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Formulation and Evaluation of Herbal Prophylactic Antiemetic Soft Lozenges for Motion Sickness

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ABSTRACT

Motion sickness, characterized by symptoms like nausea, vomiting, and dizziness, often occurs due to sensory conflicts between the visual and vestibular systems. Common treatments, such as antihistamines and scopolamine patches, may cause side effects like drowsiness. This study focuses on developing an herbal alternative, specifically prophylactic antiemetic soft lozenges, using anethole extracted from star anise, known for its antiemetic properties. The formulation is based on a PEG 6000 matrix, combined with propylene glycol as a plasticizer, microcrystalline cellulose as disintegrate, and other excipients. The study involved optimizing the formulation through an error-and-trial technique, ensuring desirable physical properties like hardness, weight uniformity, and stability. The lozenges were evaluated for moisture content, pH, dissolution time, and temperature stability, demonstrating promising results in buccal drug delivery without the common side effects associated with conventional treatments. This novel formulation provides a natural, patient-friendly solution for motion sickness, enhancing compliance and minimizing side effects.

Keywords: Motion Sickness, Anethol, PEG, Soft Lozenges.

INTRODUCTION

Motion sickness is a condition marked by symptoms such as dizziness, nausea, vomiting, and pallor, which occur due to exposure to real or perceived motion. This happens when there's a mismatch in signals from the inner ear, eyes, and other body parts that help maintain balance. Common situations that trigger motion sickness include traveling in vehicles or boats. Symptoms can range from mild discomfort to severe nausea, influenced by individual susceptibility, type of motion, and overall health. Treatment options include medications and self-care strategies, like focusing on a fixed point, avoiding heavy meals, and seeking fresh air [1, 2].

The exact neural pathway of motion sickness is complex and not fully understood. It involves interactions between the visual, vestibular (inner ear), and gastrointestinal systems. The vestibular system detects motion and sends signals to the brain, which processes this information alongside visual input. A conflict between what the eyes see and what the inner ear senses can lead to symptoms. Key brain areas, such as the cerebral cortex, cerebellum, and brainstem, are involved in this process, along with neurotransmitters like histamine and serotonin [3].

Current Treatments for Motion Sickness include Antihistamines (e.g., dimenhydrinate) to block nausea signals, Scopolamine patches that prevent nausea and Benzodiazepines (e.g., lorazepam) that reduce anxiety and nausea [4].

But there are some drawbacks of Current Treatments such as Antihistamines and scopolamine may cause drowsiness and dry mouth, Benzodiazepines can lead to dependency and sedation. Not all treatments are effective for everyone, and some may have contraindications [5].

Star anise is a spice traditionally used to alleviate nausea and digestive discomfort. Its main active ingredient, anethole, not only gives it a distinctive licorice flavor but also calms the digestive system. Anethole has several potential health benefits, including antimicrobial, antioxidant, anti-inflammatory, and antiviral properties. It may help relieve nausea in motion sickness by blocking serotonin receptors, acting on dopamine receptors, interacting with the GABA system and Reducing inflammation and oxidative stress. While star anise appears to be a promising natural remedy for nausea and soft lozenges offer effective delivery methods, existing treatments for motion sickness have limitations that warrant consideration [6]. Despite its promising effects, further research is necessary to understand anethole's mechanisms and safety.

Soft lozenges are designed to dissolve slowly in the mouth, allowing for quicker absorption compared to pills. Polyethylene glycol (PEG) is often used in these lozenges because it enhances the solubility of poorly soluble drugs. When placed in the mouth, the lozenge dissolves, releasing the medication into the saliva, where it is absorbed through the mouth's lining and enters the bloodstream [7].

Current research is attempt to formulate and evaluate PEG based soft lozenges of star anise extract for prophylactic treatment of motion sickness.

