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# FORMULATION, DEVELOPMENT AND EVALUATION OF SUGAR AND JAGGERY BASED LOZENGES OF DEXTROMETHORPHAN HYDROBROMIDE

**Prakruti Amin[1], Dhruvi Shah[2]*, Dharani Shah[3], Honey Shah[4] and Krima Shah[5]**

[1]Assistant Professor, [2,3,4,5]Research Scholar

Department of Pharmaceutics K. B. Institute of Pharmaceutical Education and Research, Gandhinagar, Gujarat.

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***Corresponding Author**
**Dhruvi Shah**
Research Scholar,
Department of Pharmaceutics K. B. Institute of Pharmaceutical Education and Research, Gandhinagar, Gujarat.

## ABSTRACT

This study presents the formulation, development, and evaluation of sugar and jaggery based lozenges containing dextromethorphan hydrobromide (DXM HBr), a widely utilized antitussive medication. The special population such as pediatric and gediatric are having difficulty in swallowing solid dosage form, so for them lozenges is a good option. Cough and Cold is a common syndrome that we find during seasonal changes, for that Dextromethorphan is used as dry cough and with growing concerns over the health implications due to excessive sugar consumption, there is a burgeoning interest in exploring alternative sweeteners for pharmaceutical formulations. Jaggery, a natural sweetener derived from sugarcane or date palm sap, offers a potential alternative due to its perceived health benefits and cultural acceptance. Various formulations were prepared utilizing different ratios of sugar and jaggery in combination with other excipients employing the heating and congealing method. During the development process, one of the frequent hurdles was the bitterness of the drug, which was successfully mitigated through the use of taste masking agents such as Kyron T-134 resin and honey. Physicochemical characterization, encompassing parameters such as weight variation, hardness, friability, disintegration time, and drug content uniformity, was conducted to assess the quality attributes of the lozenges. Furthermore, in vitro dissolution studies were performed to investigate the drug release kinetics. The results revealed that sugar and jaggery-based lozenges of DXN HBr exhibited satisfactory physicochemical properties and

drug release profiles. Notably, sensory evaluation indicated favourable acceptability, with jaggery-based formulations demonstrating enhanced palatability compared to those containing only sugar. This research underscores the potential of utilizing jaggery as a natural sweetener in pharmaceutical formulations, offering improved taste profiles while addressing concerns regarding sugar content. The backup dosage form with enhanced palatability and broader acceptability, particularly among populations seeking natural product options.

**KEYWORDS:** Pediatric, Geriatric, Dextromethorphan Hbr, Sugar, Jaggery, KyronT-134, Heating and congealing method.

## INTRODUCTION

Unleash the power of relief with lozenges-the tiny titans that dissolves discomfort away. Lozenges are solid preparation that contains one or more medicaments, usually in a flavoured, sweetened base, that are intended to dissolve or disintegrate slowly in the mouth. Generally lozenges are used for pediatric and geriatric patients because they cannot swallow solid oral dosage forms well as for medication designed to be released slowly to yield a constant level of drug in the oral cavity or to bathe the throat tissues in the solution of the drug. In the modern world, throat infection is the most prevalent illness. So, for the convenience the lozenges come into the picture. They often hailed for their therapeutic properties has made lozenges more popular remedy.[1] Lozenges are solid dosage form that are intended to be dissolved or disintegrated slowly in the mouth. Lozenges are planned 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. Drugs includes analgesics, anaesthetics, antimicrobial, antiseptic, antitussive, aromatics, astringent, corticosteroid, decongestants and demulcents, as well we can compound the single dose and multiple dose lozenges as per the particular requirements of the patient's need.[2] Common cold, cough and sore throat are minor disorders of respiratory system, usually arises due to infection in respiratory tract and autoimmune response. The number of patients suffering from cold, cough and sore throat usually increases during monsoon and winter season, owing to fluctuations in the environmental conditions. Children and women under 35 years are more prone to suffer from cold, cough and sore. Underdeveloped immune system increases the risk of exposure it is expected that children are three times more susceptible to cold and cough than an average adult. The aforementioned advantages of drug administration via the oral cavity offer new possibilities in the

