RESEARCH ARTICLE

Formulation and Evaluation of Herbal Remedy for Cough

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ABSTRACT

The most frequent reason patients seek medical assistance is because of a persistent cough, despite the fact that coughing is both a crucial defensive reflex and a universal indication of health. According to an epidemiologic study, up to 40% of people report coughing. Upper respiratory tract infections (URTIs) and the common cold are the most frequent causes of cough, but other causes include post-infectious cough, undiagnosed chronic cough, and cough brought on by pulmonary diseases like asthma, chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis, and lung cancer. The most common causes of cough in children are viral URTI, chronic bacterial bronchitis, and asthma. Whether acute or chronic, cough is linked to considerably reducing health-related quality of life. Patients with chronic cough commonly report sleep disturbance, nausea, chest pains, lethargy, social humiliation, urine incontinence, and low mood. Coughing may not be effective in certain circumstances (such as respiratory tract inflammation, neoplasia, eosinophilic bronchitis, airway irritation from various pollutants, airway hyperresponsiveness from infection, gastroesophageal reflux disease, and coughing without any known cause, also known as idiopathic cough). Opioidergic central cough suppressants, such as opioids, codeine, pholcodine, noscapine, and dextromethorphan, are useful when coughing is ineffective. Constipation, sedation, respiratory depression, dependence, drowsiness, addiction, and even mortality can result from prolonged use of these cough suppressants, which restricts their use in people. The proposed research project's objective is to develop and assess herbal dosage forms that contain the widely used spice *Piper longum L. (Piperaceae).*

Keywords: Butterscotch Candy, Jelly Candy, Lollipop Candy, *Piper longum* L.

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INTRODUCTION

The activation of vagal afferent neurons, which have their terminals in the larynx, trachea, and bronchi, causes coughing. Two types of fibres, A-delta fibers and C-fibres, are involved in the cough reflex. A delta fibre is a sensory nerve fibre, myelinated and hence transmits sensory information fast as compared to C-fibres (non-myelinated). It's possible that other vagal afferent neurons also control the reflux. Receptors that can quickly adjust to new stimuli respond well to mechanical forces. The effectiveness of synaptic transmission at the major terminal location of vagal afferent nerves, or the action potential of these nerves, profoundly affects cough when it is reduced by medication. If the cough is left untreated, it causes muscular pain, ribs may get fractured, damage to blood vessels, rupture of the diaphragm, abdominal hernia, damage of throat tissue, and blood in the cough. When a cough is non-productive, cough suppressants that act on the opioid receptors in the brain, such as morphine, codeine, pholcodine, noscapine,

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dextromethorphan, etc., work well. Constipation, sedation, respiratory depression, dependence, drowsiness, addiction, and death are only some of the negative side effects of long-term usage of these cough suppressants in humans. Concerns about the safety and bad consequences associated to the use of cough and cold medicines (CCMs) in this age group contribute to the fact that their prescription is so common among young children. The evidence-based guidelines restricted the use of cough and cold medicines.[1-3]

The suggested study aimed to produce and assess an herbal dosage form including the widely used spice *Piper longum* L. The "long pepper" plant, *P. longum* L. (Piperaceae), can be found all over the world in tropical and subtropical regions, including the Indian subcontinent, Sri Lanka, and many nations in the Middle East and the Americas. Black pepper's strong commercial and economic importance made it particularly prized by Roman emperors. Long pepper has anti-asthmatic, anti-inflammatory, antimicrobial, antioxidant and immunomodulatory activity.[4,5]

Since *P. longum* has a pungent taste, the preparation of candy was selected as a dosage form. For instance, medicated sweets have a high visual appeal, may be easily administered by young children, and would allow for faster therapeutic action. As they don't need to be diluted in water, candies are easy to use without interrupting your day. Treatment can be stopped at any time if necessary. In addition, the medications released from jelly will be in a readily accessible state since they will be dissolved or suspended in the saliva. In light of this, it is tempting to consider developing potential anti-tussive formulations based on candy formulations derived from natural materials.[6,7]