Materials and Methods

- **Extraction of Active Principles from Star Anise**:

For purpose of extraction of star anise, it is grinded into a coarse powder. 60 grams of coarse powder is placed it in a conical flask. Then ethanol is added in conical flask until it covers coarse powder of star anise. This mixture is kept for seven days stirring occasionally. After seven days mixture is filtered using filter paper. Then filtered liquid is transferred to the shallow dish and let the ethanol evaporate leaving the concentrated extract behind. Final extract is stored in cool, dark place for several months [8].

- **Formulation of Soft Lozenges**: Formulation components of soft lozenges involves base, plasticizer, accacia, microcrystalline cellulose, glycerin and colouring agent. Selection of type and concentration of formulation components of soft lozenges was done by error and trial technique. This technique involves trying out different formulations or methods and evaluating their outcomes until an optimal result is achieved. In the context of product formulation, trial and error involve testing different combinations of ingredients or adjusting their proportions until the desired properties are achieved. The active ingredient from star anise is mixed with acacia and added to the PEG base. For decision of formulae of lozenges base different proportion of PEG 6000 which serves as matrix and propylene glycol which serves as plasticizer is tried in 4 batches and most optimal batch is selected having desired properties for delivery of soft lozenges.

Table No: 1. Error and trial batches of soft lozenges

Batch No.	Melted PEG 6000	Propylene Glycol (ml)	Observations	Conclusion
1.	9.0 ml	7.0 ml	Very soft	Not optimal
2.	9.5 ml	6.5 ml	Very soft	Not optimal
3.	10.0 ml	6.0 ml	Relatively soft	Not optimal
4.	11.0 ml	4.0 ml	Desirable Hard	Optimal

PEG based soft lozenges were prepared by melting 44.0 ml of PEG 6000 at 60°C and poured it into a round bottom flask. Then 16.0 ml of propylene glycol is added and it stir until a clear mixture forms. Then 3.0 gm of microcrystalline cellulose is mixed in it. Then triturated acacia and anethole added and stirring until well mixed. Then heat is removed and flavour and color added to this melted solution. This stired thoroughly and poured the mixture into molds and let it cool until solid. Once hardened, the lozenges are removed for evaluation [9].

- **Evaluation of Soft Lozenges:**

➢ **Appearance**: Assess color, shape, and texture. The color should be uniform, and defects like lumps should be absent.

➢ **Hardness**: Hardness of PEG based soft lozenges is important to access the mechanical strength of soft lozenges which is important parameter during handling and transportation of soft lozenges. Hardness is tested by applying force on lozenges by fingers and by drop of lozenges from particular height. Hardness is found sufficient to defend mechanical force during handling [10].

➢ **Weight Uniformity**: Uneven weight of soft lozenges will affect drug content uniformity and hence pharmacological activity. For this 8 lozenges is selected and comparing their individual and average weight percent weight variation is calculated. To determine percent deviation in weight following formulae is used [11].

$$Percentage\ Weight\ Variation\ = \frac{Individual\ weight - Average\ weight}{Average\ weight} \times 100$$

Table No: 2 weight uniformity of soft lozenges

Sr.no	Initial weight	Average Weight	Weight variation (%)	Remark
1	7.5gm	7.4gm	1.3%	Acceptable
2	7.4gm	7.4gm	0%	Acceptable
3	7.5 gm	7.4gm	1.3%	Acceptable
4	7.3gm	7.4gm	-1.3%	Acceptable
5	7.4gm	7.4gm	0	Acceptable
6	7.5gm	7.4gm	1.3	Acceptable
7	7.4gm	7.4gm	0	Acceptable
8	7.3gm	7.4gm	-1.3%	Acceptable

➢ **pH:** As pH directly affects the stability, dissolution, and taste of the lozenge. Ideal range is in between 5.5 to 7.5. this pH is because of PEG 6000 which serves as base in formulation and also pH of Anethole is 7 providing best buccal absorption conditions. For test pH meter is calibrated using buffers (pH 4.0, 7.0, and 10.0). Then sample is prepared and different portions of samples are tested differently to ensure accuracy, and average value is calculated for these multiple portion. pH of PEG based soft lozenges is found 6.4 which is within limit for optimum buccal delivery [12].