administration of drugs to "problematical" sub populations like children and the elderly. These patients have special drug administration requirements as they are often unable to swallow solid dosage forms (e.g. tablets, capsules).Poor taste can also lead to medication being refused or spat out. Furthermore, the pediatric sub population is a very heterogeneous group. To cold related infection viruses in children mostly. Dextromethorphan (3-methoxy-N-methylmorphinan) is one of the most commonly used antitussive drug (Cough suppressant) in children. It is used to relive cough due to common cold, hay fever, upper respiratory tract infection, sinus, sore throat and bronchitis. Dextromethorphan hydrobromide has an opioid like structure. However, being the d-isomer, it does not possess the analgesic/addictive properties of opioids. Dextromethorphan hydrobromide was approved as a non-prescription cough medication in 1958 by the FDA. In current scenarios, dextromethorphan hydrobromide can be found in more than 125 OTC cough and cold patented products. Since liquid dosage forms are bulky and stability is a key issue, it is given either alone or in combination with analgesics (Acetaminophen), expectorants (Guaifenesin) and/or antihistamines (Brompheniramine, Chlorpheniramine and diphenhydramine). It's mainly active against the dry cough and is used in combination with expectorants to have significant effects for productive cough. Sore throats, sores, and other irritations in mouth and pharynx are common ailments that can cause pain. Although a variety of pharmaceuticals are available, both prescription and over-the-counter, to treat the pain, these pharmaceutical scan be sometimes difficult to administer to patients who are unwilling and/or unable to take conventional oral medications. For example, children and adults may have difficulty swallowing tablets or capsules. Patients may resist taking medicine in liquid form due to the medicine's unpleasant taste or texture or difficulty in swallowing. Moreover, there may be a significant time delay, sometimes twenty minutes or longer, between ingesting many oral medications and the onset of a therapeutic effect because the medications must be absorbed into the blood stream from the digestive system after the medicine is swallowed. Lozenges are inserted into the mouth. Because the tongue's bottom extremities may be damaged, buccal lozenges are well-formed and commonly utilised and are designed to be put due to their size. Between the gums and the cheek although a lozenge can last up to 30 minutes, this is dependent on the individual. By consuming the lozenge, the patient can manage the rate of excretion and absorption, until it was completely dissolved. As a result, the amount of medication supplied each time a lozenge is administered can vary significantly. Increased dilution and swallowing can also be caused by sucking and subsequent saliva production.[3] Lozenges are used for patients who are unable to swallow solid oral forms of drugs and pharmaceuticals that are meant to be released

slowly in order to generate a continuous dose of the drug in the mouth or to wash the throat tissue with a drug solution. As there are other different medications that can be delivered through the lozenge. Depending on the need of particular patient.[4]

**Advantages**

→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 flavours 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.

**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[5]

## MATERIALS AND METHODS

Dextromethorphan hydrobromide IP (Abbott pharmaceuticals), Eudragit S100(Evonik Roehm pharm polymers), Polyethylene glycol (PEG6000), Gelatin powder(Suvidh Nath laboratories), Methyl Cellulose High Viscosity 4000 Cps (Chemdyes corporation), Kyron T-134(Ajanta Pharma Ltd), Honey, Citric acid, Menthol, Sugar, jaggery, Hydroxypropyl methyl cellulose (HPMC K 100), Tartrazine solution(In-house K.B institute of pharmaceutical education and research).

## Methods

### Heating and Congealing technique

Take required quantity of sugar and jaggery and add required amount of water. Put for heating on water bath (105-110 ºC) until it become thick. Now after the base is become hard after that add excipients as per their melting point and heat it for 30 min more. Pre-lubricate and put it for 10 – 15 min pour the syrup and lozenges remove from mould. Batches formulated as per this method.

