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Lozenges Formulation and Evaluation: A Review

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ABSTRACT: Lozenges are palatable unit dosage form administrated in the oral cavity, which is the most common route and easiest way of administering a drug and have a bright future as novel method of delivering drugs for local and systemic effect. However, pediatric, geriatric patientsshow less compliance in swallowing tablets and capsules due to difficulties in swallowing and bitter taste of many drugs when formulated as liquid dosage form. The benefit of the medicated lozenges is they increase the retention time of the dosage form in the oral cavity which increases bioavailability and reduces first pass metabolism. The present review covers all aspects associated with lozenges like its advantages and disadvantages, its types and their preparation methods, criteria for selecting flavoring agents and quality control of lozenges. The medicaments which can be formulated as lozenges include local anesthetics, antihistamines, antitussives, antiseptics, decongestants, demulcents and antibiotics.

KEYWORDS:Lozenge, Troches, Pastilles, Medicaments.

I. INTRODUCTION:

Lozenges are enhanced cured dose structures expected to be sucked and held in the oral depression or pharynx containing at least one medicament. They can be set up by embellishment or by pressure. Shaped lozenges are in some cases called as pastilles, while compacted lozenges are alluded to as troches [1,2].Among the serious issues looked by numerous patients with conventionaltablet measurements structure is trouble in gulping. This issue is clearer when drinkingwater isn't effectively free to the patient taking medication. Dispersible tablet conveyance framework ischaracterized by quick deterioration, speedy dissolving, fast delivery and improved patientcompliance. Trouble in gulping (dysphagia) is a typical issue of all age gatherings, particularly the old and pediatrics, due to physiological changes related with those gatherings. Different classifications that experience issues in using customary oral measurement structures incorporate the intellectually sick, uncooperative and patients experiencing queasiness, movement affliction, unexpected scenes of hypersensitive assault or hacking. Now and then it very well might be hard to swallow conventional items because of non-accessibility of water. These issues prompted the advancement of a novel sort ofsolid oral dose structure consequently, an appealing, taste veiling plans are the need of great importance [3].

1.1ADVANTAGES:

→ It very well may be given to those patients who experience issues in gulping.
→Simple to regulate to geriatric and pediatric populace.
→ It broadens the hour of medication in the oral cavity to evoke a particular impact.
→ Foundational assimilation of medication can be conceivable through buccal cavity.
→ Taste of medication can be veiled by sugars and flavors utilized in definition.
→ It can increment in bioavailability.
→ It can decrease dosing recurrence.
→ No disintegration.
→ Do not require water for intake.
→ Less production time.
→ Less production cost.
→ Lozenge can be withdrawn if dose is not needed.

1.2DISADVANTAGES:

→Some drug may not be suitable with aldehyde candy bases e.g. Benzocaine.
→ The non-ubiquitous distribution of drug within saliva for local therapy.
→ Possible draining of drug from oral cavity to stomach along with saliva.
→ The lozenges dosage form could be used as candy by children mistakenly.

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→ A hard candy lozenges is a high temperature required for their preparation [4,5].

1.3CLASSIFICATIONOFLOZENGES:
→According to the site of action
(a) Local effect Ex. Germicides, Decongestants. (b) Systemic impact Ex. Nutrients, Nicotine.
→According to texture and composition
(a) Chewy or caramel based medicated lozenges (b) Compressed tablet lozenges (c) Soft lozenges (d) Hard sweets lozenges.

1.3.1 Chewy or caramel basedmedicated lozenges: These are the dose structure in which medicament is fused into a caramel base which is bitten as opposed to being broken down in mouth. These tablets are regularly exceptionally natural product seasoned and may have a somewhat acidic taste to cover the harsh taste of the glycerin. These tablets are particularly utilized for pediatric patients and are an extremely viable methods for directing prescriptions for gastrointestinal ingestion and fundamental use. One of the more famous lozenges for pediatric use is the chewable lozenge, or "sticky sort" candylozenges. These gelatin-based pastilles were set up by emptying the dissolve into molds or out onto a sheet of uniform thickness.