➢ **Moisture content test**: Moisture content test is very important in terms of stability of soft lozenges. For moisture content determination analytical balance is calibrated. 1 lozenge is selected as sample. Then dry aluminium weighing dish is weighed (W1-0.18 gm). Then sample is weighed with aluminium weighing dish.

➢ **Solubility Analysis**: Solubility Analysis study access ability of lozenges to dissolve in different solvents and importantly it also accesses solubility at salivary pH. For this sufficient quantity of sample is taken in beaker and solvents are introduced so sample will completely covered by sample. And system is observed for some period of time, if required stirring and shaking is also done. From above method it is found that in polar solvents such as water, Ethanol, Methanol, Acetone sample is completely soluble. In the solvents with low polarity such as Chloroform, Toluene, Hexane sample is partially soluble [13].

➢ **Dissolution Time**: Dissolution test is performed on 2 lozenges individually using dissolution apparatus 1 (paddle). Lozenges is placed at bottom of vessel (1000 ml) (Ph 6.4 using buffer) at 50 rpm and temperature is maintained at body temperature. Then dissolution apparatus is started. Sample from vessel from sampling point is taken at 5 time point as zero minute, at 5 min., at 10 min., at 15 min., at 20 min. After these 5 samples are dilutes in 100 ml volumetric flask with addition of suitable solvent. And absorbance of each sample is taken by UV-spectrophotometer at 231 nm. And concentration is determined by calibration curve method. Solution of anethole with known concentration is used as reference sample [14].

Table No: 3 Dissolution study of soft lozenges

Sr.no	Absorbance	Concentration (mcg/ml)
0 min	0.00	0.0
5 min	0.247	28
10min	0.469	53
15 min	0.699	60
20 min	0.858	97

Temperature Stability: This involves deciding temperature conditions for proper storage of PEG based soft lozenges with maximum stability. For this study hot air oven is used as temperature chambers and temperature conditions are decided. Study done with elevated temperature conditions. Such as first setting 40°C, then 50°C, then 60°C. At the temperature of 40°C lozenges was completely stable. After the 50°C it started to achieve sticky surface. At 60°C lozenges surface started to melt. During above process lozenges were frequently observed for identifying any change in them [10].

Result and discussion

➢ **Extraction of anethole**: Anethole is successfully extracted by solvent extraction method using Ethanol. And incorporated in PEG based soft lozenges.

➢ **Formulation of soft lozenges**: By using formulae obtained by error and trial technique for lozenges base, formulation is successfully developed by using following formulation table.

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Table No: 4.formulation table of soft lozenges

Sr. No.	Ingredient	Quantity
1.	PEG 6000 (melted)	44.0 ml
2.	Propylene Glycol	16.0 ml
3.	Acacia	4.5 gm
4.	Microcrystalline Cellulose	3.0 gm
5.	Menthol	2.0 gm
6.	Pea Green Colour	q.s.
7.	Anethole	800 (100mg each)

- **Evaluation of soft lozenges:**

a. Appearance of Soft Lozenges: Colour of soft lozenges is green with colour uniformity. Shape of Soft Lozenges is square.