**Table 1: Composition of lozenges.**

| Sr. no. | Ingredient (mg) | F1 | F2 | F3 | F4 | F5 | F6 |
|---|---|---|---|---|---|---|---|
| 1 | DXM Hbr | 10 | 10 | 10 | 10 | 10 | 10 |
| 2 | Eudragit S 100 | 120 | 120 | 120 | 120 | 120 | 120 |
| 3 | HPMC K 100 | 300 | 300 | 300 | 300 | 300 | 300 |
| 4 | PEG - 6000 | 2400 | 2400 | 2400 | 2400 | 2400 | 2400 |
| 5 | Sugar | 10000 | 10000 | 10000 | 10000 | 10000 | 10000 |
| 6 | Jaggery | 10000 | 10000 | 10000 | 10000 | 10000 | 10000 |
| 7 | Kyron T-134 | - | - | 0.5 | 1 | 1.5 | 2 |
| 8 | Honey | - | - | - | - | 1 | 1 |
| 9 | Gelatin powder | 10 | 10 | 10 | 10 | 10 | 10 |
| 10 | Methyl cellulose | 300 | 300 | 300 | 300 | 300 | 300 |
| 11 | Citric acid | 3600 | 3600 | 3600 | 3600 | 3600 | 3600 |
| 12 | Tartrazine solution | q.s | q. s | q. s | q. s | q. s | q. s |
| 13 | Menthol | 120 | 120 | 120 | 120 | - | - |
| 14 | Vanilla | - | - | - | - | q. s | q. s |

### Experimental work

**Identification of drug:** The drug was subjected to FT-IR studies for the purpose of characterization. IR technique is one the most powerful techniques which offers the possibility of chemical identification. Drug was mixed with potassium bromide (KBr) in 1:100 proportions and a spectrum was obtained in a range of 400–4000 $cm^{-1}$ Potassium bromide was used as a blank while running spectrum.[6,7]

### UV visible spectrophotometry determination of absorption maximum (λmax)

The DXM Hbr was subjected to UV spectroscopic analysis to find out the wavelength (max) at which it shows maximum absorbance. Stock solution of the drug (1 mg/ml) was prepared in a phosphate buffer (pH 6.8) and a 100 µg/ml solution was scanned over the wavelength range 200–400 nm to determine λmax.[8]

**Preparation of Standard Stock Solution of DXM Hbr**

Accurately weighed 10mg DXM Hbr was dissolved in 100 ml of suitable solvent to obtain a solution of 100 µg/ml.

**Preparation of calibration curve**

From the above prepared stock solution, aliquots were taken and appropriately diluted to obtain 10 to 60 µg/ml concentrations of DXM Hbr. Absorbance of each solution was measured 279.4 nm against 6.8 pH phosphate buffer as blank at specific λmax of 279.4nm. Analytical method parameters for DXM Hbr[9]

**Evaluation test**

1. **Hardness test:** To evaluate the diametrical crushing strength, 3 lozenges from each formulation were tested using a Monsanto hardness tester. The mean ± SD values were calculated. The range of hardness found at the end given below in the result table.[10]

2. **Friability test:** The friability of the 20 lozenges from each batch was tested by a friabilator. At a speed of 25 rpm for 4 min. The lozenges were then dedusted, reweighed and percentage weight loss was calculated by the equation. In friability test the results are in the range of between0.5% to 1%, so it is considered as this test is pass.[11]

   % Friability = (initial Wt. - Wt. after friability) × 100 / initial Wt.

3. **Average weight and Weight variation test:** 20 lozenges were selected and weighed collectively and individually on an electronic balance. From the collective weight, average weight was calculated. Each lozenge weight was then compared with average weight to assure whether it was within permissible limits or not. Not more than two of the individual weights deviated from the average weight by more than 7.5% for 300 mg lozenges.[12]

$$\text{Average weight} = \frac{\text{weight of 20 lozenges}}{20}$$

$$\%\ \text{weight variation} = \frac{\text{average weight-weight of each lozenges}}{\text{Average weight}}$$

**Table 2: Weight variation test standards as per USP, BP and IP.[13]**

| As per USP standards | Maximum % deviation allowed | As per IP/BP Std. |
|---|---|---|
| 130mg or less | 10% | ≤ 84 mg |
| 130 to 324mg | 7.5% | 80 to 250 mg |
| More than 325 mg | 5% | ≥ 250 mg |