Fig no 1: Chewy Lozenges

1.3.2Compressed tablet Lozenges: When the drug is heat sensitive, it could be set up by compression. The granulation strategy is like that utilized for any compacted tablets. These lozenges vary from traditional tabletsin
→ Organoleptic property
→Non disintegrating characteristics
→Slower dissolution profiles.
The lozenge 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.

Fig no 2: Compressed Lozenges

1.3.3 Soft Lozenges: Soft capsules have become well known in light of the simplicity of impromptu arrangement and materialness to a wide assortment of medications. The bases for the most part comprise of a combination of different polyethylene glycols, acacia or comparable materials. One type of these delicate capsules is the pastille, which is characterized as a delicate assortment of tablet, generally straightforward, comprising of a medicine in a gelatin, glycerogelatin or acacia: sucrose base.Soft lozenges are like a recorded type of prescription that is making a rebound the "dessert". Desserts are characterized as intensely saccharinated, delicate masses containing therapeutic specialists. The improvement in their present use is to a great extent because of the utilization of polymers (polyethylene glycols) as the framework for the measurements structure. They are anything but difficult to utilize, helpful to convey, simple to store (room temperature), and are by and large wonderful tasting. Polyethylene glycol-based capsules may tend to be hygroscopic and may relax whenever presented to high temperatures.

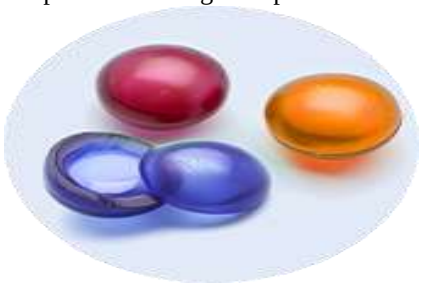

Fig no 3: Soft Lozenges

1.3.4 Hard Candy Lozenges: Hard candy lozenge are combinations of sugar and different starches in anamorphous (nanocrystalline) or smooth state. They can likewise be viewed as strong syrups of sugars. The dampness substance and weight of hard candy lozenges ought to be between, 0.5 to 1.5 % and 1.5 - 4.5 g individually. This ought to go through a moderate and uniform disintegration or

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disintegration more than 5 - 10 min., and ought not deteriorate. The temperature necessities for their arrangement is typically high henceforth heat labile materials cannot be incorporated in them. These pastilles were set up by Heating and solidifying strategy[6].

Fig no 4: Hard Lozenges

II. MANUFACTURING:

Chewy or caramel basedmedicated lozenges:

The candy base is cooked at 95-125^{O}C and moved to planetary or sigma cutting edge blender. Mass is permitted to cool to 120^{O}C. This is trailed by the expansion of whipping specialist underneath 105^{O}C. The medicaments are then added between 95-105^{O}C. Shading is scattered in humectant and added to the above mass at a temperature above 90^{O}C. Cultivating precious stones and flavor are then added beneath 85^{O}C followed by grease option above 80^{O}C. Confections are then shaped by rope forming.

2.1 Compressed tablet Lozenges:

→ Direct compression- Ingredients can be completely blended and straightforwardly compacted.

→Wet granulation-In this sugar is pounded by mechanical comminution to a fine powder (40-80mesh). Medicament is added and the mass is mixed mass. The mixed is exposed to granulation with sugar or corn syrup and screened through 2-8mesh screen. This is trailed by drying and processing to 10-30mesh size. Flavor and lubricant are then added preceding the compression.

2.2 Soft Lozenges:

Soft lozenges can be hand rolled and then cut into pieces or the warm mass can be poured into a plastic mold. Mold cavity should be overfilled if Poly Ethylene Glycol (PEG) is used, as PEG'scontract as they cool. This is not needed in the case of chocolate as it does not shrink.

