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Linkus lozenges with polyherbal extract based on their design, development, and evaluation for symptomatic relief

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Abstract
Lozenges are solid dose preparations that are meant to dissolve slowly in the mouth for therapeutic effect. Respiratory infections are frequent infections that often infect the respiratory tract, causing symptoms such as headaches and body aches, fever, sleepiness, runny nose, congestion, and cough. Humanity has employed traditional medicine and herbal mixtures to heal and treat a variety of ailments and problems. People have used natural ingredients as remedies from ancient ages. Ayurveda, Siddha, & Unani plants are formulated in different dose forms such as churna, gutika, asavas, aristasavlehas, so on and so forth. Various formulations are frequently used, with Ayurvedic reference, as a domestic remedy, or as a conventional medicine. Balguti, Sitopaladi churn and Sootshekharmatra are a few herbal preparations that are regularly utilised in various households. These formulations each possess immunomodulatory, expectorant and antacid characteristics. In our research, we repackaged classic formulas into novel unit dosage forms. Given the importance of patient satisfaction and market considering competitors with modern dosage forms, the present study included phytochemical screening of extracts utilized as well as the manufacture of lozenges containing herbal constituents. It was revealed that formulas passed quality control checks. These herbal preparations would have less negative effects and be favored by the target group.

Keywords: Sore throat, common cold, nasal congestion, runny nose

Introduction
An adult may typically experience a sore throat two to three times a year, especially children more susceptible than adults due to their immunological immaturity. One of the most typical symptoms of upper respiratory tract infections (URTIs) that prompts visits to medical practitioners' offices or nearby drug shops for treatment is an acute sore throat. Every year, about 25 percent of people in England and Wales seek medical attention for a respiratory tract illness.

60% of all antibiotic prescriptions in general practice are for respiratory tract infections, including URTIs and lower respiratory tract infections. This places a major financial burden on the healthcare system [1]. As a better and more inventive dosage form and oral confectionery product, lozenges are one of the most well-known and cutting-edge medication delivery systems. The oral route is the most popular of the many administration methods since it is simple to take, flexible, and especially patient-compliant, and it is suitable for all patients regardless of age. The creation of novel drug delivery methods for already available medications that have increased efficacy, avoid first pass hepatic metabolism do not require water consumption, and boost bioavailability together with decreased dose frequency [2].

Despite the fact that the lozenge dissolving duration is 30 minutes, these lozenge dissolve between 15 seconds to 2 minutes depending on the patient, who regulates the place of the medication's effect is accelerated by how quickly it breaks down. In order to minimize systemic drug action and maximize local drug activity, lozenges are designed to be allowed to dissolve on the back of the tongue. They gently dissolve in the mouth while being chewed or sucked, releasing their active components for targeted local action [3]. The overuse of antibiotics contributes to the rise of antibiotic resistance, a growing concern to the public health of the entire world.

As a result, it's important to urge RTI patients to explore alternative therapies, while saving antibiotics for those who have serious illnesses or are at higher risk of consequences [4].

Most lozenges may be purchased over-the-counter. Runny nose, cough, headache, trouble swallowing, enlarged lymph nodes, and a raspy voice are just a few of the symptoms of a sore throat or pharyngitis inflammation. Usually, a bacterial, viral, or fungal infection is the culprit. Formulators have worked hard to create a unique type of tablet dosage form for the oral route that swiftly degrades and breaks up in salivation without the need to swallow the dosage form whole in order to combat these problems, such as trouble swallowing and symptoms like sore throat. Varying types of lozenges have different mixtures of components and fixes. They can be applied through the mouth cavity either locally or systemically. Analgesics, sedatives, antimicrobials, and other medications are delivered via lozenges [5].

Applications for lozenges include expectorant, nasal decongestant, cough suppressant, and throat infection. Scratchiness, or irritation are all symptoms of a sore throat, which frequently get worse when you swallow. A viral infection, such as the flu or a cold, is the most frequent cause of pharyngitis, which causes a painful throat [6].

