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# FORMULATION AND EVALUATION OF HERBAL LOZENGES CONTAINING EXTRACT OF *HEDERA HELIX* FOR TREATMENT OF PRODUCTIVE COUGH.

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**ABSTRACT**:

The goal of the current research project is to formulate and assess herbal medicinal hard lozenges without added sugar. To this end, an extract of the natural plant "Hedera helix Linn." was used, along with few common excipients. Using plant extract, jaggery, corn syrup, mint extract, artificial taste and colour and other necessary excipients, the lozenges were made through the melting and molding process. These sucrose-free lozenges, which have jaggery as a base, were made with the benefit of "Diabetes mellitus" patients in mind who should not consume sugar. This study aims to evaluate and demonstrate the efficacy of formulated lozenges through the use of assessment parameters such as drug content uniformity, hardness, thickness, weight variation, friability, moisture content, and in vitro disintegration and dissolution. The taste of the drugs was masked by sweeteners and flavours used in the formulation. It is a herbal product, safe to use and convey. The formulation was ecological and economical.

## 1.Introduction [1-6]:

Lozenges are also called a “troches” or “pastilles”. Compressed lozenges are referred as “troches” and molded lozenges are referred as “pastilles”. A lozenge is a solid medication that contain one or more medicaments which are small, flavored that are designed to dissolve slowly in the mouth, providing either local or systemic effects. It includes drug and a flavouring agent & comes in variety of flavours. The term "lozenge" originates from the French word, indicates a geometry with four equal sides called “four-sided” diamond shape. They can be made using moulding or compression technique. These have been produced in pharmacies since the twentieth century and are still commercially available.

A lozenge is a potent and solid substance taken orally that dissolves in the mouth or throat & is easy to administer. They are inserted into the mouth because, the tongues bottom extremities may get damaged. It contains one or more active ingredients and is formulated in a sweet, sugary base. Lozenges are used to treat oral irritation, cough, sore throat and dry mouth conditions and can also aid in the absorption of drugs into the body. They have both local effects on the throat, such as soothing, cooling and systemic effects if the medication is absorbed through the buccal linings or ingested. Due to pleasant taste these are placed in mouth for longer time and the drug is released to have local effect.

Buccal lozenges are commonly used, due to their size and shape, as they can be positioned between the gums and the cheek for longer time, due to pleasant taste, and the drug is released to have local effect. The duration of the lozenge's effect can vary, depending on the individual, but it can last up to 30 minutes. By controlling the rate of dissolution and absorption, patients can regulate the amount of medication delivered each time they use a lozenge. Sucking of lozenge and increased saliva production can lead to dilution and swallowing of the medication. These oral preparations are particularly helpful for patients who have difficulty swallowing solid medication or for drugs that are meant to be released slowly to generate a continuous dose of the drug in the mouth or throat.

Lozenges contain a variety of drugs, including analgesics, sedatives, antihistamines, aromatics, astringents, corticosteroids, anaesthetics, antimicrobials, antiseptics, antitussives and demulcents, depending on the specific needs of the patient.

**1.1. Advantages [1,2] -**

**A) Pleasant Taste and Extended Local Activity:** Lozenges are formulated with pleasant flavours and sweeteners, making them more palatable for patients. The slow dissolution in the mouth extends the time the drug remains in the oral cavity, allowing for prolonged local activity, which is beneficial for treating throat irritations or localized issues.

**B) Minimal Equipment Required**: The preparation of lozenges does not require complex equipment, making them relatively easy and cost-effective to produce.

**C) Versatile Formulation Options:** Lozenges can be formulated with a variety of drugs, allowing for a wide range of medications to be delivered using this dosage form, based on the specific needs of the patient.

**D) Easy Administration:** Lozenges are simple to administer, making them suitable for both paediatric and geriatric patients who might have difficulty in swallowing pills or tablets.

**E) Buccal Cavity Absorption:** Some drugs can be absorbed systemically through the buccal cavity (lining of the cheek), providing an alternative route for drug delivery and avoiding first-pass metabolism in the liver.

