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Review on Lozenges

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Abstract

Lozenges are one of the widely used dosage forms. 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. Lozenges provide a palatable means of dosage form administration and enjoy its position in pharmaceutical market owing to its several advantages but it suffers from certain disadvantages too. This dosage form can be adopted for local as well as systemic therapy and a wide range of active ingredient can be incorporated in them. The present review covers more or less all aspects associated with lozenges and also throws light on the applications of lozenges.

Keywords: Lozenges, Troches, Molding

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Introduction

Lozenges are the flavored medicated dosage forms intended to be sucked and held in the mouth or pharynx containing one or more medicaments usually in the sweetened base [1,2]. Lozenges are intended to relieve oropharyngeal symptoms, which are commonly caused by local infections and also for systemic effect provided the drug is well absorbed through the buccal linings or when it is swallowed [3].

Lozenges are used for patients who cannot swallow solid oral dosage forms as well as for medications designed to be released slowly to yield a constant level of drug in the oral cavity or to bathe the throat tissues in a solution of the drug. Drugs often incorporated into lozenges include analgesics, anesthetics, antimicrobials, antiseptics, antitussives, aromatics, astringents, corticosteroids, decongestants, and demulcents. However, this is by no means an exhaustive list as many other drugs may lend themselves to delivery by a lozenge. As well, both single and multi-ingredient lozenges can be compounded, depending on the particular patient's needs [4].

Advantages and disadvantages of medicated lozenges [5-8]

Lozenges offer many advantages to formulation scientists like they avoid first pass metabolism, thus increase in bioavailability can be used for purpose of both local and systemic effect through buccal mucosa, offer better patient compliance can be given to those patients who have difficulty in swallowing and easy to manufacture and store. Medicated lozenges also have drawbacks like non-ubiquitous distribution of drug within saliva for local therapy and possible draining of drug from oral cavity to stomach along with saliva.

(d) Hard lozenges [8,9]

Classification of Lozenges [9]

Lozenges can be classified into various classes based on various methods like

(A) According to the site of action

(a) Local effect

Ex. Antiseptics, Decongestants.

(b) Systemic effect

Ex. Vitamins, Nicotine.

(B) According to texture and composition-

(a) Chewy or caramel based medicated lozenges [1]

These are the dosage form in which medicament is incorporated into a caramel base which is chewed instead of being dissolved in mouth. . Most formulations are based on the glycerinated gelatin suppository formula which consists of glycerin, gelatin, and water. These lozenges are often highly fruit flavored and may have a slightly acidic taste to cover the acrid taste of the glycerin.

(b) Compressed tablet lozenges [8,9]

When the active ingredient is heat sensitive, it may be prepared by compression. The granulation method is similar to that used for any compressed tablet. These tablets differ from conventional tablets in terms of organoleptic property, non disintegrating characteristics and slower dissolution profiles.

(c) Soft lozenges [4,7,10]

They are either meant for chewing or for slow drug release in mouth. They can be made from PEG 1000 or 1450, chocolate or sugar-acacia base while some soft candy formulations can also contain acacia and silica gel. Acacia is used to provide texture and smoothness and silica gel is used as a suspending agent to avoid settling of materials to the bottom of the mold cavity during the cooling. The formulation requires heating process at about 50 ^{0}C, hence is only suitable to heat resistant ingredients.

These are mixtures of sugar and other carbohydrates in an amorphous (non crystalline) or glassy state. They can also be regarded as solid syrups of sugars.

The moisture content and weight of hard candy lozenge should be in between, 0.5 - 1.5% and 1.5-4.5 g respectively. These should undergo a slow and uniform dissolution or erosion over 5-10 min., and they should not disintegrate.

Disadvantage: The temperature required for their preparation is high hence heat labile materials cannot be prepared.

