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FORMULATION AND EVALUATION OF LOZENGES FOR ANTI-EMETIC AND MOTION SICKNESS

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INTRODUCTION

- **Purpose of Dosage Forms**: Dosage forms are designed to ensure the proper delivery of active pharmaceutical ingredients (APIs) to achieve a desired therapeutic effect. They also help in controlling the drug's release rate, minimizing side effects, and enhancing patient compliance.
- **Solid Dosage Forms**: Solid oral dosage forms include tablets, capsules, powders, and lozenges. These forms are the most common and convenient, providing precise dosage and ease of use.
- **Importance of Formulation Design**: The formulation process ensures that the drug reaches the targeted site in the appropriate concentration at the right time. Proper formulation ensures stability, bioavailability, and the overall effectiveness of the medication.[1,2]

Lozenges as a Dosage Form

- **Definition**: Lozenges are solid preparations designed to dissolve slowly in the mouth, releasing the active ingredient for local or systemic action.
- **Types of Lozenges**
  - **Hard Lozenges**: Usually made from sugar or sugar substitutes and hardened during cooling.
  - **Soft Lozenges**: Often made with polyethylene glycol (PEG) or other soft bases, ideal for faster dissolution.
  - **Chewable Lozenges**: Ideal for children and those who find hard lozenges too uncomfortable, typically made from glycerin or gelatin.
- **Common Uses**: Lozenges are frequently used for relief from nausea, motion sickness, vomiting.[3]

Mechanism of Action

- **Local Effect**: In conditions like nausea, motion sickness, vomiting, lozenges dissolve in the mouth and provide a soothing effect directly at the site of CTZ center. Active ingredients such as ondansetron, ginger.
- **Systemic Absorption**: Certain drugs in lozenges are absorbed through the buccal or sublingual mucosa, which has rich capillary networks that allow for direct entry into the bloodstream. This mechanism bypasses the gastrointestinal tract and first-pass metabolism in the liver, providing a faster onset of action.
- **Slow Release**: The slow dissolution process ensures that the API is released gradually over an extended period, offering sustained therapeutic effects with minimal peaks and troughs.[4]

Advantages of Lozenges

- **Ease of Administration**: Lozenges are simple to administer, especially for patients who have difficulty swallowing tablets or capsules. They are ideal for those experiencing nausea or vomiting, as they do not require water.
- **Prolonged Drug Release**: Lozenges provide a slow and continuous release of the drug, which can help maintain stable drug levels over a longer period.
- **Improved Patient Compliance**: Due to their pleasant taste, easy handling, and ability to avoid unpleasant side effects, lozenges encourage higher patient adherence to treatment.
- **Bypass of First-Pass Metabolism**: Many drugs administered orally undergo first-pass metabolism, which can reduce bioavailability. Lozenges, by dissolving in the mouth, deliver the drug directly into the bloodstream or oral mucosa, bypassing this metabolic process and improving drug effectiveness.
- **Convenience**: Lozenges are portable, requiring no special storage conditions, and they can be used discreetly in various situations, such as during travel or while outdoors.
- **Taste and Masking**: Lozenges can be formulated to mask the taste of bitter medications, improving patient acceptance, especially in pediatric or

geriatric populations.[5,6]

Applications of Lozenges

- **Throat and Oral Cavity**: Lozenges are commonly used for treating nausea, motion sickness, vomiting. Active ingredients like menthol, sucrose, and herbal extracts are often added for their soothing properties.
- **Motion Sickness and Nausea**: Lozenges can be formulated with antiemetic drugs, such as ondansetron, to provide systemic relief from nausea and vomiting due to motion sickness or chemotherapy.
- **Systemic Drug Delivery**: Lozenges are increasingly used for the systemic delivery of medications such as anti-emetic (e.g. odansetrone). The buccal route of absorption allows for faster onset compared to traditional oral tablets.[7]

Mechanism of Dissolution and Release

- **Dissolution Process**: Lozenges are designed to dissolve slowly, ensuring that the drug is released gradually. The rate of dissolution is influenced by the formulation of the lozenge, including the base material (sugars or sugar substitutes), excipients, and drug solubility.
- **Buccal and Sublingual Absorption**: Drugs absorbed through the buccal mucosa bypass the gastrointestinal tract, entering the bloodstream directly through the capillaries. This provides rapid systemic effects, which is beneficial for conditions like nausea and vomiting.
- **Controlled Release Mechanism**: Many lozenges are designed to release the drug at a controlled rate over time, allowing for extended relief. This can be achieved by manipulating the base and excipient composition, including the choice of binder, acidulant, and drug solubility.[8]

Key Considerations for Lozenge Formulations

- **Taste Masking**: A major challenge in lozenge formulation is improving the taste, particularly when dealing with bitter or unpleasant-tasting APIs. Sweeteners, flavors (menthol, funnel, orange), and flavor enhancers such as citric acid can be used to mask bitterness and improve palatability.
- **Physical Properties**: The hardness, friability, and dissolution time of lozenges must be carefully controlled to ensure the desired therapeutic effect. Too soft a lozenge may break easily, while too hard a lozenge may not dissolve properly.
- **Stability**: Lozenges must be stable under various environmental conditions, including temperature and humidity. The shelf life of lozenges can be influenced by the hygroscopic nature of the excipients, which may cause them to absorb moisture and degrade over time.
- **Drug Loading**: The concentration of the active ingredient must be optimized to ensure that the lozenge delivers the appropriate dose. Higher drug loads can affect the taste and dissolution rate, so balancing these factors is critical.[9]