**F) Masking Unpleasant Taste:** The sweeteners and flavours used in lozenge formulations can effectively mask the unpleasant taste of certain medications, improving patient compliance and acceptance.

Overall, lozenges offer several advantages, making them a valuable choice for delivering medications to patients who need local or systemic effects while providing ease of administration and a pleasant experience.

**1.2. Disadvantages [1,2]-**

**A) Caution for Parents:** Parents need to be cautious, not to associate lozenges with candy and

should store them out of the reach of children to prevent accidental ingestion.

**B) Heat Stability Requirement:** Certain drugs may require heat stability, and the manufacturing process of lozenges involves heating, which may limit the use of heat sensitive drugs in this dosage form.

**C) Bitter Taste of Drugs:** Some drugs have inherently bitter tastes, and masking this taste with sweeteners and flavours in a lozenge formulation might be challenging or not entirely effective.

**D) Risk of Mistaken Use as Candy:** Lozenges can resemble candies, especially those designed to be appealing with sweet flavours. This could lead to accidental ingestion by children who might mistake them as candy.

**E) Incompatibility with Certain Candy Bases:** Some drugs may not be suitable for formulation with certain candy bases, such as aldehyde candy bases, as it could affect the drug's stability or effectiveness. For example, benzocaine might not be suitable for lozenges due to potential interactions with the candy base.

**F) Age Restrictions:** While lozenges are generally easy to administer, they may not be suitable for very young children who might not understand how to use them properly. Age restrictions may be necessary to ensure safe use. It is essential to consider these disadvantages while using lozenges asa medication and take appropriate precautions to ensure their safe and effective use.

### 1.3. Uses of Lozenges [20]-

a) To medicate mouth and throat for slow administration in cough remedies.

b) Sore throat, cough, gingivitis, pharyngitis, decongestants, and other oral and throat diseases can be treated and relieved by adding a range of medications to them.

c) Lozenges have also been used to distribute medication in a systematic manner for pain relief.

d) Local and systematic illness are commonly treated with lozenges.

## 2.Materials and Methodology [4]:

### 2.1. Materials:

The leaves of plant Hedera helix Linn. were freshly collected from local nursery from Sangli, Maharashtra, India. Jaggery, corn syrup, mint extract, artificial flavours and colours were procured from local market. Honey was purchased from the local market. All ingredients used were pure and of analytical grade.

### 2.2. Method:

### 2.2.A. Extraction of Hedera helix Linn. -

Plant material should be fresh (for example, a plant leaves) or dried. It is to be crushed, using a pestle and mortar, to provide a greater surface area. The plant material should be sufficient to fill the porous cellulose thimble. The extraction apparatus gives a greater appreciation for the process of extraction. Build a rig using stands and clamps to support the extraction apparatus. Following this, the solvent (250 ml of methanol) is added to a round bottom flask, which is attached to a soxhlet extractor and condenser. The crushed plant materials were loaded into the thimble, which was then placed inside the soxhlet extractor. The side arm was lagged with glass wool. The solvent was heated using the isomantle and began to evaporate, moving through the apparatus to the condenser. The condensate was then driped into the reservoir containing the thimble. Once the level of solvent reached the siphon it was poured back into the flask and the cycle began again. The process should run for a total 6-7 hours.

**2.2.B. Phytochemical screening** – In order to determine the presence or absence of primary and secondary metabolites, phytochemical screening of plant extracts has been carried out using a standard procedure to verify the purity of herbal medicinal products. Phytochemical tests for - Steroids, Glycosides, reducing sugar, Terpenoids, Saponins, Flavonoids, Alkaloids, Anthraquinone, were carried out adopting standard procedures, for identification of chemical constituents.

**2.2.C. Formulation of lozenges [1] –**

Technique used- Melting & Moulding

⇩

A jaggery syrup was made by mixing jaggery and water.