Table – 1: Types of Lonzenges

Sl. No	Type of centre filled lozenges	Composition	Fill weight (%)
1.	Liquid fill	Fruit juice, sugar syrup, hydro alcoholic solutions or Sorbitol solution.	10-20
2.	Fruit center	Jams and jellies whose viscosity has been modified with corn syrup or liquid sucrose	20-25
3.	Paste center	Granules and crystals formulated as paste	40
4.	Fat center	Medicament or flavor being suspended or dissolved in hydrogenated vegetable oil	25-32

Table – 2 : Formulation of Lonzenges

Ingredients	Examples
Candy base	
a. Sugar	Dextrose, sucrose, maltose, lactose.
b. Sugar free vehicles	Mannitol, sorbitol, polyethylene glycol (PEG) 600 and 800.
c. Fillers	Di calcium phosphate, calcium sulfate, calcium carbonate, lactose, microcrystalline cellulose.
Lubricants	Magnesium stearate, calcium stearate, stearic acid and PEG, vegetable oils and fats.
Binders	Acacia, corn syrup, sugar syrup, gelatin, polyvinyl-pyrrolidone, tragacanth and methylcellulose.
Coloring agents	Water soluble and lakolene dyes, FD & C colors, orange color paste, red color cubes, etc.
Flavorings agent	Menthol, eucalyptus oil, spearmint, cherry flavor, etc.
Whipping agent	Milk protein, egg albumin, gelatin, xanthan gum, starch, pectin, algin and carrageenan.
Humectants	Glycerin, propylene glycol and sorbitol.

Center filled hard Lozenges [10]

These are the hard candy lozenges with soft or liquid centers into their main body. Types of centre filled lozenges are as explained in the Table-1.

Formulation of Lozenges

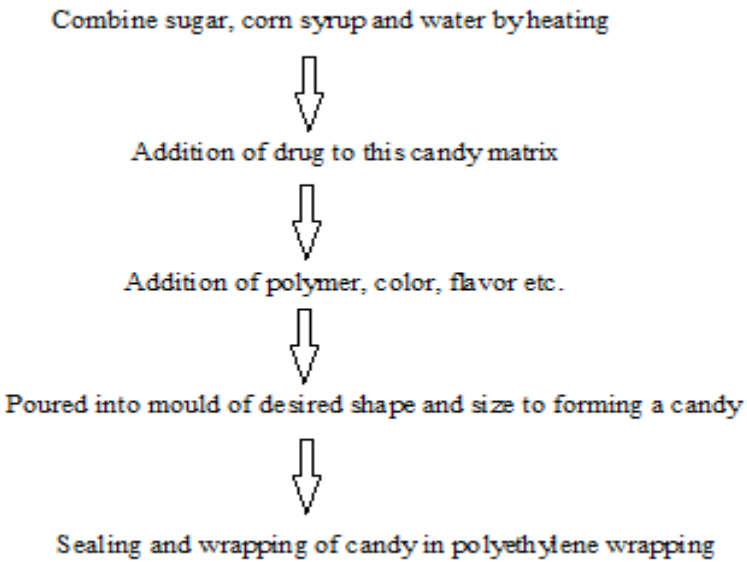
Lozenges are formulated in such a way that they are stable, provide a good medium for administration of drugs. The ingredients which are used for formulation of Lozenges are as shown in table-2.

Criteria for preparation of medicated Lozenges

- Selection of Drug Candidate
- Selection of Drug Carrier

Method of preparation of medicated Lozenges [11-13]

Technique used → heating and congealing.



General consideration for designing medicated Lozenges [14-17]

Since the development cost of a new chemical entity is very high, the pharmaceutical companies are now focusing on the development of new drug delivery systems for existing drug with an improved efficacy and bioavailability together with reduced dosing frequency to minimize side effects Typically, oral candidacies takes the form of an adherent white, curd like, circumscribed plaque anywhere within the oral cavity. There are many drugs dosage forms like lozenges, tablets, inhalers, and syrups, are in markets for the treatment of the same. The “lozenges are flavoured medicated dosage forms intended to be sucked and hold in the mouth/ pharynx. These preparations are commonly used for the purpose of local effect or systemic effect”. New drug design to this area always benefit for the patient, physician and drug industry. There are several dosage forms like in the market; there is a need for more dosage forms which acts effectively and locally as well as systematically.

Evaluation of medicated Lozenges

(A) Quality Control [9, 14, 16]

(1) Candy base – It has to be check for following parameters-Corn syrup, sugar delivery gears, Temperature, steam pressure and cooking speed of precookers and temperature, steam pressure, cooking speed and vacuum of candy base cookers.