2.3 Hard Candy Lozenges:

The candy base is cooked by dissolving required amount of sugar in one third measure of water in a candy base cooker. This is proceeded till the temperature ascends to 110^{O}C. Corn syrup is added and cooked till the temperature arrives at 145-156^{O}C. The candy mass is eliminated from the cooker and moved to a lubricated transfer container mounted onto a weight check scale where the weight of the mass is checked. This is trailed by color addition in the form of pastes, solutions or color cubes. The mass is then moved to a water-jacketed stainless steel cooling table for blending and the flavor, drug and ground rescue is added. The mass is either emptied into molds or into a lace while cooling and afterward slice to wanted length. The got lozenges are packed [7].

III. FORMULATION COMPOUNDS:

Ingredients	Examples
a) Sugar b) Sugar free vehicles c) Fillers	Dextrose, Sucrose, Maltose, Lactose. Mannitol, Sorbitol, Poly Ethylene Glycol (PEG) 600 and 800. Di calcium phosphate, Calcium sulfate, Calcium carbonate, Lactose, Microcrystalline cellulose.
Binders	Acacia, Corn syrup, Sugar syrup, Gelatin, Polyvinyl pyrrolidone,Tragacanth and Methylcellulose.
Lubricants	Magnesium stearate, Calcium stearate, Stearic acid and PEG, Vegetable oils and Fats.
Whipping agents	Milk protein, Egg albumin, Gelatin, Xanthan gum, Starch, Pectin, Algin and Carrageenan.
Coloring agents	Water soluble and Lakolene dyes, FD & C colors, Orange color paste, Red color cubes, etc.
Flavoring agents	Menthol, Eucalyptus oil, Spearmint, Cherry flavor, etc.
Humectants	Glycerin, Propylene Glycol and Sorbitol.

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Preservatives	Methyl paraben, Propyl paraben.

Table 1: Excipients used

Salt	Butterscotch, Maple, Nutty, Buttery
Bitter	Spice Wild Cherry, Licorice, Chocolate Mint, Grapefruit, Coffee, Cherry, Peach,
Acrid	Raspberry, Orange, Lemon, Lime
Sour	Raspberry, Fruits, Berries, Acacia
Oily	Syrup
Sweet	Peppermint, Anise, Wintergreen
Acrid	Fruit, Berry, Vanilla
Metallic	Citrus Berries, Mint, Grape, Marshmallow

Table 2: Flavoring agents [8].

3.1 Sugar: Sucrose, a disaccharide of glucose and fructose, is gotten from sugarcane or beet. The decision of beet or natural sweetener depends on accessibility and geological contemplations. Sucrose and sucrose items are utilized in cured capsules in view of their significance as unbiased sugars, their dissolvability properties, and their capacity as a "drier" to lessen the mass of the sweet through crystallization.

3.2 Corn syrup: Corn syrup is utilized in each sort of dessert to control sucrose and dextrose crystallization, which may prompt disintegrating. Corn syrup in suitable proportion with sucrose and dextrose permits the arrangement of a formless glass and builds up a candy with the alluring appearance. The accompanying actual properties of corn syrup are critical in the arrangement of medicated candies: thickness, density, dextrose equivalent, hygroscopicity, sugar crystallization, consistency, edge of freezing point depression, and osmotic pressure. Sucrose crystallization is experienced in different food and drug applications. In sucrose crystallization, dispersion of the sucrose from the mass answer for precious stone surface and combination of the sucrose atom into the grid structure are the average rate-restricting steps. Numerous elements can influence the development rate, including temperature, supersaturation, disturbance, and pollutants.

3.3Binders:Binders are generally used for compressed tablet that are intended to hold the particles of mass as discrete granules which include acacia, corn syrup, sugar syrup, gelatin, polyvinylpyrrolidone, tragacanth and methylcellulose, HPMC, etc.

3.4 Lubricants:Lubricants are used to avoid sticking of candy to the teeth and improve flow of final troche mixture and include magnesium stearate, calcium stearate, stearic acid and PEG, etc.