Formulation and Manufacturing Considerations

- **Excipients**: The choice of excipients such as binders (corn starch), fillers (sucrose, glucose), and stabilizers (MCC) is essential to ensure the physical integrity of the lozenge.
- **Manufacturing Process**: Lozenges can be manufactured using various techniques.
  - **Compression Molding**: A process where a mixture of active ingredients and excipients is compressed into a mold.
  - **Casting**: Liquid formulations of lozenges are poured into molds and allowed to solidify.
  - **Hot Melt Method**: Active ingredients are melted with excipients, and the molten mixture is poured into molds.
- **Quality Control**: Post-manufacturing, lozenges are tested for physical characteristics such as size, weight variation, hardness, friability, disintegration test and dissolution time to ensure consistent quality and performance.

Benefits of Lozenges

- **Sustained Release**: Lozenges provide prolonged drug release, making them ideal for managing chronic symptoms or conditions that require continuous relief (e.g., motion sickness, nausea, vomiting).
- **Accessibility**: With no need for water, lozenges are particularly beneficial in situations where other dosage forms may not be convenient or possible.
- **Non-Invasive**: Lozenges are an easy, non-invasive alternative to injections or other complicated drug delivery methods.
- **Versatility**: Lozenges can be formulated to deliver a wide variety of therapeutic agents, including those for local (e.g., motion sickness, nausea, vomiting) or systemic (e.g., antiemetic drugs) action.[9]

DRUG PROFILE

1. Generic Name

Ondansetron

2. Brand Names

Zofran®, Emeset®, Ondem®, Vomikool®, others.

3. Drug Class

5-HT₃ (Serotonin) Receptor Antagonist (Antiemetic agent).

4. Chemical Name

9-methyl-3-[(2-methyl-1H-imidazol-1-yl) methyl]-1, 2, 3, 9- tetrahydro-4H-carbazol-4-one

5. Molecular Formula

C₁₈H₁₉N₃O

6. Molecular Weight

293.36 g/mol

7. Structure
(Include a structure diagram if needed)

8. Physical Properties
- **Appearance:** White to off-white crystalline powder
- **Solubility:** Freely soluble in water and alcohol
- **Melting Point:** 178–180°C (approx.)
- **pKa:** 7.4
- **LogP:** 2.1

9. Pharmacokinetics
- **Absorption:** Rapid oral absorption; bioavailability ~60% due to first-pass metabolism
- **Distribution:** Widely distributed; plasma protein binding ~70–76%
- **Metabolism:** Extensively hepatic via CYP3A4, CYP2D6, CYP1A2
- **Elimination Half-life:** 3–6 hours
- **Excretion:** Mainly renal and hepatic (urine and feces)

10. Mechanism of Action
Ondansetron selectively blocks serotonin (5-HT₃) receptors in the central nervous system and gastrointestinal tract. This action prevents nausea and vomiting by interrupting the emetogenic signals.

11. Indications
- Chemotherapy-induced nausea and vomiting (CINV)
- Radiation-induced nausea and vomiting (RINV)
- Postoperative nausea and vomiting (PONV)
- Off-label: Gastroenteritis, pregnancy-induced nausea.[10]

LITERATURE REVIEW ON LOZENGE

1. Singh, P., et al., (2021) This study demonstrates the feasibility of using lozenges for antiemetic drug delivery, specifically with ondansetron. Lozenges are flavored solid dosage forms that slowly dissolve in the mouth, enabling the drug to be absorbed through the buccal mucosa, thereby allowing both local and systemic effects. The theoretical foundation of this approach lies in the enhancement of bioavailability via mucosal absorption and bypassing hepatic first-pass metabolism. The slow dissolution also ensures a sustained release profile, ideal for managing prolonged symptoms of nausea and vomiting. Ondansetron, a 5-HT_3 receptor antagonist, is especially suitable for such formulations due to its rapid onset of action and effectiveness when absorbed through mucosal tissues.

2. Muth, E. R., et al., (2007) This study evaluates the efficacy of high-dose ondansetron in motion sickness, a condition caused by a sensory mismatch between visual and vestibular inputs. While ondansetron effectively blocks serotonin receptors in the chemoreceptor trigger zone (CTZ), it is not as effective in targeting the vestibular system, which primarily involves histaminergic (H1) and cholinergic (M1) pathways. This theoretical distinction explains the drug's limited efficacy in treating motion sickness, even at elevated doses, and highlights the complexity of treating vestibular- induced nausea as opposed to emesis triggered by chemotherapy or anesthesia.

3. Hershkovitz, D., et al. (2009) Seasickness, a specific form of motion sickness triggered by vestibular overstimulation, represents another clinical challenge where ondansetron may not provide optimal relief. This study supports the theoretical understanding that vestibular-origin nausea involves neurotransmitters other than serotonin, such as histamine and acetylcholine. Hence, while ondansetron can modulate nausea mediated via gastrointestinal vagal afferents and central 5-HT_3 receptors, it lacks the capacity to inhibit vestibular pathways. This limits its effectiveness in preventing motion sickness despite its proven efficacy in chemotherapy or postoperative nausea contexts.

