COMPRESSED TABLET LOZENGES FORMULATION AND EVALUATION: A REVIEW

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ABSTRACT
Oral solid dosage form varies and have advantages over other dosage form. Lozenges are one of the widely used solid, unit dosage form of medicament which are meant to be dissolved in mouth or pharynx. Compressed Tablet 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, paediatric, geriatric patients show 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 Compressed Tablet Lozenges is they increase the retention time of the dosage form in the oral cavity which increases bioavailability and reduces first pass metabolism. The medicaments which can be formulated as lozenges include local anesthetics, antihistamines, antitussives, antiseptics, decongestants, demulcients and antibiotics. Lozenges are evaluated by hardness, friability, diameter and thickness, weight variation, moisture content, drug content/ assay, etc. Drug – Excipients interaction are studied by FTIR. In- vivo study, In vitro study. Compressed Tablet Lozenges provide easy administration, convenience to patient, patient compliance, and efficient treatment of low drug dosing, immediate onset of action, reduced dosage regimen, and cost effectiveness.

KEYWORDS: Compressed Tablet Lozenges, Troches, Medicaments, Excipients.

INTRODUCTION[1,2,3,4]
The pharmaceutical industry first produced lozenges and compressed tablets in the mid to late nineteenth century as a way to deliver a specific amount of a drug. Because drug quantities
are often measured in milligrams or less, another powder was needed to provide the necessary bulk as a carrier of the active ingredient. The properties of this other (nonactive) powder define tableting ability in pharmaceutical applications. Lozenges are the flavoured medicated dosage forms proposed to be sucked and held in the mouth or pharynx containing one or more medicament usually in sweetened base. Lozenges are used to relieve oropharyngeal symptoms, which are normally caused local infection and also for systemic drug absorption. Medicated lozenges are designed to increase retention of dosage form in oral cavity which increases bioavailability, reduces gastric irritation and bypasses first pass metabolism. Lozenges are used for patients who are unable to swallow solid oral dosage form as well as for the medication designed to be released slowly to yield a constant level of drug. Dissolution time of lozenges is about 30 minutes, it also depends on the patient, as patient controls the rate of dissolution and absorption by sucking on lozenges until it dissolves. Drug often incorporated into lozenges include analgesic, anti-tussives, aromatics, astringents, corticosteroids, decongestants, demulcent and many other supplement etc. Lozenges should dissolve slowly in mouth and possess some degree of smoothness, with their shape being without corners. Lozenges are formulated with various shapes, like flat, circular, octagonal, biconvex, rod shaped etc.

They are intended to treat local irritation or infection of mouth or pharynx and may also be used for systemic drug absorption. Lozenges are intended to achieve local effect as soothing and purging the throat. Lozenges are also used for systemic effect provided the drug is well absorbed through the buccal linings or when it is swallowed. Since the sublingual lozenges may be impractical due to their size, buccal lozenges are formulated and have been extensively used and are intended to be placed between the cheek and the gums. Though the lozenge dissolution time is about 30 minutes, this depends on the patient; as the patient controls the rate of dissolution and absorption by sucking on lozenge until dissolves. Sucking and the subsequent production of saliva may also lead to increased dilution of the drug and accidental swallowing. Lozenges can be prepared by molding (gelatin and/or fused sucrose and sorbitol base) or by compression of sugar-based tablets. Molded lozenges are sometimes referred to as pastilles, whereas compressed lozenges may be referred to as troches. They 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 bath the throat tissues in a solution of the drug. Lozenges historically have been used for the relief of minor sore throat pain and irritation and have been used extensively to deliver topical
anesthetics and antibacterial. Today they are used for drugs like analgesics, anesthetics, antimicrobials, antiseptics, antitussives, aromatics, astringents, corticosteroids, decongestants, and demulcents and other classes and combinations.

**DEFINITION**[^5]

“Lozenges are solid dosage form containing the flavoring and sweetening agents that are intended to dissolve or disintegrate slowly in the mouth or oral cavity”. They are most often used for localized effect into oral cavity and can also show systemic effect if it is well absorbed in the buccal lining and pharynx.

**ADVANTAGES**[^6,7]

- It broadens the hour of medication in the oral cavity to evoke a particular impact.
- It very well may be given to those patients who experience issues in-gulping.
- Simple to regulate to geriatric and paediatric populace.
- 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 decrease dosing recurrence.
- It can increment in bioavailability.
- No disintegration.
- Do not require water for intake.
- Less production time.
- Lozenge can be withdrawn if dose is not needed
- Less production cost.

**DISADVANTAGES**

- 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.
- For a hard candy lozenges required a high temperature for their preparation.

**Types of Lozenges**[^8,9,10]

Lozenges are classified into various methods 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 lozenges
   b) Compressed tablet lozenges
   c) Soft lozenges
   d) Hard candy lozenge

❖ Compressed Tablet Lozenges
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
1. Organoleptic property
2. Non disintegrating characteristics and

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.