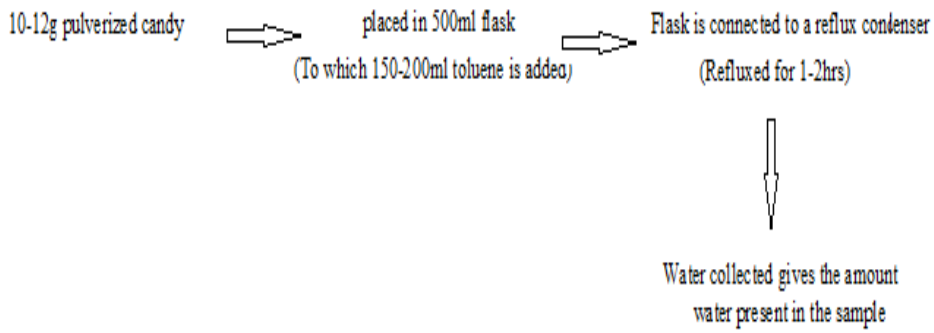
(2) Moisture analysis -

a) Gravimetric method- 1g of sample is placed in vacuum oven at 60-70^{o}C for 12-16hrs. After specified period of time, weigh the sample and moisture content is calculated by subtraction of final weight from initial weight.

Moisture Content =Initial weight – final weight

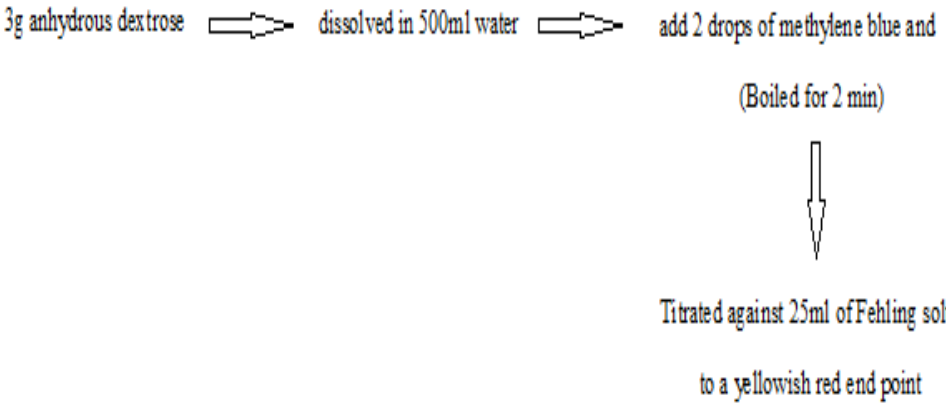
b) Karl Fisher titration- A sample calculated to contain 10-250mg water is taken in titration flask and titrated with Karl Fischer reagent.

c) Azeotropic distillation method



(3) Determination of sugar and corn syrup ratios-This is done by "Dextrose equivalent method: Lane Eynon Titration method".

(4) Percentage reducing sugars-



$$\text{Percent reducing sugar} = \frac{\text{Reducing sugar factor} \times 100}{\text{Sample wt.}/250 \times \text{Vol. of sample solution consumed by Fehling's sol}^{n}}$$

(5) Salvage solutions- Determined using a refractometer.

(6) Forming checks- Involves a check on candy rope diameter.

(7) Cooling checks- Visual inspection is performed in order to analyze any stress cracking due to rapid cooling, air bubble formation, surface cracking and black specks.

(B) Physical and Chemical Testing [12, 13]

(1) Diameter and thickness- Diameter of the lollipop is important for uniformity of lozenges size. It can be measured using Vernier Calipers. The extent to which the diameter of the lozenges deviated from ± 5% of the standard value.

(2) Hardness- The resistance of lozenges to shipping or breakage under conditions of storage, transportation and handling before usage depends on its hardness. The hardness of lollipops can be measured by using Monsanto hardness tester. The hardness was measured in terms of kg/cm^2.

(3) Weight Variation- The USP weight variation test is done by weighing 20 lozenges individually, calculating the average weight and comparing the individual weights to the average.

$$\textbf{Weight Varation} = \frac{\textbf{Average weight} - \textbf{Initial weight}}{\textbf{Average weight}}$$

(4) Drug excipients interaction studies- Determined by FTIR.

(5) Friability - Determined by Roche Friabilator operated at 25rpm for 4min.

(6) In-vitro drug release- This is carried out in USP II paddle type dissolution apparatus.

(7) Drug content- Appropriate number of lollipop are crushed and dissolved in an appropriate solvent and the absorbance of the solution is measured spectrophotometrically.