4. Griddine, A., et al., (2023) This review offers a broad pharmacological overview of ondansetron, a highly selective 5-HT_3 receptor antagonist. It blocks serotonin both peripherally at vagal nerve endings in the gastrointestinal tract and centrally in the CTZ of the medulla. The drug is widely used for nausea and vomiting associated with chemotherapy, radiation, and surgical procedures. However, its lack of anticholinergic or antihistaminic properties means it is poorly suited for motion sickness, which is more effectively managed by drugs acting on the vestibular system. This theoretical limitation further underscores the need to explore combination therapies or alternative agents for comprehensive motion sickness management.

5. Sahu, S. K., et al., (2019) Though not directly related to antiemetic therapy, this study presents essential formulation strategies for developing lozenges. It emphasizes principles such as the selection of compatible excipients, taste-masking techniques, and controlled-release design. These principles are directly transferable to the development of ondansetron lozenges, where achieving a balance between palatability and pharmacokinetics is crucial for ensuring patient compliance and therapeutic efficacy. Additionally, the use of natural additives in lozenges can inspire combination formulations that integrate both synthetic and herbal components for dual therapeutic actions.

6. Sharma, M., et al., (2017) This study highlights the use of lozenges for delivering chlorhexidine, an antibacterial agent, demonstrating the effectiveness of oromucosal delivery for both local and systemic action. It shows how lozenges can maintain a sustained drug concentration in the saliva, facilitating prolonged therapeutic effects. Applying similar principles to ondansetron lozenges supports their potential use in delivering consistent antiemetic activity through gradual dissolution and absorption. The buccal route also enables

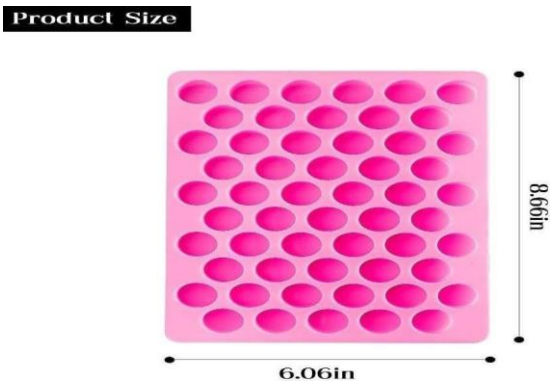
rapid relief without the need for water or swallowing, making it particularly useful for patients experiencing continuous nausea, especially in motion sickness or post-chemotherapy scenarios.

AIM

The aim of this study is to formulate and evaluate Ondansetron lozenges for the management of motion sickness. The goal is to develop a convenient, effective, and patient- friendly dosage form that offers rapid relief from nausea and vomiting associated with motion sickness, with sustained drug release over an extended period.

OBJECTIVES

1. **Formulation Development**
   - To formulate Ondansetron lozenges using appropriate excipients, including sugar, liquid glucose, citric acid, ginger and flavoring agents, ensuring the right texture, stability, and taste.
2. **Physicochemical Evaluation**
   - To evaluate the physicochemical properties of the lozenges, such as.
   - **Weight variation** to ensure uniformity.
   - **Hardness** to assess the mechanical strength.
   - **Friability** to determine the durability during handling.
   - **Drug content uniformity** to ensure consistent therapeutic dosage across all lozenges.
3. **Dissolution and Drug Release**
   - To assess the **dissolution time** and **drug release profile** of Ondansetron from the lozenges in suitable mediums (e.g., artificial saliva or phosphate buffer, pH 6.8) and ensure it provides a sustained release effect.
4. **Evaluation of Organoleptic Properties**
   - To evaluate the **color, taste, and texture** of the lozenges to ensure they are acceptable to patients, especially children and elderly individuals who are sensitive to taste and texture.
5. **Stability Testing**
   - To perform **stability studies** on the formulated lozenges under different storage conditions to determine their shelf life and ensure they maintain their therapeutic efficacy over time.
6. **Patient Compliance Evaluation**
   - To analyze the ease of **administration and patient compliance** with the Ondansetron lozenges compared to traditional tablets or injections, focusing on the potential benefits for pediatric, geriatric patients and pregnant women, and those suffering from motion sickness during travel.
7. **Comparative Study**
   - To compare the **efficacy of Ondansetron lozenges** with other conventional oral dosage forms (e.g., tablets, syrups) for motion sickness, particularly in terms of onset of action and sustained release.
8. **Optimization of Formulation**
   - To optimize the lozenge formulation to ensure that it meets all the necessary pharmacokinetic requirements, such as rapid onset of action and controlled release for prolonged therapeutic effect.
9. **To Provide a Novel Drug Delivery System**
   - To provide a novel, patient-friendly, and convenient drug delivery system that improves the therapeutic management of motion sickness, especially for patients who have difficulty swallowing tablets or using injections.
10. **Optimization of Taste and Palatability**
    - To optimize the **taste masking** techniques for the formulation of Ondansetron lozenges, ensuring the palatability of the product by utilizing suitable flavoring agents, sweeteners, and acidulants (e.g., citric acid) to mask any unpleasant taste of the drug.