Aparajita is the common name for the recurrent plant *Clitoria ternatea* (Fabaceae). They have pinnate leaves. The single, 4- to 5-cm-long, deep blue blooms have a very short pedicellum. Pods have a flat, linear form and are 6–12 cm long and 0.7–1.2 mm broad. Brown or black coloured seeds range in length from 4.5 to 7 mm and width from 3 to 4 mm. It is available all throughout India [7]. For stomatitis, hematemesis, sleeplessness, epilepsy, psychosis, purgative, and cathartic purposes, the entire plant and seed extracts are utilized. In addition to being a well-known antibacterial and anti-inflammatory herb for centuries, the herb has also been used as an anti-inflammatory, anti-diabetic, antipyretic, analgesic, and antiemetic agent. It has been mentioned in several ayurvedic treatises, including charaka samhita and sushruta samhita.

Benefits of lozenges

1. Simple delivery to young and old patients
2. Local and systemic effects via oral cavity
3. Extended pharmacological action
4. Increased interaction time with the patient
5. Prevent drug hepatic metabolism
6. Do not require water for ingestion
7. Appropriate for individuals with dysphagia
8. Drug therapy may be discontinued if dose is not required
9. Formula modification in accordance with patient needs
10. Shorter manufacturing time
11. Low production costs
12. Ads flavors and a pleasing aftertaste
13. Increased patient adherence

Ingredients [8-11]

Ginger

It is made of *Zingiber officinale* (Family: Zingiberaceae) rhizomes that have had their black outer skin scrapped off and dried in the sun. Oleo-resin, which is mostly found in ginger and possesses fragrant, carminative, and expectorant properties Fresh ginger's key ingredient, gingerol, may strengthen the immune system and protect the respiratory system. It often appears as a yellow, pungent oil with a spicy-sweet scent.

Clove

A tree (Myrtaceae) called *Syzygium aromaticum* produces cloves as its aromatic flower buds (Eugenia caryophyllus). They originated in Indonesia's Maluku Islands, often known as the Moluccas. Used as an antiviral and an analgesic. The presence of Eugenol and other components in the flower bud causes these effects

Turmeric

They are dried *Curcuma longa* rhizomes (Zingiberaceae). Due to its bright yellow colour, turmeric is one of the spices that is frequently used in Indian cuisine. It has antiseptic properties, making it useful for respiratory ailments including the common cold, bronchitis, cough, and other upper respiratory issues. It also lowers kapha, making it useful for clearing throat mucus. It is employed in cosmetic goods since it protects skin as well. It includes curcuminoids, the main component of which is curcumin, which has a wide range of medicinal uses.

Honey

It is a saccharine liquid that the hive bee, *Apismallifera*, Apisdorsata, and other species of *Apis* deposit in the honey comb (from the nectar of flowers) (Fam: Apidae). Honey is a well-known natural treatment for both dry and wet cough

Liquorice

It is possible to extract a sweet flavour from the root of Glycyrrhiza glabra (Family: Leguminosae). The licorice plant is a perennial herbaceous legume that is indigenous to India and portions of southern Europe. In India, it is also referred to as mulethi and Jestamadh, and it is frequently used in the Ayurvedic medical system to treat a variety of respiratory illnesses. Used as a demulcent and expectorant. Glycyrrhenic acid, which is present, is the cause of these characteristics

Tulsi

Tulsi is frequently used in ayurveda and naturopathic treatments to aid in the natural healing of the human body. Both the leaves and the blossoms of tulsi are useful. The miracle plant has also been classified in ayurvedic texts as stimulant, antipyretic, and fragrant in character. The herb tulsi is often employed to treat respiratory issues. Asthma may be treated with it and it is also used to treat headaches, sore throats, and fevers.