MATERIAL AND METHODS

Materials

Dried fruit Powder of *P. longum L.* was purchased from a local vendor of Ayurvedic Pharmacy, Pune, Maharashtra, India. Plain, unflavored, pasteurized butter, sucrose, and baby corn seeds procured by local purchase, Pune, Maharashtra, India. Corn syrup USP was prepared by standard laboratory method using baby corn seeds. Rock salt and honey was obtained from Shivam Enterprises, Pune and Dabur India Ltd., respectively. Glycerine and gelatin were procured from Research–Lab Fine Chem. Industries, Mumbai (Maharashtra, India). All of the other chemicals and materials were of analytical grade and did not need to be cleaned any further before they were used.

Methods

Preparation of ethanolic extract of P. longum L.

A total of 125 gm *P. longum* L. fruit powder was packed in a filter paper and it was placed in the thimble of soxhlet extractor. The powder was exhaustively extracted by continuous soxhlet extraction using ethanol (99.99%) for 3 days at 45 to 50°C. Then extract was separated and concentrated on a water bath. Then the extract was subjected for preliminary phytochemical screening and the other half is kept for evaporation at 40 to 45°C.[8]

Preparation and evaluation of flavored selected compositions of candies of ethanolic extract of P. longum L.

- *Flavoured lollipop candy of P. longum L.*

Cleaned candy molds were lubricated with molten, unflavored butter of a well-known Indian brand. The candy base was prepared using granulated sugar and corn syrup USP followed by the addition of water in a stainless steel (SS) vessel. This solution is heated on a cooking gas burner's medium flame until vigorous boiling (144–148°C). The required quantity of *P. longum* L. ethanolic extract was added into the syrupy mass with continuous stirring. This hot candy mass was poured into lubricated mold cavities and colored plastic straw was immersed (vertically) into each filled mold. Candies are allowed to settle by congealing at ambient temperature (Table 1).

- *Flavoured butterscotch candy of P. longum L.*

To prepare butterscotch candy, required quantities of granulated sugar and water were mixed in SS vessel, followed by a gradual addition of corn syrup USP with constant stirring. This mixture was heated on a cooking gas burner's medium

Table 1: Formulation of flavored candy of *P. longum L.*
(Formula for 15 units of each type of candy)

Sr. No.	*Name of the ingredient*	*Lollipop candy*	*Butterscotch candy*	*Jelly candy*	*Role of the ingredient*
		(Quantity in gm)			
1	Ethanolic extract of *P. longum* L.	2.43	2.43	2.43	Active
2	Granular sugar	87.5	60	25	Sweetening agent
3	Corn syrup USP	18.75	8	-	Plasticizer & for control of crystallinity
4	Rock salt	-	1	-	Active
5	Butter	-	1	-	Lubricant for casting candies
6	Honey	-	5	-	Sweetening agent & for imparting Smooth texture
7	Gelatin	-	-	100	Jelling agent
8	Glycerin	-	-	25	
9	Water	q.s	q.s	q.s	Vehicle
10	Chocolate	2–3 drops	2–3 drops	2–4 Drop	Flavoring agent

flame until vigorous boiling. Addition of extract of *P. longum* L. followed by addition of rock salt, butter and honey into syrupy mass with continuous stirring until the commencement of boiling. This mixture is heated on a medium gas burner flame until vigorous boiling. Candy syrup was poured on a cleaned, lubricated tray and candies by congealed at ambient temperature. Candies of appropriate shapes were cut using a sharp stainless steel knife.

- *Flavoured jelly candy of P. longum L.*

Required quantities of gelatin and granulated sugar were mixed in S.S. vessel followed by addition of glycerin and water with constant stirring. Extract of *P. longum* L. was added in the above mixture. This whole mixture was heated on medium gas burner flame till vigorous boiling. Hot candy mixture was poured into mould cavities with vertical immersion of plastic straw. Candies were allowed to settle by congealing at ambient temperature.