PLAN OF WORK

1. **Preliminary Research and Literature Review**

- **Task:** Conduct an extensive review of the literature concerning motion sickness, current drug treatments, and lozenge formulations.
- **Objective**
  - To understand the pathophysiology of motion sickness.
  - To evaluate the current role of Ondansetron in managing motion sickness and other conditions.
  - To explore the use of lozenges as a drug delivery system, including various formulation techniques and excipients.
- **Outcome**
  - A comprehensive literature review outlining the need for a novel Ondansetron delivery system (lozenges).
  - Identification of key excipients and methods for the formulation of lozenges.

2. **Selection of Materials and Formulation Development**

- **Task:** Select appropriate excipients (e.g., sweeteners, binders, texture inhancer, stabilizer, lubricant and flavoring agents) and decide on the formulation method (melt- based or alternative methods).

- **Objective**
  - Develop the initial formulation based on factors like solubility, drug stability, and desired release characteristics.

- Choose excipients that provide an optimal texture, stability, and bioavailability.

- **Outcome**
- A finalized formulation recipe and prepared excipients ready for lozenge production.

3. Preparation of Ondansetron Lozenges

- **Task:** Prepare the Ondansetron lozenges by following the chosen formulation and method. The preparation process involves mixing the active ingredient with the excipients, melting the base, and molding.
- **Objective**
- To prepare lozenges with uniform drug distribution and correct mechanical properties.
- To maintain the drug's stability during the preparation process.
- **Outcome**
- A batch of prepared Ondansetron lozenges for further evaluation.

4. Evaluation of Physicochemical Properties

- **Task:** Evaluate the physicochemical properties of the lozenges, including:
  - **Weight Variation:** Weigh 10 lozenges and calculate the average weight and deviations.
  - **Hardness Test:** Use a Monsanto Hardness Tester to measure the strength of the lozenges.
  - **Friability Test:** Assess the friability using a Roche Friabilator to ensure lozenges can withstand handling and transport.
  - **Disintegration Time:** Test the disintegration time in purified water or phosphate buffer.
- **Objective**
- To ensure the lozenges meet acceptable pharmaceutical standards and maintain consistent drug content.
- **Outcome**
- A report on the quality of the lozenges in terms of their physical and mechanical properties.[11,12,13]

5. Organoleptic Evaluation (Taste, Color, Texture)

- **Task:** Evaluate the taste, color and texture of the lozenges using human panels and sensory evaluation. Focus on palatability, flavor masking, and overall acceptability.
- **Objective**
- To optimize the organoleptic properties of the lozenges, ensuring that they are pleasant for pediatric, pregnant women and geriatric patients.
- **Outcome**
- Data on the overall acceptability and taste preferences of the lozenges, along with adjustments made based on feedback.

6. Dissolution Study

- **Task:** Conduct in vitro dissolution testing of the lozenges in purified water (or a similar buffer solution) to simulate the conditions of the oral cavity. Measure the release profile of Ondansetron.
- **Objective**
- To confirm the controlled, sustained release of the drug from the lozenge.
- To ensure that the drug release profile is consistent with therapeutic needs.
- **Outcome**
- Dissolution data, including the percentage of drug released over time, to assess the suitability of the lozenges for sustained action.[14,15,16]

7. Stability Studies

- **Task:** Conduct accelerated and long-term stability studies of the lozenges under various environmental conditions (e.g., temperature, humidity) to assess their physical, chemical, and mechanical stability over time.
- **Objective**
- To evaluate the shelf-life and long-term stability of the lozenges.
- To ensure the drug remains potent and the lozenges maintain their desired characteristics (e.g., hardness, appearance, taste).

8. Patient Compliance and Preference Study

- **Task:** Conduct a survey or clinical trial involving a sample of patients (preferably those prone to motion sickness, such as travelers) to assess their preference and compliance with the lozenge dosage form.
- **Objective**
- To measure patient satisfaction, ease of use, and preference for lozenges over traditional tablet or injection forms.
- To understand the impact of the lozenge's palatability, ease of administration, and effectiveness in managing symptoms of motion sickness.
- **Outcome**
- Insights into how the lozenges are received by the target population, including data on usability, patient compliance, and preference.

9. Comparative Study with Existing Dosage Forms

- **Task:** Compare the effectiveness of Ondansetron lozenges with currently available dosage forms for motion sickness (e.g., tablets, injections). This can include evaluating the onset of action, duration of action, and patient compliance.
- **Objective**
- To determine if the lozenge formulation provides superior convenience, onset of action, and patient satisfaction compared to other forms.
- **Outcome**
- Data comparing the lozenges with existing products in terms of patient feedback, therapeutic efficacy, and overall effectiveness in managing motion sickness.

