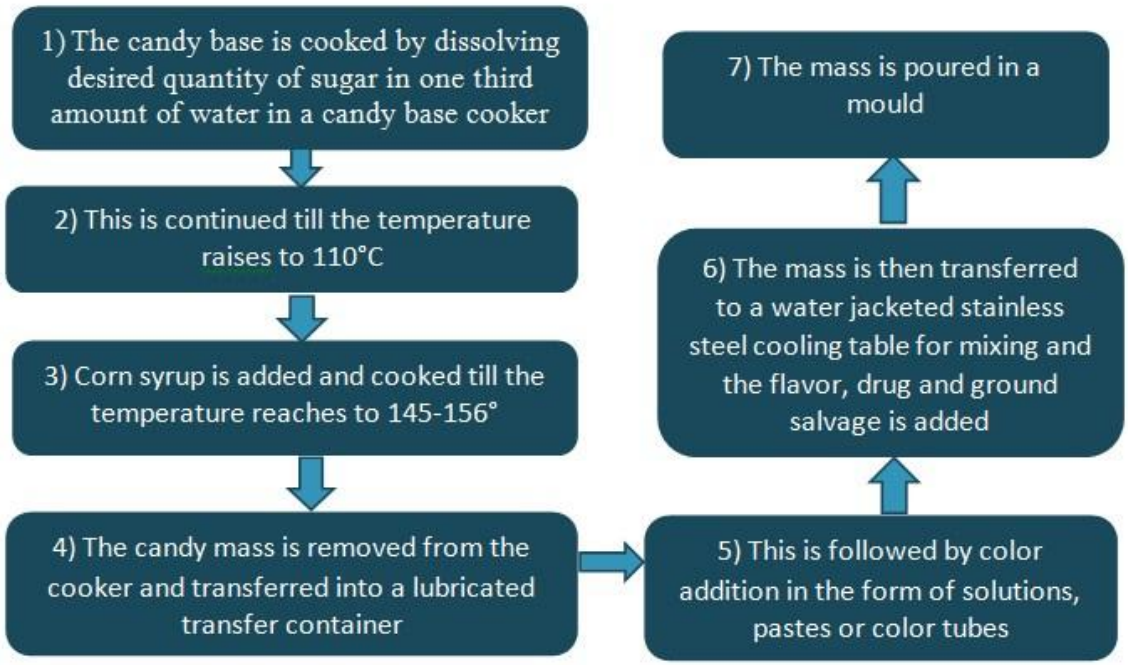
Acidulents: Citric acid, tartaric acid, fumaric acid, malic acid are used as acidulents. These are added to candy base to strengthen the flavor characteristics of the finished products.

Colours: Colours approved by FD and C like orange, red, green, yellow.

Flavour: Menthol, eucalyptus oil, spearmint, and cherry flavour.etc.

Medicament:2-4% medicament can be incorporated in the hard candy lozenges.