⇩

Jaggery was dissolved in a small amount of water and heated to 110°C until it forms a viscous syrup.

⇩

The temperature was then lowered to 90°C, and the drug and other ingredients were added.

⇩

The mixture was then poured into mould to form lozenges.

⇩

To protect them from moisture, the lozenges were wrapped in aluminium foil and stored in desiccators.

**Table 4.1.- Formulation table containing extract of Hedera helix (Batches B1-B9)**

| Ingredients | B1 | B2 | B3 | B4 | B5 | B6 | B7 | B8 | B9 |
|---|---|---|---|---|---|---|---|---|---|
| Hedera helix extract(g) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Jaggery(gm) | 38 | 39 | 40 | 41 | 42 | 43 | 44 | 45 | 46 |
| Corn syrup(gm) | 13 | 14 | 15 | 16 | 16.1 | 16.2 | 16.3 | 16.4 | 16.5 |
| Water(ml) | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 |
| Mint extract(ml) | 0.9 | 1 | 1.1 | 1.2 | 1.3 | 1.4 | 1.4 | 1.5 | 1.5 |
| Colour | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. |
| Flavour | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. |

20 lozenges were prepared from each batch.

**3.Evaluation of lozenges [1-4] -**

Evaluation Tests for Lozenges are as follows-

(**A) Determination of organoleptic properties -**

The determination of organoleptic properties involves a visual inspection of the lozenges to assess their appearance, colour, odour and shape. This evaluation is done to ensure that the lozenges meet the desired visual characteristics and quality standards.

**(B) Dimensions-**

**(i) Thickness uniformity** -

In the evaluation process, six lozenges were randomly selected from each batch, and their thickness was measured using vernier calliper.

**(ii) Diameter -**

The diameter, size, and shape of lozenges depend on the selected mould. The lozenges of different sizes and shapes can be prepared, but generally, they are circular with either flat or biconvex faces.

**(C) Hardness** -

Hardness or crushing strength (Fo) of a lozenge is the force needed to break it in diametric compression using a Monsanto hardness tester. To determine the hardness of formulation, six lozenges were selected for testing. The lozenges were held between the two jaws of the tester along their oblong axis. Initially, the reading should be 0 kg/cm². Then, a constant force was applied by rotating the knob until the lozenges fractured. The value noted at this point represents the hardness of the lozenge and is measured in kg/cm². This test provides valuable information about the lozenge's mechanical strength and durability, ensuring their quality and integrity during handling and use.

**(D) Weight variation** -

Weight variation testing involves randomly selecting ten lozenges from a batch and individually weighing them. The average weight of these ten lozenges were calculated. To pass the weight variation test, no more than two individual lozenges weights should deviate from the average weight. This test ensures that the lozenges in the batches are consistent in terms of weight, quality and dosage standards.

**(E) Friability -**

Determined by Roche friabilator operated at 25rpm for 4min.

**(F) In vitro dissolution studies -**

USP Type 2 (paddle apparatus) was used for this study. Formulated lozenges were placed in 900 ml phosphate buffer of pH 6.8. The temperature was kept up at 37°C and mixed at a speed of rotation of 50 rpm. At 5 min time interval, a 5 ml aliquot of the sample was withdrawn and the volume was replaced with an equal measure of plain buffer kept at 37°C. The obtained samples were filtered and measured at 250 nm using UV– visible spectrophotometer.

**(G) Moisture content -**

By the gravimetric method, 1 g sample was weighed and placed in an oven at 60–70°c for 12–16 hrs. Final weight was determined and its weight was rechecked. Percentage friability is given by the equation.

$$\% f = (\text{initial weight} - \text{final weight}/\text{initial weight}) \times 100.$$

**(H) Drug content -**

5 mg of lozenges were dissolved in 50 ml of phosphate buffer solution of pH 6.8 for 4 hrs. on a rotary shaker. The filtered solution was measured using a UV–visible spectrophotometer.