Evaluation of Flavored Candies of *P. longum* L.

Appearance

All candy units' appearance was assessed visually for gloss, homogeneity.

Surface texture

Surface texture of the candies was assessed by touch and noted as either smooth or rough. Moreover, a magnifying glass also noted the presence or absence of cracks on the surface.

Organoleptic characteristics

All candy units' Color and odor were assessed by subjective perception, while the panel of taste evaluated the balance of sweet-sour taste.

Average weight

The individual unit of candy is weighed and the weights were noted accurately. The average weight of each candy unit was calculated.

Hardness

The hardness of candy was determined using tablet hardness tester following a similar procedure reported for testing the hardness of tablet.

pH

It is determined by dissolving the candy in distilled water, filtering the suspension using Whatman filter paper no. 1 and the pH (average) of clear filtrate was noted.

Disintegration time

Six candies were put in a machine for breaking up that had sliding discs and distilled water as the breaking up medium. The medium was kept at a temperature of 25°C. The time it took to break up all six candies was written down, and the average time was figured out.

Drug content

In a 50 mL volumetric flask, candies were dissolved in 10 mL of methanol, and the amount was brought up to 50 mL with a pH 6.8 phosphate buffer. This 1-mL solution is put into a 50 mL volumetric jar with pH 6.8 phosphate buffer and sonicated for 30 minutes. Then, filter paper is used to separate the mixture. 328 nm was used to measure how much this fluid could soak up light.

Dissolution studies pH 6.8 phosphate buffer for lollipop candy

For this study, candy from each formulation type was subjected to dissolution study using dissolution test apparatus type II. The dissolution study was carried out in 900 mL of pH 6.8 phosphate buffer at 100 rpm, 37 ± 1°C for 15 minutes or till complete disintegration of the candies. The sample was withdrawn at a 3-minute sampling interval. With a UV-visible spectrophotometer (double beam) Shimadzu 1800, the absorbance was recorded at 328 nm.[9]

Stability Study of Candies

The selected experimental formulations of candies of *P. longum* L. were subjected to short term stability study using the following test condition.[10]

Duration of study

30 days

Temperature conditions

From 2 to 8°C and room temp (30–35°C) Frequency of testing the sample: 0, 15, and 30 days. The tests performed were (Table 2);

- Appearance
- Organoleptic characteristics
- Hardness
- Disintegration time
- Drug content

Table 2: Characteristics of flavored candy containing ethanolic extract of *P. longum* L.

Sr. No.	*Characteristic*	*Lollipop candy*	*Butterscotch Candy*	*Jelly candy*
1	Appearance	Flower	Flower	Flower
2	Surface texture	Smooth	Smooth	Smooth
		Organoleptic characteristics		
3	Color	Brown	Brown	Brown
4	Odor	Characteristic	Characteristic	Characteristic
5	Taste	Slightly pungent	Slightly sour	Slightly pungent
6	Average weight (gm)	10.56 ± 1.41	11.01 ± 1.21	10.11 ± 1.01
7	Hardness	13.93 ± 1.21	6.91 ± 0.98	Pliable
8	pH	6.42 ± 0.092	6.15 ± 0.12	6.70 ± 0.098
9	Palatability	Good	Good	Good
10	Disintegration time (min)	3.14 ± 0.24	2.31 ± 0.98	Non-disintegrating
11	Drug content	95.68 ± 1.23	96.84 ± 1.43	97.45 ± 0.95

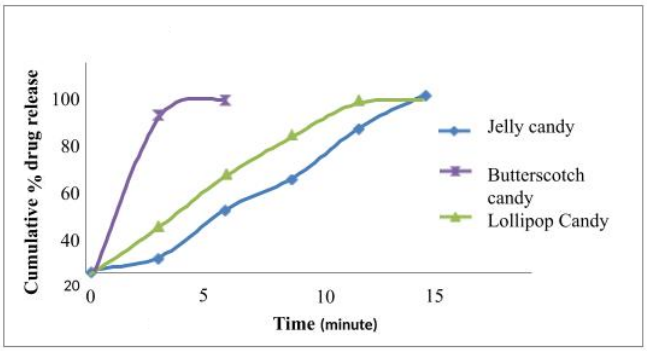

Figure 1: Graphical representation of *in-vitro* drug release

Table 3: Stability data of candies of *P. longum L.* extract.