Manufacturing Process



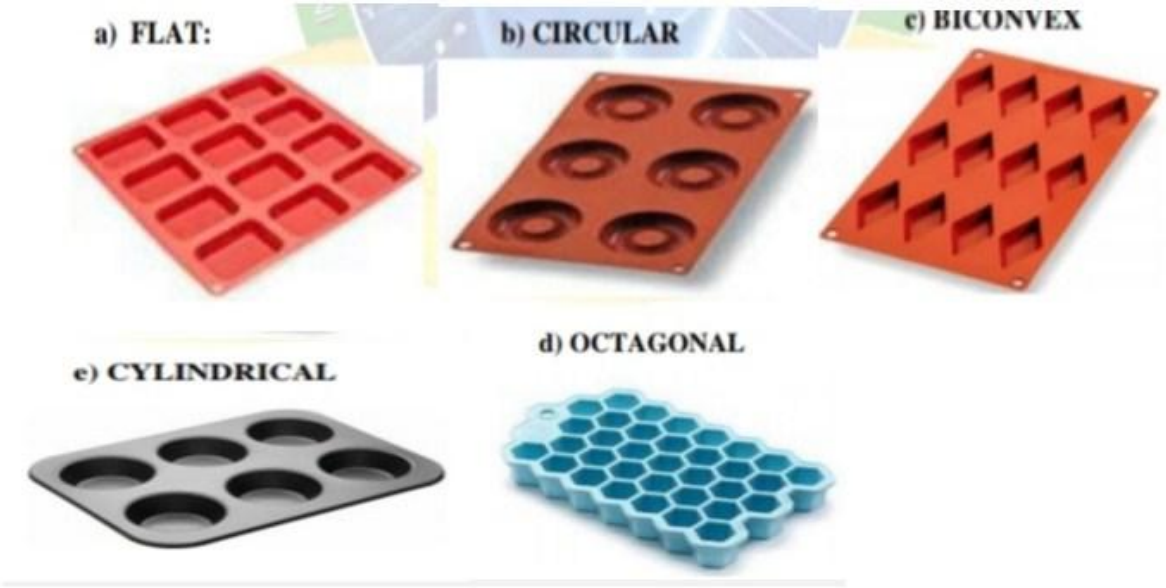


Figure 2: Lozenges moulds

Table 1: Excipients used

Sr.no	Ingredients	Example
1.	a) Sugar b) Sugar free vehicles c) Fillers	Dextrose, sucrose, maltose, lactose. Mannitol, sorbitol, polyethylene glycol (PEG) 600 and 800. Di calcium phosphate, calcium sulfate, calcium carbonate, lactose microcrystalline cellulose.
2.	Lubricants	Magnesium stearate, calcium stearate, stearic acid and PEG, vegetable oils and fats.
3.	Binders	Acacia, corn syrup, sugar syrup, gelatin, polyvinyl pyrrolidone, tragacanth and methylcellulose.
4.	Coloring agents	Water soluble and lakolene dyes, FD & C colors, orange color paste, red color cubes, etc.
5.	Flavoring agents	Menthol, eucalyptus oil, spearmint, cherry flavor, etc.
6.	Whipping agents	Milk protein, egg albumin, gelatin, xanthan gum, starch, pectin, algin and carrageenan
7.	Humectants	Glycerin, propylene glycol and sorbitol.

Table 2: Flavoring agents

Flavors	Examples
Salty	Butterscotch, Maple, Nutty, Buttery
Bitter	Coffee,Liquorice, Mint, Chocolate, Peach, Grapefruit, Cherry
Acrid	Fruit, Berry, Lemon, Orange, Raspberry, Vanilla, Lime
Sour	Acacia, Raspberry, Berries, Fruits
Oily	Syrup
Sweet	Peppermint, Anise, Vanilla
Metallic	Mint, Grape, Marshmallow, Citrus, Berries

EVALUATION OF MEDICATED LOZENGES: Theprepared lozenges were evaluated for parameters like weight variation, hardness, drug content, thickness, diameter, friability, moisture content, in-vitro dissolution test &stability.

I. Thickness & Diameter
The thickness of the lozenges was measured using Vernier calipers or screw gauge. The lozenges were inserted between the jaws after making sure that the pointer was set to zero. The readings of main scale and Vernier scale were measured. This is measured in mm. The mean thickness and diameter is calculated.

Figure 3: Vernier caliper

II.Weight Variation: According to weight variation test, The 20 lozenges were selected randomly and each of them weighed individually and collectively on a digital weighing balance. Average weight per lozenges was calculated from the collective weight. Then the weights of the individual lozenge were compared with the average wt. to determine the weight variation.

Figure 4: Digital weighing balance

III. Friability test: Friability was determined by using Roche friabilator.The 20 lozenges were taken on a friabilator and were operated for 4 min at 25 rpm. Then the lozenges were taken after 4 min and they were then made free from the dust and reweighed. Then the % friability was calculated and % loss was calculated.

Fig.5. Roche friabilator

IV. Drug content: Appropriate no. of lozenges are crushed and dissolved in an appropriate solvent and the absorbance of the solution is measured spectrophotometrically.

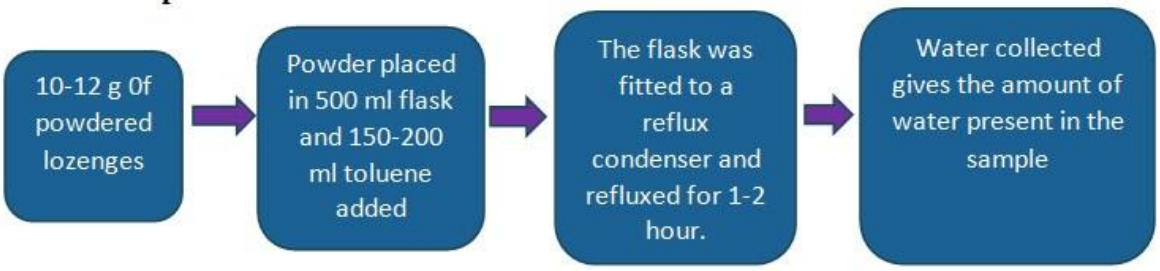
V. Hardness: The hardness of lozenge was measured using **MONSANTO HARDNESS TESTER,** where the force required to break the lozenge was noted. 3 lozenges were tested.