**(I) Stability studies –**

The stability studies for lozenges were performed for optimized formulation batch (B5) at 40°c for 90 days as per ICH guidelines. The lozenges were assessed for various parameters such as hardness, weight variation, drug content, moisture content, and drug release according to procedures mentioned previously by analysing the samples after every 1 month.

**(J) pH Determination-**

It is an important parameter of evaluation in herbal lozenges. pH is a measure of the acidity or alkalinity of a solution and may have an impact on the stability, efficacy and sensory properties of the product. The pH of herbal lozenges can be determined using a pH meter or pH paper. A small amount(1gm) of the lozenge is dissolved in water(100ml), and the pH of the resulting solution is measured. The acceptable pH range for herbal lozenges depends on the specific product and its intended use. Typically, a pH range of 5.5 to 7.5 is acceptable for most herbal lozenges.

**(K) In Process testing-**

**(i) Determination of sugar and corn syrup ratio-**

The test was carried out using Dextrose equivalent method/ percentage reducing sugar.

3g of dextrose was taken in beaker, to it 500ml of distilled water and 2 drops of methylene blue were added. It was boiled for 2 mins and titrated against 25ml of Fehling's Solution (End Point- Yellowish red colour).

$$\text{Percentage Reducing Sugar} = \frac{\text{Reducing Factor x10}}{\text{(Sample weight/250) x volume of Fehling's solution}}$$

**(L) Batch release testing-**

In addition to the usual quality control procedures and the above in-process tests, batch-release testing includes dosage uniformity and a test for grittiness was performed by partially dissolving lozenges under running tap water until one-third to one-half has been removed. No grittiness must be felt when rubbed between thumb and forefinger.

**(M) Wetting Time and water absorption ratio-**

A piece of tissue paper folded twice was kept in a Petri dish (internal diameter 5.5 cm) containing 6 ml of purified water. A lozenge having a small amount of Rosaline dye powder on the upper surface was placed on the tissue paper. The time required to develop a red colour on the upper surface of the lozenge was recorded as the wetting time. The same procedure without Rosaline dye powder was followed for determining the water absorption ratio R which was determined according to the following equation.

$$R = \frac{(Wa - Wb) \times 100}{Wb}$$

where, Wb = Weights of lozenges before use.

Wa = Weights of lozenges after use.

**(N) Mouth dissolving time-**

The time taken by the lozenge to dissolve completely was determined by placing each lozenge in separate beaker containing 100 ml phosphate buffer pH 6.8 at 50 rpm using mechanical stirrer and time was noted at 37° C.

**(O) Karl Fisher titration-**

A sample of the prepared lozenge was taken and dissolved in 10-250ml of water, which was then titrated with Karl Fischer reagent.

**(P) Fourier transform infrared (FTIR) spectroscopy-**

FTIR spectroscopy was estimated by utilizing Shimadzu FTIR spectrophotometer to detect the interaction between the excipients and Drug (Hedera helix Linn.). The excipients and drug were finely ground with potassium bromide to set up the pellets at 600 psi and spectra were examined in the range of 400 and 4000 $cm^3$.

**4. Storage -**

This lozenge formulation should be kept away from direct sunlight and out of reach of children, as per label instruction. It should be kept away from moisture. Room temperature and refrigerator temperature are often advised based on the requirements of both, the drug and the base used in the lozenge formulation.

**5. Packaging of lozenges-**

Lozenges are usually hygroscopic in nature hence an involute and multiple packing system should be used in order to maintain its stability during marketing. The single unit of lozenge was wrapped in a moisture impervious liner. These wrapped lozenges were then placed in a tamper proof or water-resistant glass, polyvinyl chloride or metal container. Finally, these were over-wrapped using aluminium foil or sheet.