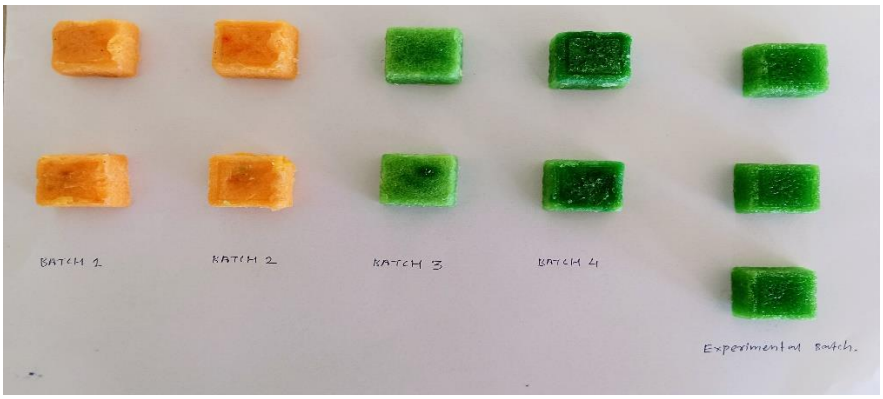

Fig no 1: Formulation of soft lozenges

b. Hardness: Hardness of soft lozenges is found to be optimal so it can withstand mechanical shock and will not break and also show optimum release profile in buccal cavity for better buccal absorption.

c. Weight Uniformity: 3 lozenges has 0% weight variation and another 3 and 2 lozenges have 1.3% and -1.3% weight variation respectively. There is no significance weight variation found in batch. Hence there is acceptable weight variation limit.

d. pH (Potential for Hydrogen): when tested by pH meter pH is found to be 6.4 , which within the ideal range also matches with salivary pH. This range is optimum for buccal absorption for delivery of active principle of formulation.

e. Moisture Content: Percent moisture content is calculated using following formulae and it is found to be 0.48%. Which do not affect significantly stability of product.

f. Solubility Analysis: After checking solubility in different solvents it is found that sample is soluble in water, Ethanol, Methanol. But in low polarity solvent such as chloroform, toluene and Hexane it is partially soluble.

g. Dissolution time- For dissolution time graph of Time vs Concentration is as follow:

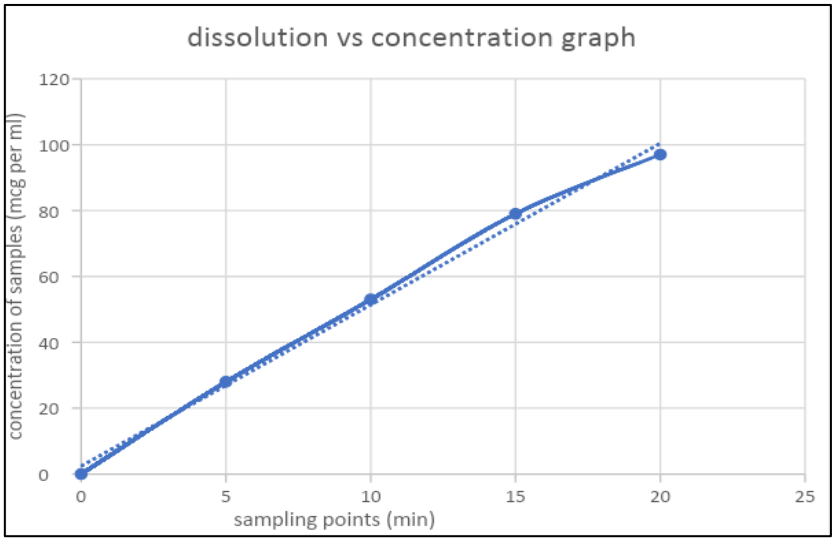

Fig no 2: Graph of dissolution vs concentration

h. Temperature Stability: After introducing Soft Lozenges at various temperature conditions it is found that PEG is stable till 55°C. But after this as temperature rises PEG based lozenges surface started to melt and star becoming soft.

Conclusion

PEG-based soft lozenges were successfully prepared using the pour and mold method for buccal drug delivery. The active compound from star anise was efficiently extracted through maceration. The formulation of the lozenges was optimized using an error and trial approach. PEG served as the base, and propylene glycol acted as a plasticizer. The lozenges were developed and evaluated effectively for buccal delivery.

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