4. **In vitro mouth dissolving time:** Mouth Dissolving time was determined by each batch formulation using USP disintegration apparatus, where lozenges were placed in each tube of the apparatus and time taken for the lozenges to dissolve completely was noted by using 100ml phosphate buffer of pH 6.8 at 37$^{o}$C. This test was done in triplicate.[14]

5. **In vitro drug release study:** *In vitro* release studies of lozenges from all formulations were performed according to USP XVIII apparatus II, paddle method (Dissolution testapparatus-Electro lab, Mumbai, India). Paddle speed was maintained at 50 rpm and 900 ml of pH 6.8 phosphate buffers was used as the dissolution medium. Samples (10 ml) were collected at predetermined time intervals (every 5minutes) and replaced with equal volume of fresh medium, filtered through a Whatman filter paper, and analyzed with a UV–Visible spectrophotometer at λ = 279.4nm. Drug concentration was calculated from a standard calibration plot and expressed as cumulative % drug dissolved.[15]

## RESULT AND DISCUSSION

### FT-IR Results

Identification of the drug sample DXM Hbr was confirmed from the FTIR spectrophotometer (Model-8400S, Shimadzu, Kroyoto, Japan). Spectra obtained by KBr pellet method. The FTIR spectrum of drug is shown in Figure.

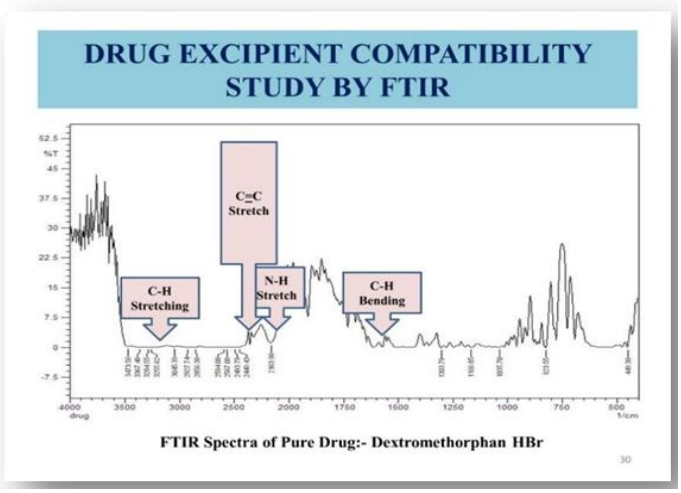


**Figure 1: FT-IR study of pure drug – Dextromethorphan Hbr.**

The characteristic peaks of pure drug dextromethorphan hydro bromide as c-h stretching is at 3255.62 $cm^{-1}$ , c=c stretch is at 2449.43 $cm^{-1}$, n-h stretch 2163.98 $cm^{1}$ and c-h bending is at 1600 $cm^{-1}$ by which we can say that all the values are in its range and drug is in its free state. Presence of the drug in the formulations and confirms the compatibility of drug with the polymer.

**UV visible spectrophotometry determination of absorption maximum (λmax)**

Stock solution of the DXM Hbr (10 mg/100ml) was prepared in a phosphate buffer (pH 6.8) and a 100 µg/ml solution was scanned over the wavelength range 200–400 nm. DXM Hbr exhibited maximum absorption at 279.4 nm.

**Calibration Curve DXM Hbr Hbr**

Calibration Curve in Phosphate buffer pH 6.8 Accurately weighed 10mg DXM Hbr was dissolved in 100 ml of Phosphate buffer pH 6.8to obtain a solution of 100 µg/ml. From the above prepared stock solution, aliquots were taken and appropriately diluted to obtain 10,20,30,40,50,60,70.80 and 90 µg/ml concentrations of DXM Hbr. Absorbance of each solution was measured in triplicate at 279.4 nm. against 6.8 pH phosphate buffer as blank at that specific λmax. The absorbance of each concentration is shown in table and the calibration curve is shown in figure.