Raw material for Compressed Tablet Lozenges
1. Tablet base or vehicle
   a) Sugars: Dextrose, Nu-tab, Royal T, Di-pac, Sugar tab, Honey tab, Mola tab
   b) Sugar free vehicles: Sorbitol, Mannitol, Poly ethylene glycol-8000,
   c) Other fillers: Dicalcium phosphate, calcium sulphate, calcium carbonate, Lactose, Micro crystalline cellulose
2. Binders: Acacia, corn syrup, Sugar syrup, Gelatin, Polyvinylpyrrolidone, Tragacanth, Methyl cellulose.
3. Colours: Water soluble dyes and Lakolene dyes

❖ Manufacturing of Compressed Tablet Lozenges
The heat liable ingredients i.e heat sensitive ingredients are not possible to formulate by procedure same as that of soft lozenges, hard lozenges. Simply the compression method is applicable for such type of ingredients, same as like compressed tablet. The only difference
between them is non-disintegrating and slower dissolution profile. The granulation method is used in compressed lozenges.

a) Direct compression

Manufacturing of compressed tablet lozenges can either be direct compression and wet granulation. In direct compression, ingredients are thoroughly mixed and then compressed.

b) Wet granulation

In wet granulation, sugar content is pulverized by mechanical commination to a fine powder (40-80 mesh size). Medicament is added and thoroughly blended. The blended mass is subjected to granulation with sugar or corn syrup and screened through 2-8 mesh screens. This is followed by drying and milling to 10-30 mesh size. Flavor and lubricant are then added prior to compression.[7]

Lozenges Compression Sequences

A) Die –filing
B) Weight adjustment
C) Compression hardness

<table>
<thead>
<tr>
<th>S. No</th>
<th>Ingredients</th>
<th>Examples</th>
<th>Role</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Candy base</td>
<td>Dextrose, sucrose, maltose, lactose. Mannitol, sorbitol, PEG 600 &amp; 800.</td>
<td>These are the used as sweetening agent and impart the taste masking properties.</td>
</tr>
<tr>
<td>2.</td>
<td>Fillers</td>
<td>Di calcium phosphate, calcium sulfate, calcium carbonate, lactose, microcrystalline cellulose.</td>
<td>These are the used to Improve the flowability,</td>
</tr>
<tr>
<td>3.</td>
<td>Lubricants</td>
<td>Magnesium stearate, calcium stearate, stearic acid and PEG, vegetable oils and fats.</td>
<td>These are the used to avoid sticking of candy to the teeth.</td>
</tr>
<tr>
<td>4.</td>
<td>Binders</td>
<td>Acacia, corn syrup, sugar syrup, polyvinylpyrrolidone, gelatin, tragacanth, and methylcellulose.</td>
<td>These are the used to hold the particles.</td>
</tr>
<tr>
<td>5.</td>
<td>Coloring agents</td>
<td>Water soluble and lakolene dyes, FD &amp; C colors, orange color paste, red color cubes, etc.</td>
<td>These are the used to inhance appearance and organoleptic properties of dosage form.</td>
</tr>
<tr>
<td>6.</td>
<td>Flavorings agent</td>
<td>Menthol, eucalyptus oil, spearmint, cherry flavor, etc.</td>
<td>These are the used to give a taste.</td>
</tr>
<tr>
<td>7.</td>
<td>Whipping agent</td>
<td>Milk protein, egg albumin, gelatin, xanthan gum, starch, pectin, algin and carrageenan.</td>
<td>These are the used in toffee-based confection.</td>
</tr>
<tr>
<td>8.</td>
<td>Humectants</td>
<td>Glycerin, propylene glycol and sorbitol.</td>
<td>They improve chew mouthfeel properties.</td>
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</table>

Table 1: Material of Lozenges and their functions.
Evaluation of Lozenges\cite{11,12,13,14}

- **Physical and chemical testing**
  - **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.

- **Diameter and thickness**
  
  A vernier calliper is the instrument used for the determination of diameter and thickness of the lozenges.

- **Friability**
  
  Roche 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

  \[
  \% \text{ friability} = (1 - \frac{W_t}{W}) \times 100
  \]

  Where, \( W \) = initial weight of lozenges

  \( W_t \) = weight of lozenges after revolution.

- **Weight 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.

- **Drug Excipients interaction studies**
  
  Fourier transfer infrared analysis i.e. FTIR is used to study the Drug-Excipients interactions.

- **Disintegration 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 37\(^\circ\)C.
✓ **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°C ± 2°C maintain between dissolution studies.

✓ **Drug 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.

✓ **Moisture analysis**
Moisture analysis can be done by using three methods like.

- **Gravimetric analysis**
  Weigh accurately about 1g 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, once again weigh the sample and moisture content can be calculated by subtraction of initial weight from initial weight. Formula used for calculation moisture content is Moisture content = Initial weight – Final weight.

- **Azeotropic distillation method**
  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.

- **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.
Stability studies
The stability studies were performed to measure physical as well as the chemical stability of the drug, which may perhaps the organoleptic properties of the lozenges. Accelerated stability study was conducted as per ICH guidelines (zone IV) at 45°C and 75% relative humidity over a period of seven weeks. Sufficient number of optimized formulations were packed in amber coloured screw capped bottles and kept in incubator maintained at 37°C. Samples were taken at intervals of 15 days to estimate the drug content and to evaluate organoleptic properties.

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.

Medication Given Through Lozenges
Medicaments Drug candidates which can be incorporated in lozenges, belong to one of the following categories:
1. Antiseptics
2. Local anaesthetics
3. Antibiotics
4. Antihistaminic
5. Antitussives
6. Analgesics
7. Decongestant
8. Antifungal

CONCLUSION
Compressed Tablet 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. Lozenges are organoleptically acknowledged plan by the pediatric and geriatric 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 Lozenges are medicated confections that have been developed about 20th century ago and are still under commercial production. Most of the preparations are available over the counter products and are very economic dosage forms. They are designed for local as well as systemic therapy. A
wide range of actives can be incorporated within their structure. Lozenges enjoy an important position in pharmacy and will continue to remain so in future.

REFERENCES

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