**6. Result and Discussion-**

### 6.1. FT-IR results of Hedera helix Extract-

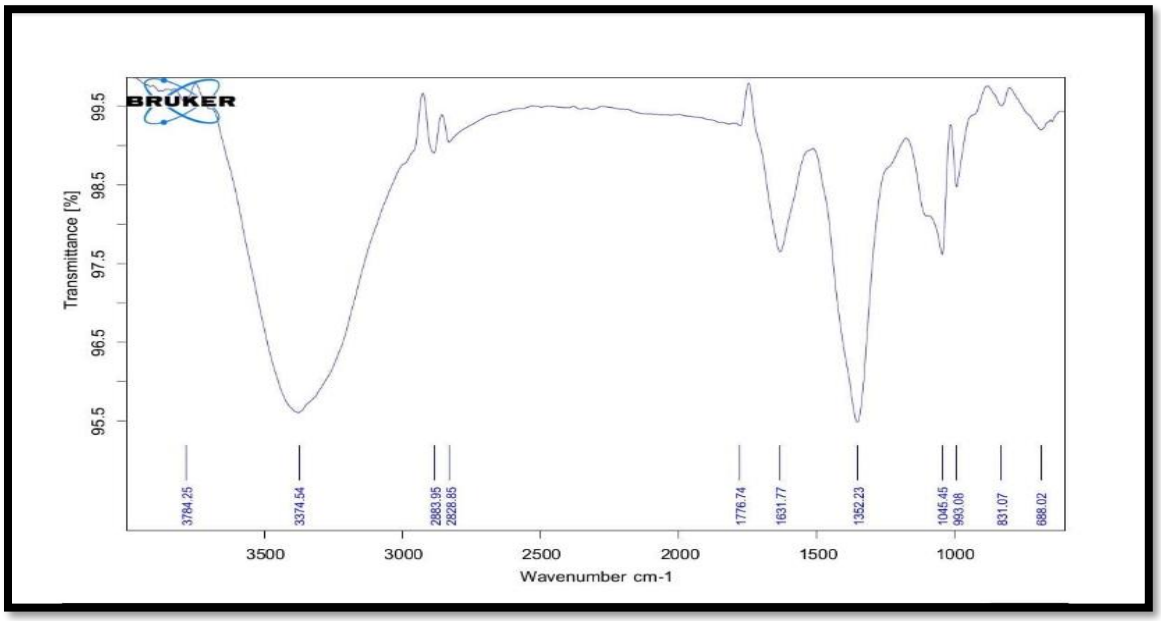



**Fig.6.1.-I.R. Interpretation of *Hedera helix* .**

| Bond | Functional Group | Frequency |
|---|---|---|
| O-H | Alcohol | 3374.54 |
| C=O | Anhydride | 1776.74 |
| C=N | Imine/Oxime | 1631.77 |
| N=O | Nitro | 1352.23 |
| C-N | Aromatic Amine | 1045.45 |
| C-H | Alkene | 993.08 |
| C-Cl | Chloride | 688.02 |
| C-H | Aromatic | 831.07 |

**Table 6.1.-Results of I.R. of Hedera helix formulation.**

| Batches | Hardness (kg/cm2) | Thickness (mm) | Weight (gm) | Diameter (mm) | Drug content (%) | Friability | Moisture content | Disintegration time (min) |
|---|---|---|---|---|---|---|---|---|
| B1 | 10 | 6.1 | 3 | 11 | 98.5 | 2.80 | 0.88 | 10.32 |
| B2 | 10.2 | 7.2 | 3 | 10 | 96 | 2.91 | 0.91 | 15 |
| B3 | 10.3 | 6.7 | 3 | 9 | 98.2 | 2.95 | 0.95 | 15.50 |
| B4 | 10 | 6.6 | 4 | 12 | 97.1 | 2.95 | 0.82 | 16.32 |
| B5 | 11 | 7.3 | 3 | 12 | 95.8 | 2.98 | 0.80 | 20.11 |
| B6 | 10.1 | 7 | 3.9 | 15 | 98.3 | 2.87 | 0.93 | 18.20 |
| B7 | 10.5 | 6.9 | 3 | 11 | 98.5 | 2.97 | 0.88 | 20.30 |
| B8 | 10.2 | 6.3 | 4 | 14 | 98.4 | 2.87 | 0.81 | 17.25 |
| B9 | 10.4 | 6.4 | 3 | 8 | 96.2 | 2.96 | 0.90 | 22.05 |