Material and Method [12-16]

Flowers of *Clitoria ternatea* were procured at a local market. Aluminum sheets precoated with silica gel (60 F254, 20 cm × 20 cm with 250 µm layer thickness) were purchased from Merck, Darmstadt, Merck (Germany). AR grade ethanol, AR grade methanol, and AR grade ethyl acetate (AR grade), Instrumentation and chromatographic conditions The medication was separated chromatographically on aluminum plates precoated with silica gel 60 F254, (10 cm 10 cm with a layer thickness of 250 m). On the plate, samples were applied. The mobile phase was an 80:20 v/v mixture of ethyl acetate and hexane. 10 cm: 10 cm chloroform: methanol (15:1) The CAMAG twin trough glass chamber was utilized for linear ascending development of TLC plate under 16 min saturation conditions

Preparation of Extract
Clitoria ternatea flower powder was made and dried at 400 °C. The coarse powder was extracted in a soxhlet apparatus with ethanol. It was dried to yield a 5% yield of alcoholic extract.

Lozenge preparation
Flowers from *Clitoria ternatea* were crushed in mortor and pastle and shifted through a sieve attached to a mechanical shifter. The residual material was reground and transferred once more to produce powder. The excess material was discarded. Purified water was placed in a water bath and heated to 60-70 degrees Celsius. Sugar was added to boiling water and heated with continuously mixed until it was completely dissolved. Than grinded powder of *Clitoria ternatea* added into obtain sugar syrup and other component were added and mixed together for 5 to 10 minutes using a stainless steel spatula. The material was poured into the lozenges forming molds, which is fitted with oval shaped dies to form lozenges of appropriate size, shape, and weight. The average weight of produced lozenges were tested as needed in accordance with the specified standard weight. The prepared lozenges were sent through a three-deck-cooling conveyer and subsequently through a metal detector. The lozenges were placed in polybags to cool to room temperature. The lozenges were kept in a room that was kept at 28 degrees Celsius and 50 percent relative humidity until the pillow packing was completed. Formulation details given in (Table 1).

Table 1: Formulation Chart of Fluoxetine Hydrochloride Lozenges.

Ingredients (mg)	Control	F1	F2	F3	F4
Aparajita	0	5.5	6	7.5	8
Clove	5	2	2	2	3
Ginger	10	12.5	12	10.5	10
Cardamom	1	2	2.5	2	2.5
Liquorice	7	6	6	5.5	5.5
Turmeric	3	2	3	2	2
Tulsi	6	3	3.5	3.5	3
Honey	1	1	1	1	1
Sugar	20	20	20	20	20

Determination of ash values
The total ash technique is intended to determine the total quantity of material left after ignition. This comprises both "physiological ash," which is formed from plant tissue, and "non-physiological ash," which is the remnant of foreign materials (such as sand and dirt) sticking to the plant surface.

Evaluation of Aparajita Lozenges
Determination of organoleptic properties organoleptic properties were examined by visual inspection of lozenges for appearance, color, and shape.

Measurement of pH
The acidity or alkalinity of a lozenges was indicated by using lab pH meter, a scale from 1.0 to 14.0. 1% W/V solution of candy was prepared by dissolving 1 g candy in 100 ml distilled water and its pH was recorded.]

Weight variation
Ten lozenges were randomly selected from each batch and individually weighed. The average weight and standard deviation of 10 lozenges were calculated. The batch passes the test for weight variation test if not more than 2 of the individual lozenges weight deviates from the average weight.

Thickness
Six lozenges were selected randomly from each batch and thickness was measured using Venire caliper Thickness can vary with no change in weight due to difference in the density of granulation and the pressure applied to the lozenges, as well as the speed of the tablet compression machine.

Hardness
Hardness or crushing strength is the force required to break a lozenge in a diametric compression using Monsanto Hardness Tester. For each formulation, the hardness of six lozenges was determined. The lozenges were held along its oblong axis in between the two jaws of the tester. At this point, reading should be 0 kg /cm then, constant force was applied by rotating the knob until the lozenges fractured. The value at this point was noted in kg/cm.