MATERIALS

Material	Description
Ondansetron	Active pharmaceutical ingredient (API) used to prevent nausea and vomiting. A selective 5-HT3 receptor antagonist used as the Active Pharmaceutical Ingredient (API). Prevents nausea and vomiting by blocking serotonin receptors in the brain and gut.
Sugar (Sucrose)	Base material providing sweetness and contributing to the lozenge's structure. Acts as a bulking and sweetening agent. Enhances palatability, masks API taste, and forms solid lozenge structure through crystallization.
Liquid Glucose (Glucose Syrup)	Acts as a plasticizer, making the lozenges more flexible and preventing brittleness. plasticizer and humectant. Maintains moisture, prevents brittleness and crystallization, adds sweetness and viscosity
Citric Acid	Acidulant used to adjust pH and enhance flavor. A weak organic acid for pH adjustment and flavor enhancement. Stabilizes formulation, adds tanginess, and can improve API solubility.
Flavoring Agent	Such as mint, orange and funnel to mask bitterness and improve taste. Natural or synthetic flavors (e.g., mint, orange, fennel) to mask unpleasant taste and improve patient compliance.
Colorant (optional)	Food-grade colorant to improve the visual appeal of the lozenge. Food- grade dyes or natural pigments to enhance visual appeal. Can indicate flavor or dosage strength.
Binding Agents (Optional)	Includes corn starch or microcrystalline cellulose (MCC). Binds ingredients, improves texture, and enhances lozenge strength.
Magnesium stearate	To improve consistency and prevent stickiness. Common lubricant and manufacturing and prevents lozenges from sticking
Ginger extract	Natural anti-nausea. Natural herbal antiemetic. Works with Ondansetron for enhanced relief and adds a warm, spicy flavor.[17]

EQUIPMENT

Equipment	Description
Balance (Analytical Scale)	For accurate measurement of excipients, API, and final lozenge weight.
Heat Source (Water Bath/Hot Plate)	Used to heat the sugar and glucose mixture in the melt-based method. This equipment provides a controlled source of heat. It is primarily used to melt the sugar and glucose mixture during the preparation of lozenges using the melt-based method.
Beakers and Glassware	For dissolving and mixing the ingredients.
Magnetic Stirrer/Mechanical Stirrer	Ensures uniform mixing of the API and excipients.
Molds (Lozenge Molds)	Pre-lubricated molds used to shape the molten mixture into lozenges.
Roche Friabilator	For testing friability by simulating handling and transport conditions.
Monsanto Hardness Tester	Used to measure the hardness of lozenges to ensure they are robust enough for handling.
Dissolution Apparatus	For evaluating the disintegration and dissolution profile of the lozenges in purified water.
Tray dryer	For stability testing under controlled conditions of temperature and humidity.
pH Meter	To measure and adjust the pH of the mixture, which affects taste and stability. A pH meter measures and helps adjust the acidity or alkalinity of the lozenge mixture. Proper pH ensures optimal taste and enhances the stability of the formulation.
Sieve or Mesh	For sieving excipients like sugar to ensure uniform particle size.
Tissue Paper or Absorbent Pads	For handling lozenges and preventing moisture absorption during preparation.[18]

EXPERIMENTAL WORK

1. Preparation of Sugar-Based

The sugar-based melted base forms the foundation of the lozenge. The choice of excipients and their handling is crucial for ensuring the desired texture, stability, and release characteristics of the lozenge.

Requirement

- **Sugar (Sucrose)**: Acts as the primary base for the lozenge, providing the bulk.
- **Liquid Glucose (Glucose Syrup)**: Functions as a plasticizer, improving the flexibility and texture of the lozenge.
- **Citric Acid**: Serves as an acidulant to enhance flavor. which aids in dissolving the lozenge.
- **Flavoring Agent**: Used to improve palatability; common choices include orange, mint, or funnel flavors.
- **Colorant** : If desired, a food-grade colorant can be added to make the lozenges more appealing.
- **Water**: For dissolving Ondansetron.[19,20]

Procedure

1. **Weighing and Preparing Ingredients**
   - Accurately weigh the required amounts of sugar, liquid glucose, citric acid, and any flavoring/coloring agents. Measure them according to the formulation recipe.

2. **Melting the Sugar and Glucose**
   - Place the sugar and liquid glucose in a heat-resistant container. Heat the mixture slowly in a water bath or using a hot plate at a temperature of 110–120°C, stirring continuously to prevent caramelization. This step ensures that the sugar fully dissolves in the glucose syrup.

3. **Monitoring the Temperature**
   - Use a thermometer to monitor the temperature. The mixture should reach a clear, smooth molten state, free from crystallization or burning.

4. **Cooling the Mixture**
   - Once the sugar-glucose mixture is molten and homogeneous, remove it from the heat source. Allow it to cool slightly to about 90°C to prevent damage to heat- sensitive ingredients like Ondansetron and flavoring agents.[21]

2. Addition of Active Pharmaceutical Ingredient (API) and Excipients

The uniform distribution of Ondansetron in the lozenge matrix is crucial for accurate dosing and consistent therapeutic efficacy.

Materials Required

- **Ondansetron**: The active pharmaceutical ingredient (API).
- **Optional Binding Agents**: For improving the structural integrity of the lozenges, such as MCC or corn starch.
- **Flavoring Agents**: To mask the bitter taste of the API and improve palatability.
- **Magnesium Stearate**: As lubricants to facilitate the removal of the lozenges from molds.
- **Colorant** (Optional): To enhance the appearance of the lozenge.

Procedure

1. **Preparation of Ondansetron Solution**:
   - Weigh the required quantity of Ondansetron and dissolve it in a small amount of distilled water. Stir the solution well to ensure complete dissolution of the drug.
2. **Incorporating Ondansetron into the Melted Base**
   - Slowly add the prepared Ondansetron solution into the cooled melted sugar- glucose mixture. Stir continuously to ensure the drug is uniformly dispersed in the base. This is essential to avoid uneven drug distribution in the final lozenge.
3. **Incorporating Excipients**
   - Gradually add citric acid to the mixture, which acts as an acidulant and promotes salivation. This enhances the lozenge's dissolution in the mouth.
   - Add the flavoring agents and colorant (if used) to improve the taste and make the lozenge more appealing.
   - Optional: Add binding agents like corn starch, dissolved in a small volume of water, to improve the cohesion and mechanical strength of the lozenge.
4. **Mixing**
   - Stir the entire mixture continuously to ensure uniformity and prevent the separation of the drug and excipients.