**Table 6.2.- Evaluation of lozenges for post formulation parameters.**

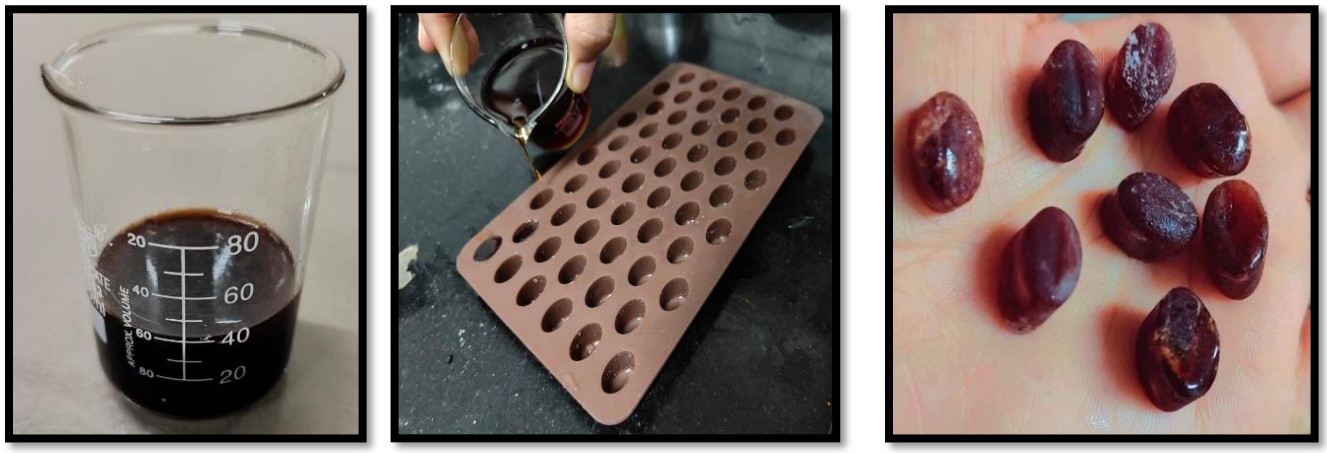
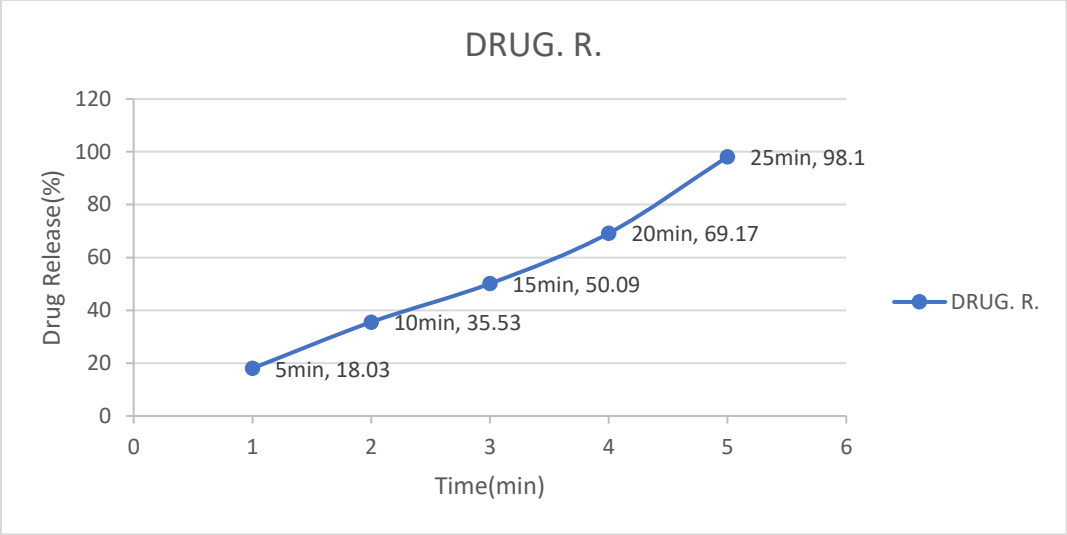