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

Moisture content
Moisture content done by the gravimetric method, 1 g sample was weighed and placed in an oven at 60–70°C for 12–16 h. Final weight was determined to utilize a delicate muslin fabric and its weight was rechecked. Percentage friability is given by the equation.

$$\% F = (\text{Initial Weight} - \text{Final weight}/\text{Initial weight}) \times 100$$

Friability
The friability of sample of twenty lozenges were measured using a Roche Friabilator. Twenty pre weighed lozenges were rotated at 25 rpm for 4 minutes. The lozenges were taken out and de-dusted and were reweighed and the percentage of weight loss was calculated. Friability was found to be less than 1% in the range of 0.15% to 0.99%.

Percentage friability = [(Initial Weight – Final Weight) /Initial Weight] x 100

Disintegration Time
Disintegration time is the interval required for complete disappearance of a lozenges or its particles from the tester net. Disintegration test of the prepared lozenges was performed according to USP30, using a disintegration tester through the disintegration medium of phosphate buffer with pH 6.2 maintained at 37±0.5 °C.

Results

Table 2: Phyto-Chemical Analysis of *Clitoria ternatea*

Test	A	Et H Ex
% yield	40%	20%
Carbohydrates	+	+
Volatile Oil	+	+
Flavonoid	+	+

Thin-layer chromatography & Ash value

The Rf values of extract was found to be 0.48 by using mobile phase ethyl acetate: n-hexane at the ratio of (80:20 v/v) (Figure 1). Total ash value of *Clitoria ternatea* was found to be 13%.

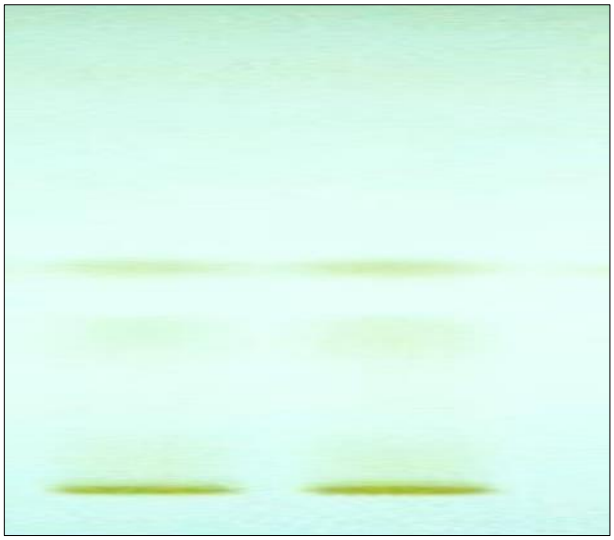


Fig 1: Thin-layer chromatography of *Clitoria ternatea Extract*

Evaluation of Lozenges

Table 3: Preliminary evaluation of *Clitoria ternatea*

Parameter	Control	AF1	AF2	AF3	AF4
Shape	Oval	Oval	Oval	Oval	Oval
Colour	Brown	Brown	Brown	Brown	Brown
Taste	Sweet	Sweet	Sweet	Sweet	Sweet
Flavour	Spicy	Spicy	Spicy	Spicy	Spicy
Nature	Solid	Solid	Solid	Solid	Solid