3.5Coloring agents: Coloring agents are incorporated into medicated lozenges for product identification, good appearance and masking of physical degradation. Colorants are mainly used to impart a distinctive appearance to the pharmaceutical dosage forms.Dyes and other organic colorants may degrade by heat or light via oxidation, hydrolysis, photo oxidation, etc. and their compatibility with drug, excipients, and process conditions should be studied before selection.

3.6Flavoring agents: Flavor refers to a mixed sensation of taste, touch, smell, sight and sound. Flavors are composed of different organic chemicals, such as hydrocarbons, alcohols, aldehydes, ketones, acids, esters or lactones. The low volatility and low molecular weight, usually lower than 400 Daltons, are responsible for a range of sensorial sensations attributed to the flavors.

3.7Preservatives:

Since hard candy lozenges are hygroscopic, the water content may increase and bacterial growth may occur if they are not properly packed. The presence of water would dissolve some sucrose; the resulting highly concentrated sucrose solution is bacteriostatic in nature and would not support bacterial growth [9].

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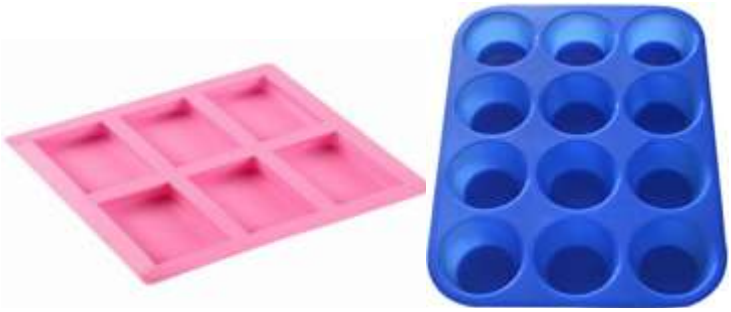
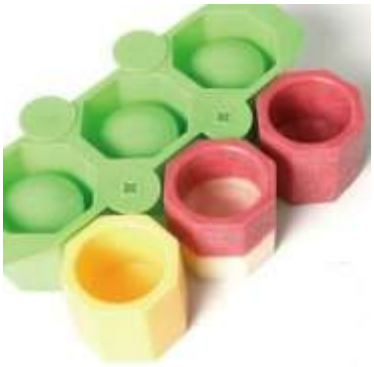
IV. DIFFERENT SHAPES OF LOZENGES MOLDS:

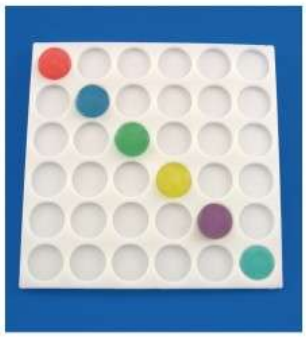


A) Fig no 5: Flat mold

B) Fig no 6: Cylindrical mold



C) Fig no 7: Octagonal mold



D) Fig no 8: Biconvex Mold

E) Fig no 9: Circular mold

V. QUALITYCONTROLOF LOZENGES:

5.1 Physical and chemical testing

5.1.1 Hardness:

Hardness of the lozenges is determined by Pfizer or Monsanto hardness tester. The resistance of lozenges to shipping or breakage under conditions of storage, transportation and handling before usage depends on its hardness.

5.1.2 Diameter and thickness:

A Vernier caliper is the instrument used for the determination of diameter and thickness of the lozenges.

5.1.3 FriabilityRoche:

Friabilator is used for the determination of friability of lozenges. Apparatus is rotated at 25 rpm for 4 min. Initial weights of lozenges are taken and they are placed in friabilator. After the revolution the lozenges were de-dusted and weighed again. The observed value not be more than 1%.

Friability is calculated by following formula

% friability = (1- Wt. / W) × 100

Where, W= Initial weight of lozenges Wt.= Weight of lozenges after revolution.

5.1.4Weight variation:

Twenty lozenges were randomly selected and individually weighed using an electronic balance. The average weight and standard deviation of 20 tablets was calculated or initial weight is compared with the calculated average weight.

