REVIEW ON FORMULATION AND STANDARDIZATION OF HERBAL LOZENGES

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ABSTRACT

The lozenges are palatable solid unit dosage form administered in the oral cavity. It is dissolved in mouth or pharynx and produces local or systemic effects. Lozenge dosage form is more beneficial method because of good patient compliance due to its taste, increased bioavailability, reduced gastric irritation, reduced first pass metabolism, and increased onset of action. The caramel based soft candy lozenges, hard candy lozenges, and compressed tablet lozenges are available in the market. Herbal formulations are used by mankind to cure various ailments and they are still very popular. Herbal lozenges were prepared by melting and moulding technique. The prepared herbal lozenges were subjected to various parameters like macroscopic evaluation, friability, hardness, uniformity of weight, disintegration time, pH, salt content, total sugar, test for heavy metals (lead, cadmium, mercury, arsenic), aflatoxins, shelf life, ash value, swelling index, moisture content, extractable matter, thin layer chromatography, UV spectrophotometry, etc which are comply with the standards mentioned in AYUSH Guidelines. This review covers more or less all aspects associated with the formulation and evaluation of the Herbal Lozenges and also throws light on various herbal lozenges available in the market.

KEYWORDS: Herbal lozenges, Lozenges, Parameters, AYUSH, Standardization.

INTRODUCTION

Herbal medicine has been recognized by the World Health Organization as an important component of primary health care in large countries like India. Lozenges are used to coat the throat tissue with a single-drug solution for patients who have difficulty swallowing solid
oral dosage forms and for medications that need to be released slowly to deliver a consistent dose in the oral cavity. Lozenges contains one or more medicaments that are dissolved into the oral cavity. It can be made by moulding or compression of sugar-based tablets. It facilitates administration for pediatric patients. Large doses of medication can be easily administered. Lozenges prolong the time a dose form is retained in the oral cavity, increasing bioavailability, reducing stomach discomfort, and avoiding first-pass metabolism. They are economic, safe logistics for the patient and easiest way of drug administration. No nursing is required, which means the patient can take it without any help. Oral dosage forms also have drawbacks if the patient suffers from chronic vomiting, they may not be the first choice of medication. They may not be a good choice in the case of a non-cooperative patients as children and infants. They are not suitable for emergencies and unconscious patients. This review covers more or less all aspects associated with the formulation and evaluation of the Herbal Lozenges and also throws light on various herbal lozenges available in the market.

A brief history
James Lofthouse was born in 1842 in Lancaster, England, and founded his pharmacy in 1865 in Fleetwood, on the Fylde coast. Fleetwood was a burgeoning fishing town at the time, and the North Atlantic fishing trawlers were swarming with fishermen suffering from bronchial problems. James took control of the situation by creating an exceptionally strong bronchial mixture with methanol, eucalyptus oil, capsicum, and liquorice that could be placed into sugar cubes and swallowed. Glass bottles, however, were not suitable containers for his customers, who grumbled that they would break in rough seas. As a result, he reformed the mixture into a solid – a lozenge made of the same elements dispersed in a sugar and gum foundation massed with water, then rolled, cut into shapes, and backed. Fishermen would come into his pharmacy and ask for "an ounce of friends" or "a bag of fisherman's lozenges" because of the popularity of this formula - hence the name "Fisherman's Friend."

Types of lozenges
- Chewable Lozenges
- Hard Lozenges
- Soft Lozenges
- Compressed Lozenges
Preparation of different kind of Lozenges Preparation of Chewy or caramel based lozenges

The candy base was prepared in a planetary or sigma blade mixer at 95-125°C. Allow the mass to cool to 120°C. The whipping agent is then added at a temperature below 105°C. Between 95 and 105°C, the medications are added. At a temperature of 90°C, the colour substance was disseminated in humectant and then added to the above mass. Below 85°C, seeding crystals and flavours are introduced. After that, lubrication is added if the temperature rises above 80°C. Rope forming is used to finish the candy.

Preparation of hard candy lozenges

To make the candy base, melt the necessary amount of sugar in 1/3 cup of water in a candy base cooker until the temperature reaches 110°C. Corn syrup was added, and the mixture was heated until it reached a temperature of 145-156°C. The candy mass was removed from the cooker and placed in a greased transfer container that was attached to a weight check scale. The colours are then added in the form of solutions, pastes, or colour cubes. The flavourings, medication, and ground salvage were added to the mass on a water-jacketed stainless steel cooling table for mixing. While cooling, the material was poured into the mould or dragged onto a ribbon and cut to the required length. The lozenges are then wrapped in a suitable wrapper.

Preparation of soft lozenges

Melting and mould techniques were used to make soft lozenges. The jaggery was melted in a water bath before being combined with the remaining components (powder) to create a uniform mixture. After that, the mixture was placed into a stainless-steel mould.