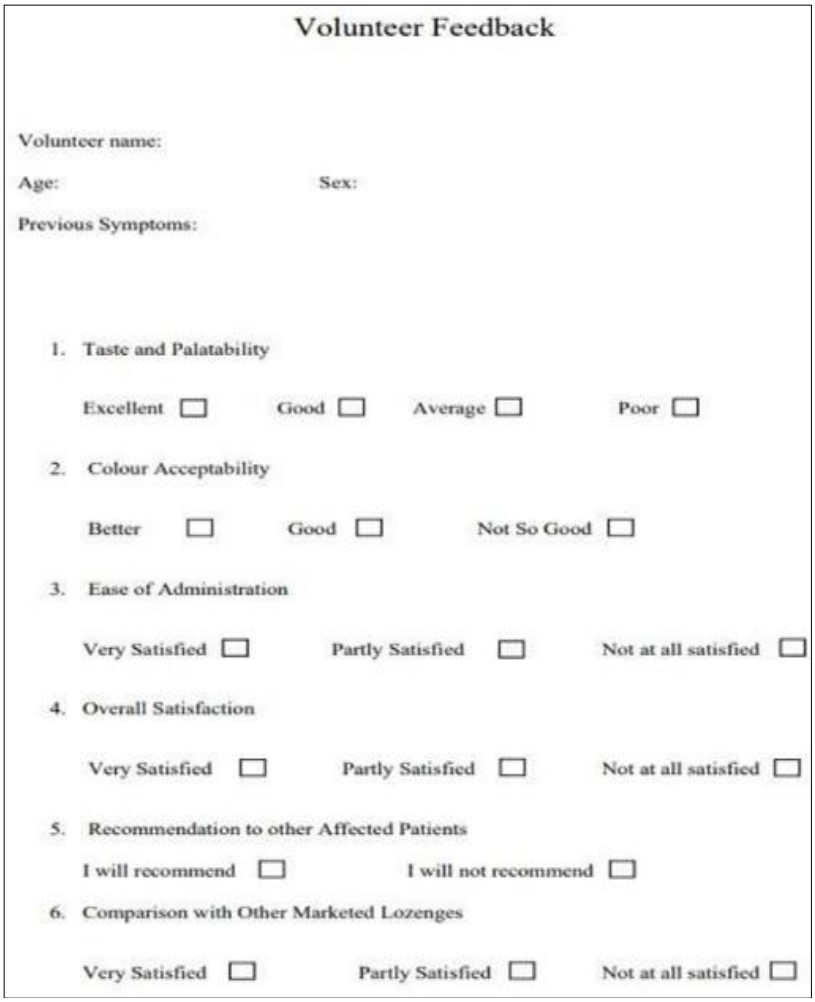
The hardness (n=5), friability (n=5), thickness (n=5), weight uniformity (n=5) and disintegration time (n=5) of prepared lozenges were evaluated and results are given (Table 4)

Table 4: Evaluation of Formulation

Parameter	Control	AF1	AF2	AF3	AF4
Hardness Kg/ cm2	14.3	10.3	12.4	13	13
Thickness (mm)	5.3	5.7	5.12	5.9	5.8
Diameter	17.10	16.89	15.31	16.92	16.89
Weight uniformity (mg)	231.4	291.4	227.2	195.4	310.2
Friability	0.63	0.52	0.85	0.65	0.71

Table 5: Feedback Questionnaire Average Score

Parameters	Average Score
Colour Acceptability	4
Taste and Palatability	3
Ease of Administration	5
Safety	5
Recommendation to other flu patients	5
Comparison with other marketed lozenges	4
Overall Satisfaction	4


Volunteer Feedback

Volunteer name:

Age: Sex:

Previous Symptoms:

1. Taste and Palatability

Excellent ☐ Good ☐ Average ☐ Poor ☐

2. Colour Acceptability

Better ☐ Good ☐ Not So Good ☐

3. Ease of Administration

Very Satisfied ☐ Partly Satisfied ☐ Not at all satisfied ☐

4. Overall Satisfaction

Very Satisfied ☐ Partly Satisfied ☐ Not at all satisfied ☐

5. Recommendation to other Affected Patients

I will recommend ☐ I will not recommend ☐

6. Comparison with Other Marketed Lozenges

Very Satisfied ☐ Partly Satisfied ☐ Not at all satisfied ☐

Fig 2: Questionnaire Pattern for Polyherbal Lozenges

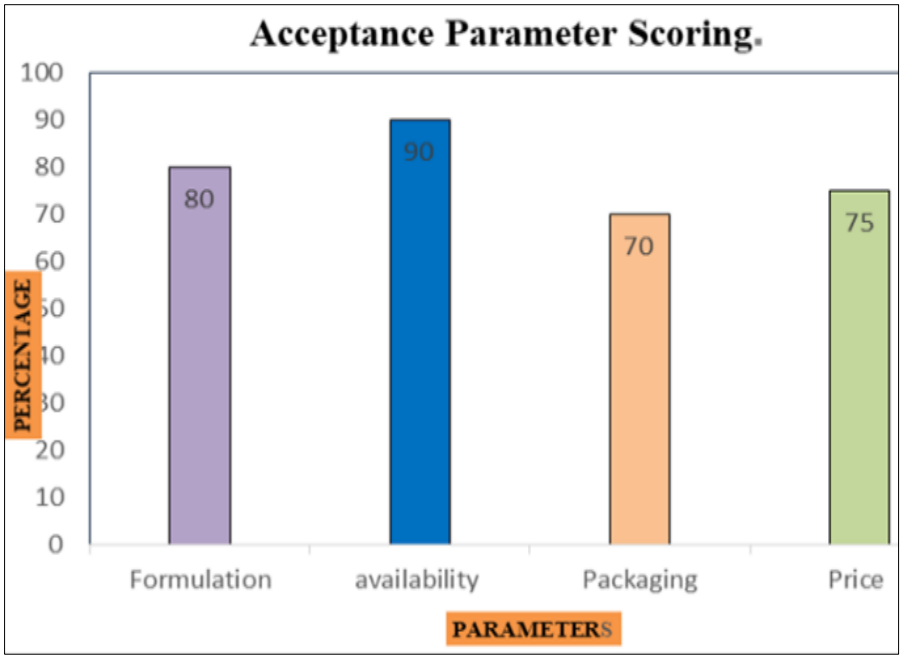


Fig 3: Acceptable Parameters Rating

Economic survey

Market cost per lozenge, with 100 individuals obliged to pay: Rs 3

Criteria for scoring

The greatest score is 5, while the lowest is 1. The acceptability requirements of the any lozenge from markets were studied using survey data from 100 volunteers. Figure 3 depicts the findings in terms of acceptability criteria scoring.

Discussion

Formulations AF1 through AF4 had a rough texture that seemed dull. Control batch preparation did not include any drugs. AF2–AF4 formulations include *Clitoria ternatea* and have a gooey look. The forms of the lozenges were based on the shape of the molds used.

Various evaluation tests were done on the prepared lozenges. The outcomes of lozenge post-formulation factors such as hardness, weight fluctuation, thickness, diameter, and friability. All of values in the tables were observed to be within the limits with no notable variation. Because all of the components were free flowing, the lozenges produced had uniform weight due to uniform mold fill. A good mechanical strength and durability to mechanical and physical stress conditions were shown by the achieved hardness range. The aparajita flower was used to make herbal lozenges along with other natural ingredients like curcuma longa, clove, cardamom, ocimum sanctum, and honey. The produced lozenges were examined, TLC and ash values were used as quality control parameters. The necessity for storage conditions arises from the observation that formulations were gaining ambient moisture during storage, necessitating the need for adequate packaging. The best dose forms for children and geriatric patients will be lozenges. *Clitoria ternatea* is regarded as a useful plant in both of the recent drug development fields due to its variety of therapeutic applications**.** (Figure 4, 5, 6, 7)

Fig 4: Control Batch

Fig 5: Batch F1

Fig 6: Control Batch F2

Fig 7: Batch F3

Fig 8: Batch F4

Conclusion

Different plants have been used to make Polyherbal lozenges. While reinforcing the concept that Polyherbal lozenges may compete with the conventional lozenges on the market, several procedures were taken to ensure that the qualitative, quantitative, and physical attributes of the completed product fulfilled the standards outlined in GMP standards and criteria. The development of the Polyherbal lozenges involved a careful examination of the herbs, dose optimization, and evaluation of identification and quantification using very sophisticated instrumental methods for evaluations. A survey with a questionnaire was used to examine the efficacy. The quality and efficacy of the Polyherbal lozenges have been supported by the conducted study. This study demonstrates that the lozenges are adequate dose form for the symptomatic treatment of cold and flu. The standardization, which gives an accurate and efficient method for creating the identification, repeatability, and quality system in herbal lozenges for the common cold and flu. As a result, the lozenges meet all the criteria and are more effective in treating the flu and the common cold (As per the survey on 100 patients). Therefore, people with cold and flu symptoms might benefit from taking this formulation.

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Conflict of interest

The authors declare no conflict of Interest

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