5.1.5Drug Excipients interaction studies:

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Fourier TransformInfraRed analysis i.e., FTIR is used to study the Drug-Excipients interactions.

5.1.6Disintegration test:

USP Disintegration apparatus is used to determine the disintegration time of lozenges. Disintegration time is noted in pH 6.8 phosphate buffer or artificial saliva at 37ºC.In- vitro drug dissolution study. Rate of drug absorption is determined by the rate of drug dissolution of the lozenges. Rate of dissolution and bioavailability is directly related to efficacy of lozenges. This study is carried out by using USP II Dissolution type apparatus (paddle type). Dissolution study was carried out in 900 ml of buffer pH 6.4 or use artificial saliva by USP II paddle method at 100 rpm. Samples were withdrawn at 5 min time interval and replaced immediately with an equal volume of fresh buffer or artificial saliva and were analyzed spectrophotometrically. Temperature $37^{O}C \pm 2^{O}C$ maintain between dissolution studies.

5.1.7Drug content:

Drug content is done by taking an appropriate number of lozenges being crushed and dissolved in a suitable solvent and the absorbance of the solution is measured spectrophotometrically**.** As the candy base manufacture is commenced, a check on following parameters is performed: Corn syrup and sugar delivery gears; temperature, steam pressure and cookingspeed of precookers and temperature, steam pressure, cooking speed and vacuum of candy base cookers [10].

5.2 Moisture Analysis:

Gravimetric, Karl Fisher titration and Azeotropic distillation methods are used to determine the moisture content of lozenges. In gravimetric method, sample (1g) is weighed and placed in vacuum oven at 60-70℃ for 12-16hrs. Final weight is subtracted from initial and the difference in moisture content is calculated. Karl Fischer titration involves calculating a sample to contain 10-250mg water in titration flask and titrated with Karl Fischer reagent. In azeotropic distillation method, 10- 12g candy is pulverized and placed in 500ml flask to which 150-200ml toluene is added. Flask is connected to a reflux condenser and is refluxed for 1-2hrs. Water collected gives the amount of water present in the sample [10].

5.3 Microbial Test for Lozenges:

Microbial test for lozenges is performed to check the presence of any bacterial, mold or spore contamination in raw materials, cooling tunnels, finished products, machinery, environmental conditions and storage drums. Laboratory microbial testing should include the various counts such as total plate, total coliform, yeast and mold, E. coli, Staphylococcus and Salmonella. Stability Testing Stability testing of lozenges is carried out under following conditions:

→1-2months at 60℃
→ 3-6months at 45℃
→9-12months at 37℃
→ 36-60months at 25 and 40℃

5.4 Stability testing of packaged products:

The final packs of lozenges are subjected for stability testing under following conditions:

→25℃at 80% RH for 6-12months
→ 37℃at 80% RH for 3 months
→ 25℃at 70% RH for 6-12 months [11].

Storage:

Lozenges 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:

Hard candies are hygroscopic and frequently prone to absorption of atmospheric moisture. Considerations must include the hygroscopic nature of the candy base, storage conditions of the lozenges, length of time they are stored and the potential for drug interactions. These products should be stored in tight containers to prevent drying. This is especially true of the chewable lozenges that may dry out excessively and become difficult to chew. If a disposable mold with a cardboard sleeve is used, it is best to slip this unit into a properly labelled, sealable plastic bag. Packaging should be proper and attractive [12].

VI. CONCLUSION:

Lozenges are organoleptically acknowledged plan by the pediatric and geadiatric patients. They are the one of the simplest courses of medication administration. They are easy to get prepared and store. lozenges produce both local and systemic impact during administration. They are utilized to join a wide scope of active ingredients. Improved and enhanced lozenges hold a prime spot in drug market. They are relied upon to procure more interest in drug creation as imaginative measurement structure for the powerful medications which appear to be an ideal dose structure. The majority of the medicated chewable

tablets are accessible as OTC items and are extremely modest when contrasted with other dose structure. lozenges appreciate a significant situation in drug store and will keep on excess so in future.

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