Preparation of compressed tablet lozenges

Direct compression or wet granulation are two methods for making compressed tablet lozenges. The components are well combined and then compacted in direct compression. Sugar was finely powdered (40-80 mesh size) by mechanical stimulation in wet granulation. The medication was then added and carefully mixed. The granulated mass was screened with 2-8 mesh screens after being granulated with sugar or corn syrup. After that, the material was dried and milled to a size of 10-30 mesh. Prior to the compression process, flavours and lubricants are applied.[7]
Herbal lozenges available in the Indian market

There are a lot of herbal lozenges in the market and some of the herbal lozenges are as follows:

- Dabur Honitus
- Himalaya Koflet-H
- Ricolaf
- Turmgel, Zeal

Table 1: Herbal lozenges available in the market.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Herbal lozenges</th>
<th>Ingredients</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Dabur Honitus Flavours (Honey, Lemon, Mint, Orange)</td>
<td>Amla, Ginger, Honey, Liquorice, Turmeric.</td>
<td>Sore throat, Pain and Infection.</td>
</tr>
<tr>
<td>2</td>
<td>Himalaya Koflet-H (Ginger flavour)</td>
<td>Trikatu {Indian long pepper (Piper longum Linn), Ginger (Zinger officinale Rosc), Black pepper (Piper nigrum Linn)}</td>
<td>Treatment of Pharyngitis, Laryngitis, Cough of varied etiology.</td>
</tr>
<tr>
<td>3</td>
<td>Himalaya Koflet-H (Lemon flavour)</td>
<td>Honey, Terminalia chebula, Trikatu, Alpina galanga, Acacia catechu.</td>
<td>Soothing relief from sore throat.</td>
</tr>
<tr>
<td>4</td>
<td>Himalaya Koflet-H (Orange flavour)</td>
<td>Honey (Madhu), Lavanga (Clove).</td>
<td>Soothing relief from sore throat.</td>
</tr>
<tr>
<td>5</td>
<td>Ricolaf</td>
<td>Extract of Ricolas herb mixture, Isomalt, menthol.</td>
<td>Used to relieve cough. Used to treat a sore throat.</td>
</tr>
<tr>
<td>6</td>
<td>Turmgel (Cool Mentholyptus, Orange, Tulsi)</td>
<td>Turmeric extract, Excipients, Flavour.</td>
<td>Tackles viral cough, cold, sore throat and enhances immunity.</td>
</tr>
<tr>
<td>7</td>
<td>Zeal</td>
<td>Yastimadhu (Glycyrrhiza glabra), Amla (Emblica officinalis), Sunthi (Zingiber officinale), Pudina (Mentha arvensis).</td>
<td>Used for sore throat and motion sickness.</td>
</tr>
</tbody>
</table>

Evaluation of herbal lozenges

Macroscopic evaluation

The macroscopic evaluation was done by visual observation of the product.

Friability test

The prepared lozenges can be frozen using a Roche Friabilator set to 25 RPM for 4 minutes.

Hardness test

Hardness of the lozenges was determined by Pfizer or Monsanto hardness tester.\[6\]

Uniformity of weight

Uniformity of weight can be determined by weighing 5 lozenges individually, the average
weight was calculated and the percent variation of each tablet was determined.

**Disintegration test**
According to USP30, disintegration test of the prepared lozenges was performed using a disintegration tester through the disintegration medium of phosphate buffer with pH 6.2 maintained at 37 ± 0.5°C.[8]

**Determination of pH**
The pH of the candy was determined by dissolving the candy in distilled water and pH was recorded.[9]

**Determination of Sugar and Corn syrup ratio**
The “Dextrose equivalent method and Lane Eynon Titration method” are used to accomplish this.

**Determination of percentage of reducing sugar**
In 500 mL of water, 3 g of anhydrous dextrose was dissolved. 2 drops of methylene blue were added to the solution and titrated against 25 mL of Fehling's solution (cupric tartrate) to a yellowish red endpoint.[7]

\[
\text{Percentage reducing sugar} = \frac{\text{Reducing sugar factor} \times 100}{\text{Sample weight/250} \times \text{Volume of sample solution consumed by Fehling’s solution}}
\]

**Test for heavy metals**
Heavy metals that are present in herbal products from the medicinal plants causes serious hazards on human health. Due to the above reason, WHO recommends permissible limits for these hazardous heavy metals (Table. 2). The Heavy metals (lead, cadmium, mercury, arsenic) was determined by using Atomic Absorption Spectroscopy method.

**Table 2: Permissible limit of heavy metals in herbal drugs as per WHO.**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Heavy metals</th>
<th>WHO prescribed limits in ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Cadmium</td>
<td>0.20</td>
</tr>
<tr>
<td>2.</td>
<td>Lead</td>
<td>10.00</td>
</tr>
<tr>
<td>3.</td>
<td>Arsenic</td>
<td>10.00</td>
</tr>
<tr>
<td>4.</td>
<td>Mercury</td>
<td>1.00</td>
</tr>
<tr>
<td>5.</td>
<td>Copper</td>
<td>20.00</td>
</tr>
<tr>
<td>6.</td>
<td>Zinc</td>
<td>50.00</td>
</tr>
</tbody>
</table>
Preparation of calibration standard solution

Preparation of calibration standard solution of Lead and Cadmium
10 mL of 1000g/mL lead standard reference solution and 1 mL of 1000g/mL cadmium standard reference solution were pipetted into a 100 mL volumetric flask and diluted to volume with HPLC grade water. This yielded a solution with a lead concentration of 100 g/mL (solution A) and a cadmium concentration of 10 g/mL (solution B). The stock solution for the calibration standard solution was made from these two solutions. Calibration standards for lead were made by mixing suitable amounts of standard working solution A with HPLC grade water at five different concentrations: 100, 200, 400, 800, and 1000 g/L. Similarly, cadmium calibration standards were made by mixing suitable amounts of standard working solution B with HPLC grade water at five different concentrations: 10 g/L, 20 g/L, 40 g/L, 80 g/L, and 100 g/L.