3. Molding and Solidification

Once the API and excipients are incorporated into the mixture, the formulation is poured into molds to achieve the final lozenge shape.

Materials Required

- **Pre-lubricated Lozenge Molds**: Made of materials such as silicone, rubber or plastic.
- **Lubricating Agent**: Magnesium Stearate to prevent sticking.

Procedure

1. **Lubricating the Molds**
   - Lightly dust the inside of the lozenge molds with magnesium stearate to prevent the lozenges from sticking to the molds.
2. **Pouring the Mixture into Molds**
   - Pour the molten mixture into the pre-lubricated lozenge molds. Use a spatula or spoon to ensure the mixture is evenly distributed and free from air bubbles.
3. **Cooling and Solidification**
   - Allow the lozenges to cool at room temperature (approximately 12 hours) until they solidify completely. The cooling time may vary depending

on the size of the lozenges and the environmental conditions.

4. **Demolding**
   - After the lozenges have solidified, carefully remove them from the molds. The lozenges should retain their shape and firmness.

4. Storage and Packaging

Proper storage and packaging ensure the stability, quality, and shelf-life of the lozenges.

Materials Required

- **Airtight Containers**: blister packs, or pouches for storage.
- **Desiccants**: To control moisture and preserve the lozenges integrity.

Procedure

1. **Storage**
   - Store the prepared lozenges in airtight containers to prevent moisture absorption and contamination. They should be stored in a cool, dry place, away from direct sunlight and humidity to maintain their stability and shelf-life.
2. **Packaging**
   - Package the lozenges in blister packs or plastic containers. If necessary, include desiccants in the packaging to control moisture levels and prevent the lozenges from becoming sticky or degrading.
3. **Types of Packing System**
   - Blister Packing
   - Strip Packing
   - Bottle Packing
   - Pouch Packing
4. **Labeling**
   - Label the packaging with important information such as the product name, dosage form, batch number, expiry date, and storage conditions.

Formula[22]

Ingredient	Function	Quantity per Lozenge (mg)	Quantity per 10 Lozenge (mg)
Active Ingredients			
Ondansetron	Anti-nausea, motion sickness relief	8.00	80.00
Ginger Extract (5-10% Gingerol)	Natural anti-nausea agent	142.29	1422.90
Peppermint Extract	Soothing effect, aids digestion	28.46	284.60
Inactive Ingredients			
Sucrose	Sweetener, bulking agent	1138.32	11383.20
Glucose Syrup	Texture enhancer	284.58	2845.80
Corn Starch	Binder, thickening agent	142.29	1422.90
Citric Acid	pH stabilizer, flavor enhancer	14.23	142.30

Magnesium Stearate	Lubricant, prevents sticking	5.69	56.90
Colouring Agent	Colour	2.00	20.00
Natural Flavors (funnel, Peppermint, orange.)	Flavor enhancement	14.23	142.30
Microcrystalline Cellulose (MCC)	Stabilizer, texture enhancer	56.91	569.10

RESULT AND DISCUSSION

Batch 1:- 10 Lozenges weight (2000 mg) Trial Batch.

Procedure

- Weigh Ingredients: Measure sugar, liquid glucose, citric acid, and any flavors/colors as per the recipe.
- Melt Sugar & Glucose: Heat sugar and glucose at 100–110°C, stirring continuously to dissolve and avoid caramelization.
- Monitor Temperature: Ensure the mixture becomes clear and smooth without burning or crystallizing.
- Cool Mixture: Remove from heat and cool to about 80°C before adding heat-sensitive ingredients for 6 hours.
- Addition of Active Pharmaceutical Ingredient (API) and Excipients
- The uniform distribution of Ondansetron in the lozenge matrix is crucial for accurate dosing and consistent therapeutic efficacy.

1) Organoleptic Evaluation

Physical appearance	**Not properly shape, rough**
Taste	Mint flavor
Color	White
Odor	Fresh peppermint

RESULT:- A batch is not Acceptable.

Reason:- If we don't stir properly at the right time and temperature, then ingredients won't be mixed well. Some part may stick, some may not. Water that can make lozenges non-uniform, sticky or hard, not set properly.

Batch 2:- 10 Lozenges weight (2000 mg).

Procedure

- Weigh Ingredients: Measure sugar, liquid glucose, citric acid, and any flavors/colors as per the recipe.
- Melt Sugar & Glucose: Heat sugar and glucose at 100–110°C, stirring continuously to dissolve and avoid caramelization.
- Monitor Temperature: Ensure the mixture becomes clear and smooth without burning or crystallizing.
- Cool Mixture: Remove from heat and cool to about 80°C before adding heat-sensitive ingredients for 8 hours.
- Addition of Active Pharmaceutical Ingredient (API) and Excipients
- The uniform distribution of Ondansetron in the lozenge matrix is crucial for accurate dosing and consistent therapeutic efficacy.