**Table 3: Calibration of DXM HBr drug on different stock solution concentrations.**

| Sr. no. | Concentration of DXM HBr drug (mg/ml) | Absorbance |
|---|---|---|
| 1 | 0 | 0 |
| 2 | 10 | 0.055 |
| 3 | 20 | 0.067 |
| 4 | 30 | 0.069 |
| 5 | 40 | 0.077 |
| 6 | 50 | 0.084 |
| 7 | 60 | 0.096 |
| 8 | 70 | 0.098 |
| 9 | 80 | 0.12 |

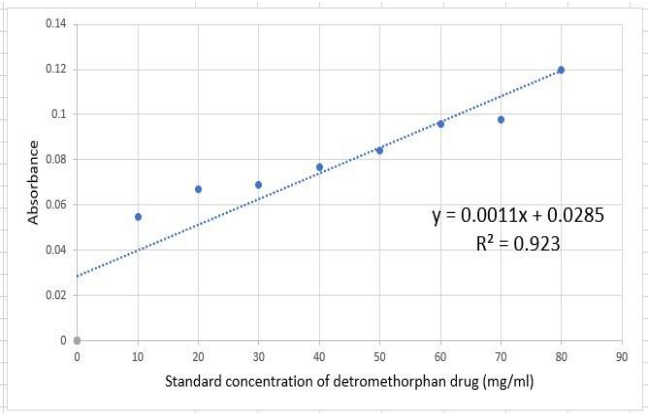


**Figure 2: Calibration curve of dextromethorphan hydrobromide and $R^2$ value.**

→ Here the $R^2$ value of DXM HBr is 0.923 (near to 1) which interprets that there is the positive and good correlation between the concentration of stock solution and absorbance, on increasing the concentration the absorbance is also increasing.

**Examination of hard sugar lozenges**

**Table 4: Organoleptic examination of sugar lozenges.**

| Parameter | Observation |
|---|---|
| Shape | Bulb spherical shape |
| Colour | Cherry red and shiny red |
| Texture | Shiny and smooth |
| Taste | Individual examination |

During the organoleptic examination of sugar based candy lozenges the relative taste score was not preferable without using taste masking agent. After performing taste masking we get desirable result withn in ion exchange resin Kyron T -134.

**Examination of hard jaggery lozenges**

**Table 5: Organoleptic examination of jaggery lozenges.**

| Parameter | Observation |
|---|---|
| Shape | Bulb spherical shape |
| Colour | Milky brown in colour |
| Texture | Shiny, greasy and smooth |
| Taste | Individual examination |

In organoleptic examination of jaggery based lozenges candy the relative taste score was not much bad as compare to test score obtained in sugar based lozenges. Honey does not show up that much betterment in taste as compared to the taste score obtained in ion exchange resin Kyron T -134.

**Results of evaluation parameters**

**Table 6: Evaluation parameters for prepared lozenges batches.**

| Batch formulation | Hardness $Kg/cm^3$ | Weight variation(mg) | Friability (%) | In vitro mouth dissolving time(min) |
|---|---|---|---|---|
| B1 | 3.02±0.006 | 2.01±0.003 | 1.12±0.153 | 25±0.004 |
| B2 | 4.24±0.005 | 2.21±0.002 | 1.27±0.005 | 24±0.002 |
| B3 | 2.14±0.006 | 2.16±0.003 | 1.60±0.12 | 29±0.003 |
| B4 | 2.16±0.008 | 2.71±0.001 | 1.80±0.008 | 28±0.003 |
| B5 | 3.14±0.006 | 2.21±0.003 | 1.77±0.006 | 27±0.001 |
| B6 | 2.16±0.005 | 2.22±0.004 | 1.04±0.006 | 29±0.007 |

During the evaluation test, discrepancies in observations between batches B1, B2, and B5 were attributed to variations in the concentration of the hardening agent. Conversely, batches B3, B4, and B6 exhibited similar observations. The friability of the samples ranged approximately between 0.5% to 1%, with batch B6 demonstrating friability close to 1%. Hardness measurements of the prepared batches fell within the range of 2.14±0.006 to 4.24 ±0.005 kg/cm^2. In vitro dissolution times in simulated mouth conditions ranged from 24±0.002 to 29±0.007 minutes.