Preparation of calibration standard solution of Arsenic and Mercury
1 mL of arsenic and mercury standard reference solution (1000 g/mL) were pipetted into a 100 ml volumetric flask and diluted to volume with HPLC grade water. This resulted in an arsenic and mercury solution with a concentration of 10 g/mL (solution C). This solution was then utilised to make a calibration standard solution as a stock solution. Calibration standards for arsenic and mercury were made by mixing suitable amounts of standard working solution C with HPLC grade water at three different concentrations: 5 g/L, 10 g/L, and 20 g/L.

Sample preparation
About 5.0 ± 0.01g (for lead, cadmium, and arsenic) dry herbal powder were weighed accurately in an iodine flask separately, and 10 mL of concentrated HNO₃ was added to each flask separately (for mercury 0.5 mL of H₂SO₄ was added with this). At 95 °C ± 5 °C, the iodine flasks were refluxed for 1 hour. After cooling the sample solutions, 5 mL of concentrated HNO₃ was added to each flask. The flasks were again refluxed at 95 °C ± 5 °C for about 1 hour. The technique was repeated till the digestion was complete. The solution was reduced to 5 mL by evaporation. After cooling the solutions, 10 mL of concentrated HCl was added to each flask.¹⁰

Aflatoxins
Aflatoxins are toxic secondary metabolites formed by fungal species namely mostly Aspergillus flavus and Aspergillus parasiticus. Aflatoxin present as contaminants in Agro based products causes primary health hazards due to its toxicity and potency. Detection and
Quantification of aflatoxins are usually carried out by various methods including Thin Layer Chromatography (TLC), High-Performance Liquid Chromatography (HPLC), ELISA (Enzyme linked immunosorbent assay) and Electrochemical immunosensor (ECI). The Aflatoxins (B1, B2, G1 and G2) was determined by using TLC methods. It is one of the most often used separation techniques that uses stationary phase made up of either alumina or silica or cellulose immobilized on an inert support such as plastic or glass called Matrix. Usually, the mobile phase is a combination of Methanol: Acetonitrile: Water. Several types of mycotoxins can be detected in single sample using TLC.

**Stability testing for lozenges**
The following conditions are applied to lozenges:
- 1-2 months at 60°C
- 3-6 months at 45°C
- 9-12 months at 37°C
- 36-60 months at 25°C

The following conditions are applied to lozenges in their final packaging:
- 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

**Determination of total ash value**
The total ash value was designed to measure the amount of material remaining after ignition. It is a physiological ash derived from plant tissue and a remnant of an external substance adhering to the surface of plants.

**Determination of swelling index**
It is the number of mL of one gram of herbal substance taken by the swelling under certain conditions.

**Determination of moisture content**
This test is used to determine the water content of a substance by drying the sample at a given temperature. The moisture content of the formulation was determined by dried the weighed amount of the formulation in hot air oven at 120°C till constant weight obtained and calculate the moisture content.
Determination of extractable matter
This method determines the number of active constituents extracted by the solvent from a given herbal product. It is used for materials that do not yet come out with appropriate chemical or biological ratings. The extraction value was determined according to the procedure given in the WHO guidelines.

Determination of microbial contamination
This method Checks for any bacterial, mould or spore contamination in raw materials, finished products, machinery, refrigeration tunnels, environmental conditions and storage drums.

Determination of TLC
The Thin layer chromatography is particularly valuable for the standardisation of small-scale contaminants. Because it is effective, easy and the equipment needed is inexpensive, the technique is often used to evaluate herbal product and their products.

UV VISIBLE Spectrophotometry
UV Visible Spectrophotometer analysis provides quality and quantity standards. But markers required for qualitative analysis. Attempts are being made to study the ultraviolet spectrophotometric analysis of herbal materials to understand quality and quantitative parameters without markers.\[6\]

RESULTS AND DISCUSSION
Based on the optimization of the parameters, the lozenges could be prepared by the melting and moulding method using the sugar base. Quality control parameters such as macroscopic evaluation, friability, hardness, uniformity of weight, disintegration test, pH, total sugar and corn syrup ratio, test for heavy metals, aflatoxins, stability, ash value, swelling index, moisture content, alcohol extraction, thin layer chromatography and UV analysis can be done by using AYUSH guidelines.

CONCLUSION
From the above investigation, it has been concluded that herbs are used to make effective lozenges. It provides excellent patient complaint and innovative dosage forms.

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REFERENCES