Sr. No.	*Characteristic*	*Initial findings*	*Findings after stability study*
		Lollipop candy	
1	Appearance/ consistency	Smooth	No gross change
2	Color	Dark brownish	Dark brownish
3	Odor	Characteristic	Characteristic
4	Taste	Blend of Sweet-slightly Pungent	Blend of Sweet-slightly Pungent
5	Shape	Flower	Flower
6	Stickiness	Non-sticky	Non-sticky
7	Palatability	Good	Good
7	Hardness	14.01 ± 0.83	13.86 ± 0.51
8	Disintegration time	3.01 ± 0.095	2.95 ± 0.088
8	Drug content	96.12 ± 1.23	95.41 ± 1.31
		Butterscotch candy	
1	Appearance/ consistency	Smooth	No gross change
2	Color	Dark brownish	Dark brownish
3	Odor	Characteristic	Characteristic
4	Taste	Blend of sweet-slightly pungent	Blend of sweet-pungent-acidic
5	Shape	Cube	Cube
6	Stickiness	Non sticky	Non sticky
7	Palatability	Good	Good
8	Hardness	7.11 ± 0.096	6.98 ± 0.16
9	Disintegration time	2.51 ± 0.14	2.21 ± 0.14
8	Drug content	97.12 ± 0.76	96.98 ± 0.38
		Jelly candy	
1	Appearance/ consistency	Smooth	No gross change
2	Color	Dark brownish	Dark brownish
3	Odor	Characteristic	Characteristic
4	Taste	Blend of sweet-slightly pungent	Blend of sweet-pungent
5	Shape	Flower	Flower
6	Stickiness	Non-sticky	Non-sticky
7	Palatability	Good	Good
8	Hardness	Pliable	Pliable
9	Disintegration time (min)	Non-disintegrating	
8	Drug content	97.04 ± 0.54	96.89 ± 0.89

RESULTS AND DISCUSSION

All medicated candies were brown in color due to the addition of chocolate flavor. Taste of medicated candies was slightly sweet and pungent due to the addition of *P. longum L.* extract. The addition of extract does not affect the pH of candies. Disintegration time and hardness of medicated candies decreased due to adding extract as extract may impair the crystallization process. Effect of the addition of extract on disintegration time was negligible as the concentration of gelatin is high and impairs the crystallization process.

Drug Release

The cumulative percent of drug release was determined based on the amount of drug in the *P. longum* L. extract in each candy. Figure 1 shows a picture of how drugs get into the body.

Release of extract from candies is as follows.

Butterscotch candy > lollipop candy > Jelly candy

The lollipop, butterscotch and jelly candies belong to the class of non-crystalline and gummy candies, respectively. The lollipop and butterscotch were distinguished by their smoothness, indicating the absence of crystals and fast drug release was observed from this dosage form.

Drug release from jelly candy was found to be very slow; hence, it may give sustained release due to the presence of gelatin. Stability studies were carried out as per standard procedures (Table 3).

Thus, the flavored lollipop, butterscotch and jelly candies possessed a smooth surface good palatability. The candies retained a characteristic odor and had no sign of microbial growth on the surface. The sample was placed in stability with negligible change in their pH values, disintegration time, hardness, and drug content.

CONCLUSION

The ethanolic extract of *P. longum* L. belonging to the family Piperaceae has demonstrated excellent anti-tussive activity when formulated as candies. Moreover, the prepared lollipop, butterscotch and jelly candies have good palatability. Hence, the formulations of candies may be considered as lead formulations. More extensive studies can be carried out to establish the validity of the claim for its clinical safety and efficacy using different flavored candies for oral delivery systems.

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