Fig.6. MONSANTO hardness tester

VI. Moisture content analysis: Moisture content in the lozenge was determined by using **Helium Moisture Balance** apparatus. Sample was weighed and crushed in mortar from that 1 gm of sample weight and placed in a desiccator for 24hrs after sample was weighed and moisture content is determined by moisture balance apparatus or by abstracting the final weight with initial weight of lozenges. Moisture analysis can be done by using 3 methods like:

a. Gravimetric analysis: Weigh accurately about 1 g of sample and note the initial weight. It is then placed in a vacuum oven at 60-70°C for 12-16 hours. After specific period of time, weigh againthe sample and the moisture content can be calculated by subtraction of final weight from initial weight. Moisture content can be calculated by:
Moisture content: Initial weight – final weight

b. Azeotropic distillation method



C. Karl Fisher titration

A sample of the prepared lozenges is calculated to contain 10-250 mg water is taken in titration flask and then it is titrated with Karl fisher reagent.

VII. Mouth dissolving time test : The time taken by lozenge to dissolve completely was determined by the USP disintegration apparatus where hard lozenge were placed in each tube of apparatus and time taken for the lozenge to dissolve was noted by using phosphate buffer of PH 6.4 at 37°C. The test was performed 3 times and average dissolving time was calculated and presented with standard deviation.

VIII. In-vitro dissolution studies: In-vitro dissolution studies were carried out using dissolution test apparatus type II (paddle type) at 100 rpm and 37 +0.5°C PH 6.8 buffer containing 2% SLS was used as dissolution medium for in-vitro dissolution studies. A lozenge was placed in each flask of the dissolution apparatus and sample of 5 ml were withdrawn at predetermined time travels for 60 min in order to maintain sink conditions an equal volume of medium was replaced. The sample was analyzed by using UV visible spectrophotometer at specific nm and % drug released was calculated. This experiment was done in triplicate and the average % released was calculated.

Fig.7. Dissolution apparatus

IX. Drug excipient interaction studies: Determined by FTIR.

X. Microbial check: In this, the presence of any bacterial, mold or spore contamination is checked in raw materials, finished products, machinery, cooling tunnels, environmental conditions and storage drums. Laboratory microbial testing should include the following counts:

- Total plate
- Total coliform
- Yeast and mold
- E.coli
- Staphylococcus
- Salmonella

XI. Stability testing

1) Lozenges are subjected to stability testing under following conditions:
- 1-2 months at 60°C
- 3-6 months at 45°C
- 9-12 months at 37°C
- 36-60 months at 25°C and 4°C

2) Stability testing of products in package
- 25°C at 80% RH for 6-12 months
- 37°C at 80% RH for 3 months
- 25°C at 70% RH for 6-12 months

Storage: These preparations should be stored away from heat and out of the reach of children.They should be protected from extremes of humidity. Depending on the storage requirement of both the drug and base, either room temperature or refrigerated temperature is usually indicated.

Packaging: Since the lozenges are hygroscopic in nature, a complex and multiple packaging is used. The individual unit is wrapped in a polymeric moisture barrier material which are then placed in tight or moisture resistant glass, polyvinyl chloride

or metal container that is over wrapped by aluminum foil or cellophane membrane.

Application of Lozenges

- Lozenges are used for the treatment of local as well as systemic disorders.
- A variety of drug candidates can been incorporated in them for the treatment and relief from conditions of oral as well as throat infections such as oral thrush, sore throat, cough, gingivitis, pharyngitis, decongestant, etc.
- Lozenges are also have been used to deliver the drug systemically for smoking cessation and pain relief.

Table 3: Various marketed preparations

Sr. No.	Marketed brand	Drug	Use
1	Sore throat lozenges	Menthol & Benzocaine	Oral anesthetic
2	Strepsils	2,4Dichlorobenzyl alcohol+amylmetacresol	Sore throat
3	ORAC 99k	Turmeric	Ayurveda proprietary medicine
4	Prospan	Hrdera helix extract	Chesty cough relief
5	Cepacol	Menthol, benzocaine	Sore throat
6	Nicorette	Nicotine	Smoking cessation
7	Zinc lozenges	Vitamin C, ecbinacea	Dietary supplement
8	Difflampus	Benzydiamine hydrochloride	Anesthetics

CONCLUSION

Lozenges are medicated confections that have been developed about 20th century ago and are still under commercial production. They are designed for local as well as systemic therapy. The formulation of lozenges is an easy and time saving process. These will have additional advantages of patient compliance, convenience and comfortless for efficient treatment including low dose, immediate onset of action, reduced dosage regimen and economic. Lozenges enjoy an important position in pharmacy and will continue to remain so in future.

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