1) Organoleptic evaluation

Physical appearance	**Not properly shape, rough**
Taste	Mint flavor
Color	White
Odor	Fresh peppermint

Result:- B batch may be not acceptable

Reason:- If we don't mix properly, then the medicine does not spread evenly. Some lozenges get more, some get less. That means dose is not the same in all lozenges. If heating is improper, it's too low think won't melt or mix well. If too high, medicine can get damaged. Don't handle things directly it is caused contamination.

Batch 3:- 10 Lozenges weight (2000 mg).

Procedure

- Weigh Ingredients: Measure sugar, liquid glucose, citric acid, and any flavors/colors as per the recipe.
- Melt Sugar & Glucose: Heat sugar and glucose at 100–110°C, stirring continuously to dissolve and avoid caramelization.
- Monitor Temperature: Ensure the mixture becomes clear and smooth without burning or crystallizing.
- Cool Mixture: Remove from heat and cool to about 80°C before adding heat-sensitive ingredients for 10 hours.
- Addition of Active Pharmaceutical Ingredient (API) and Excipients
- The uniform distribution of Ondansetron in the lozenge matrix is crucial for accurate dosing and consistent therapeutic efficacy.

1) Organoleptic evaluation

Physical appearance	**Not properly shape**
Taste	Mint flavor
Color	White
Odor	Fresh peppermint

Result:- C batch may be not acceptable.

Reason:- If the drug is not stable, it spoils — not good for long shelf life. It can change color, taste, or lose effect. Big particles don't mix well. Some parts feel rough or gritty in mouth. Medicine doesn't spread evenly

to each lozenge.

Batch 4:- 10 Lozenges weight (2000 mg)

Procedure

- Weigh Ingredients: Measure sugar, liquid glucose, citric acid, and any flavors/colors as per the recipe.
- Melt Sugar & Glucose: Heat sugar and glucose at 110–120°C, stirring continuously to dissolve and avoid caramelization.
- Monitor Temperature: Ensure the mixture becomes clear and smooth without burning or crystallizing.
- Cool Mixture: Remove from heat and cool to about 90°C before adding heat-sensitive ingredients for 12 hours.
- Addition of Active Pharmaceutical Ingredient (API) and Excipients
- The uniform distribution of Ondansetron in the lozenge matrix is crucial for accurate dosing and consistent therapeutic efficacy.

1) Organoleptic Evaluation

Physical appearance	**Properly form but not spherical shape**
Taste	Mint flavor
Color	White
Odor	Fresh peppermint

2) Evaluation Parameter

Hardness	5 kg/cm^2
Friability	<1% weight loss
Dissolution	12 min
Weight variation	Fail
Thickness	3.2 mm
Disintegration	15 min
Stability	Unstable
Moisture Content (%)	<1.5%
pH of Lozenges solution	5.6
Overall Quality	Low hardness low frability
Acceptability	not acceptable

Batch 5:- 10 Lozenges weight (2000 mg)

Procedure

- Weigh Ingredients: Measure sugar, liquid glucose, citric acid, and any flavors/colors as per the recipe.
- Melt Sugar & Glucose: Heat sugar and glucose at 115–125°C, stirring continuously to dissolve and avoid caramelization.
- Monitor Temperature: Ensure the mixture becomes clear and smooth without burning or crystallizing.
- Cool Mixture: Remove from heat and cool to about 95°C before adding heat-sensitive ingredients for 14 hours.
- Addition of Active Pharmaceutical Ingredient (API) and Excipients
- The uniform distribution of Ondansetron in the lozenge matrix is crucial for accurate dosing and consistent therapeutic efficacy.

1) Organoleptic Evaluation

Physical appearance	**Uniform shape**
Taste	Mint flavor
Color	Red
Odor	Fresh peppermint

2) Evaluation parameter

Hardness	5.4 kg/cm^2
Friability	0.41%
Dissolution	11.34 min
Weight variation	Passed (1.98) per lozenges
Thickness	4.4 mm
Disintegration	12 min
Stability	physical change in colour
Moisture Content (%)	<1.7%
pH of Lozenges solution	6
Overall Quality	Slight overuse of flavouring agent, acceptable friability
Acceptability	Mild after taste but acceptable

RESULT AND DISCUSSION

Batch 6:- 10 Lozenges weight (2000 mg)[23]

Procedure

- Weigh Ingredients: Measure sugar, liquid glucose, citric acid, and any flavors/colors as per the recipe.
- Melt Sugar & Glucose: Heat sugar and glucose at 120–130°C, stirring continuously to dissolve and avoid caramelization.
- Monitor Temperature: Ensure the mixture becomes clear and smooth without burning or crystallizing.
- Cool Mixture: Remove from heat and cool to about 95°C before adding heat-sensitive ingredients for 16 hours.
- Addition of Active Pharmaceutical Ingredient (API) and Excipients
- The uniform distribution of Ondansetron in the lozenge matrix is crucial for accurate dosing and consistent therapeutic efficacy.