Table – 4: Therapeutic applications of medicated Lozenges [17]

S.No.	Therapeutic uses	Examples
1.	Anesthetic	Lidocaine, benzocaine
2.	Analgesic	Fentanyl, codeine, ketamine
3.	Antifungal	Clotrimazole, miconazole, amphoteresin B
4.	Smoking cessation	Nicotine
5.	Nausea relief	Ondansetron, promethazine, ginger root

(C) Microbial check [11]

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

(D) Stability testing [9]

(1)Lozenges are subjected to stability testing under following conditions-

- 1-2 months at 60^oC
- 3-6 months at 45^oC
- 9-12 months at 37^oC

- 36-60 months at 25° C and 4°C.

(2) Stability testing of product in package-

Lozenges in their final packs are subjected to following conditions for stability testing:

- 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.

Conclusion

The formulation of lozenges is an easy and time saving process. It is a formulation which is more organoleptically accepted particularly by the pediatrics patients. Medicated Lozenges will be ideal dosage forms for pediatric patients. These will have additional advantages of patient compliance, convenience and comfortness for efficient treatment including low dose, immediate onset of action, reduced dosage regimen and economic. This will offer better innovative dosage form. Lozenges enjoy an important position in pharmacy and will continue to remain at the same in future.

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Table - 3: Marketed Lozenges and their ingredients

Sl. NO	Product	Main Ingredients	Other Ingredients	Indication	Marketed by
1.	VICKS®	Menthol	ascorbic acid, citric acid, eucalyptus oil, FD&C Blue No. 1, FD&C Red No. 40, flavor, liquid glucose, sucrose.	sore throat	Procter and Gamble manufacturing company
2.	THERA ZINC®	Zinc (Gluconate)	Vitamin A (Acetate) 500 IU, A proprietary blend of Slippery Elm Bark (Ulmus Fulva) f Echinacea (4:l), Propolis, Elderberry, Larch and Mullein. Natural flavors.	common cold and flu	Quantum health care
3.	NICORETTE®	Nicotine	aspartame, calcium polycarbophil, flavor, magnesium stearate, mannitol, potassium bicarbonate, sodium alginate, sodium carbonate, xanthan gum	smoking cessation	Perrigo company
4.	STREPSILS®	Amylmetacresol, dichlorobenzyl alcohol	Hexylresorcinol, sucrose, glucose, levomenthol, blackcurrant flavour (contains propylene glycol), carmoisine edicol (E122), patent blue V (E131).	Sore throat and blocked nose	Reckitt Benkiser healthcare Ltd.
5.	CLOTRIMAZOLE LOZENGE®	Clotrimazole	Croscarmellose Sodium Dextrates, magnesium stearate, Cellulose Microcrystalline, Povidone	Oral thrush	Perrigo company
6.	SUCRETS®	Dextromethorphan Hydrobromide	Corn Syrup, D&C Yellow 10,Hydrogenated Palm Oil, Menthol, N&A Honey Lemon Flavor, Sugar	Sore throat	Insight Pharmaceuticals
7.	CEPACOL®	Menthol,	cetylpyridinium chloride	Sore throat	Combe incorporated

		benzocaine	(Ceepryn®), glucose, peppermint oil, propylene glycol, sucrose, yellow 10		
8.	VIGROIDS®	Liquorices	Maize starch, menthol, kaolin, tragacanth, eucalyptus oil, peppermint oil, tolu tincture	Expectorant	Ernest Jackson and Company Ltd.
9.	CHLORASEP--TIC®	Benzocaine	Corn Syrup, FD&C Red #40, Flavor, Glycerin, Soy Lecithin, Sucrose, Water	Relief of minor sore throat and mouth pain	Prestige Brands lnc.
10.	LOCKETS®	Eucalyptus and menthol	Sugar, Glucose syrup, Honey, Glycerol, Citric Acid, Vitamin C, Monopropylene Glycol, Colors E122 and E142.	Nasal congestion and sore throat	Wrigley Company
11.	KOFLET-H®	Madhu	Haritaki, Trikatu, Kulanjana (Alpinia galanga) Khadira (Acacia catechu) Oils. Lavanga, Sukshmaila (Elettaria cardamomum), Darusita (Cinnamomum zeylanicum, Sugar base q.s	Alleviate cough and quickly relieves throat irritation	Himalaya Herbal Healthcare
12.	SUALIN®	Glycyrrhiza glabra	Aadhatoda vesica, ocimum sanctum, mentha arvensis, pimpenella anisum, eucalyptus citriodora zeylanicum, piper cubaba.	Influenza, bronchitis, sore throat, cold and cough, congestion of head and lungs	Hamdard (WAKF) Laboratories