**Fig.6.2-Prepared Lozenges**

| TIME (Min) | DRUG RELEASE (%) |
|---|---|
| 5min | 18.03 |
| 10min | 35.53 |
| 15min | 50.09 |
| 20min | 69.17 |
| 25min | 98.1 |

**Table.6.3-Percentage cumulative drug release of formulation.**




**Graph: Time Verses % Drug release of formulation.**

### 6.2. Drug release kinetics of optimized formulation batch (B5)-

| Optimized formulation | Zero Order | First Order | Higuchi | Hixson-crowell | Korsemeyer peppas |
|---|---|---|---|---|---|
| Batch | R2 | R2 | R2 | R2 | R2 |
| B5 | 0.9796 | 0.9732 | 0.8424 | 0.9908 | 0.9918 |

**Table.6.4.- Drug release kinetics**

### 7. Stability of optimized formulation B5.

| Parameters | Day 0 | After 1 month | After 2months | After 3 months |
|---|---|---|---|---|
| Hardness | 11 | 10.4 | 10 | 9.8 |
| Weight | 3 | 2.9 | 2.2 | 2 |
| % friability | 2.98 | 3 | 3 | 3 |
| %Drug content | 95.8 | 95.5 | 94.9 | 94.3 |
| Moisture content | 0.80 | 0.80 | 0.75 | 0.72 |

**Table.7.1.- Stability results**

### 8. Discussion-

The lozenges were prepared using melting and moulding method with various ingredients, including Jaggery, Hedera helix extract, corn syrup, mint extract, colours, and other excipients. The formulated lozenges underwent various characterization tests to ensure their quality and efficacy. These tests included drug content uniformity, hardness, thickness, weight variation,

friability, moisture content, in vitro dissolution and disintegration, all were conducted using following pharmaceutical standard methods. An accelerated stability study was performed in compliance with ICH guidelines at elevated temperature and humidity conditions. The study confirmed that there was no significant interaction between the drugs, flavours and colours and the prepared formulation remained stable over a seven-week period. The taste of drug was masked with flavouring agents, making the herbal lozenges more palatable for diabetic patients as well as other users.

Therefore, it is a safe product, due to use of herbal drug and very less excipients. It is quick & simple technique. Also, it is Easy to use & convey. The product was found to be eco-friendly and cost-effective. All evaluation tests met the requirements specified in the pharmacopeia (IP - Indian Pharmacopoeia). After evaluating nine batches, it was determined that Batch No.5. gave best results and performed best within the standard limits, making it the optimized batch for further production and distribution.

## 9.Conclusion-

Several allopathic lozenges for cough are available in market, containing high concentration of sucrose. With the increasing demand & interest for natural products in medicine, the demand for these lozenges is promising. The market is likely to grow, providing natural & effective alternative to allopathic medicines. These natural, herbal, sucrose free lozenges in addition to marketed lozenges provide a suitable alternative to allopathic lozenges, more acceptable to diabetic patients.

The formulation of lozenges is a straightforward and an efficient process, making it a preferred choice of medication, especially among patients who find difficulty in swallowing due to bitter taste, find them more acceptable. Medicated lozenges are ideal dosage forms for children due to their ease of administration, patient compliance, convenient and comfort during treatment. They offer additional advantages such as lower the dose, immediate onset of action, reduced dosage frequency and cost effective. Lozenges represent an innovative dosage form that holds a significant place in the field of pharmacy. Their popularity is likely to continue in the future, because of their positive attributes and benefits in terms of patient experience and treatment outcomes. Overall, lozenges provide a promising and effective solution for administering medication in most patients.

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