**In vitro dissolution profile of lozenges**

**Table 7: % Drug Release from prepared lozenges.**

| Time(min) | | %Drug Released | | | | |
|---|---|---|---|---|---|---|
| | B1 | B2 | B3 | B4 | B5 | B6 |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 5 | 44.71 ±01 | 39.91± 02 | 45.08 ±03 | 49.96 ±04 | 82.08 ±03 | 79.25 ±05 |
| 10 | 56.20 ±03 | 48.09 ±03 | 52.05 ±04 | 54.06 ±07 | 89.28 ±05 | 91.33 ±07 |
| 15 | 59.41 ±07 | 54.09 ±05 | 66.63 ±06 | 76.09 ±08 | 94.93 ±06 | 97.28 ±09 |
| 20 | 67.05 ±08 | 68.65 ±06 | 77.01 ±08 | 82.01 ±09 | 96.22 ±07 | 97.79 ±10 |
| 25 | 76.09 ±09 | 79.87 ±07 | 84.01 ±09 | 88.03 ±11 | 97.82 ±10 | 98.33 ±11 |
| 30 | 84.92 ±10 | 88.43 ±09 | 91.20± 11 | 95.62 ±12 | 98.5±13 | 99.02 ±14 |

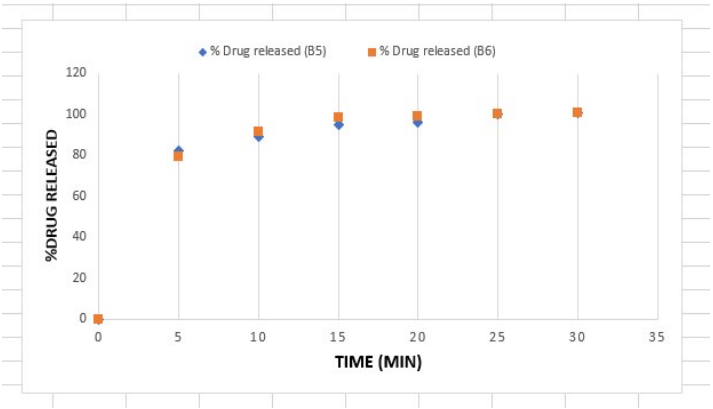


**Figure 3: Dissolution profile of lozenges B5 and B6.**

All lozenges formulations released more than 99% of the drug within 30 minutes [Figure 3]. *In vitro* cumulative % drug released, formulation B6 was considered to be better formulation among all of the nine formulations tested in this study.

## CONCLUSION

In present study focuses on the formulation, development, and assessment of hard candy lozenges containing dextromethorphan hydrobromide (DXM HBr), utilizing sugar and jaggery as base materials. These lozenges are intended for therapeutic use as a cough suppressant. The selection of lozenges over conventional tablet or capsule forms is primarily motivated by their enhanced patient compliance, particularly among geriatric and pediatric populations. Additionally, lozenges offer extended oral cavity retention, lasting over 30 minutes, thereby minimizing the challenges associated with swallowing medications. A key aspect addressed in this study is taste masking, crucial for improving patient acceptability. Taste masking was achieved through the incorporation of honey and Kyron T-134 ion exchange resin to mitigate the inherent bitterness of DXM HBr. Two base materials, sugar and jaggery, were employed in the formulation process, and various evaluation parameters were applied to compare their efficacy in producing optimal lozenges. Through rigorous quality control assessments, it was determined that the optimized batch among the six evaluated batches was B6 (Jaggery-based lozenges containing Kyron T-134 ion exchange resin and DXM HBr). This conclusion was drawn based on several criteria: Hardness testing indicated values within the range of 1 to 4 kg/cm², meeting the established criteria for acceptability. Weight variation testing demonstrated that not more than two lozenges deviated beyond the permissible limit of 7.5%, thus meeting the set standards. In-vitro dissolution testing revealed the highest percentage of drug release within the desired timeframe of 30 minutes for batch B6. Friability testing showed results within the range of 0.5% to 1%, meeting the specified criteria for acceptable lozenge integrity. Given that all evaluation parameters fell within the appropriate ranges for batch B6, it was deemed the optimized formulation. This study underscores the potential of utilizing jaggery-based lozenges containing taste-masking agents for enhanced drug delivery and patient adherence in the management of cough symptoms. Future research may explore further optimization strategies to validate the efficacy and safety of these formulations in diverse patient population

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