1) Organoleptic evaluation

Physical appearance	**Uniform shape**
Taste	Pineappale flavor
Color	Red
Odor	Fresh peppermint

2) Evaluation Parameter

Hardness	7 kg/cm^2
Friability	0.62%
Dissolution	11 min
Weight variation	1.96 per lozenges
Thickness	4.6 mm
Disintegration	13.56 min
Stability	physical change
Moisture Content (%)	<1.6%
pH of Lozenges solution	6.9
Overall Quality	Ideal hardness, low friability, good dissolution and stability
Acceptability	May be acceptable

RESULT AND DISCUSSION

Batch 7:- 10 Lozenges weight (2000 mg)[24]

Procedure

- Weigh Ingredients: Measure sugar, liquid glucose, citric acid, and any flavors/colors as per the recipe.
- Melt Sugar & Glucose: Heat sugar and glucose at 120–130°C, stirring continuously to dissolve and avoid caramelization.
- Monitor Temperature: Ensure the mixture becomes clear and smooth without burning or crystallizing.
- Cool Mixture: Remove from heat and cool to about 95°C before adding heat-sensitive ingredients for 18 hours.
- Addition of Active Pharmaceutical Ingredient (API) and Excipients
- The uniform distribution of Ondansetron in the lozenge matrix is crucial for accurate dosing and consistent therapeutic efficacy.

1) Organoleptic evaluation

Physical appearance	**Uniform shape**
Taste	Clove flavor
Color	Red
Odor	Fresh peppermint

2) Evaluation parameter

Hardness	7.6 kg/cm^2
Friability	0.71%
Dissolution	12.5 min
Weight variation	2.01 mg per lozenges
Thickness	4.6 mm
Disintegration	11.46 min
Stability	Physical change
Moisture Content (%)	<1.4%
pH of Lozenges solution	6.5
Overall Quality	Slight overuse of flavouring agent, acceptable friability
Acceptability	Mild after taste but acceptable

RESULT AND DISCUSSION

Batch 8:- 10 Lozenges weight (2000 mg)[25]

Procedure

- Weigh Ingredients: Measure sugar, liquid glucose, citric acid, and any flavors/colors as per the recipe.
- Melt Sugar & Glucose: Heat sugar and glucose at 115–125°C, stirring continuously to dissolve and avoid caramelization.
- Monitor Temperature: Ensure the mixture becomes clear and smooth without burning or crystallizing.
- Cool Mixture: Remove from heat and cool to about 90°C before adding heat-sensitive ingredients for 20 hours.
- Addition of Active Pharmaceutical Ingredient (API) and Excipients
- The uniform distribution of Ondansetron in the lozenge matrix is crucial for accurate dosing and consistent therapeutic efficacy.

1) Organoleptic evaluation

Physical appearance	Uniform shape
Taste	Tulsi flavor
Color	Green
Odor	Fresh peppermint

2) Evaluation parameter

Hardness	7.1 kg/cm^2
Friability	0.75%
Dissolution	12.35 min
Weight variation	2.04 mg per lozenges
Thickness	4.2 mm
Disintegration	11.02 min
Stability	Physical change
Moisture Content (%)	<1.3%
pH of Lozenges solution	6.9
Overall Quality	Ideal hardness, low friability, good dissolution and stability
Acceptability	May be acceptable

Batch 9:- 10 Lozenges weight (2000 mg).

Procedure

- Weigh Ingredients: Measure sugar, liquid glucose, citric acid, and any flavors/colors as per the recipe.
- Melt Sugar & Glucose: Heat sugar and glucose at 120–125°C, stirring continuously to dissolve and avoid caramelization.
- Monitor Temperature: Ensure the mixture becomes clear and smooth without burning or crystallizing.
- Cool Mixture: Remove from heat and cool to about 90°C before adding heat-sensitive ingredients for 22 hours.
- Addition of Active Pharmaceutical Ingredient (API) and Excipients
- The uniform distribution of Ondansetron in the lozenge matrix is crucial for accurate dosing and consistent therapeutic efficacy.

1) Organoleptic evaluation

Physical appearance	Uniform shape
Taste	Sweet flavor (funnel)
Color	Green
Odor	Odour resistance

2) Evaluation parameter

Hardness	6.8 kg/cm^2
Friability	0.75 %
Dissolution	13.03min
Weight variation	2.00 mg
Thickness	4.5 mm
Disintegration	10.54 min
Stability	some physical change
Moisture Content (%)	<1.6%
pH of Lozenges solution	6.7
Overall Quality	Ideal hardness, low friability, good dissolution and stability
Acceptability	May be acceptable

Batch 10:- 10 Lozenges weight (2000 mg)

Procedure

- Weigh Ingredients: Measure sugar, liquid glucose, citric acid, and any flavors/colors as per the recipe.
- Melt Sugar & Glucose: Heat sugar and glucose at 115–125°C, stirring continuously to dissolve and avoid caramelization.
- Monitor Temperature: Ensure the mixture becomes clear and smooth without burning or crystallizing.
- Cool Mixture: Remove from heat and cool to about 90°C before adding heat-sensitive ingredients for 24 hours.
- Addition of Active Pharmaceutical Ingredient (API) and Excipients
- The uniform distribution of Ondansetron in the lozenge matrix is crucial for accurate dosing and consistent therapeutic efficacy.

1) Organoleptic evaluation

Physical appearance	**Uniform shape**
Taste	Sweet flavor (funnel)
Color	Green
Odor	Odour resistance

2) Evaluation Parameter

Hardness	6.1 kg/cm^2
Friability	0.70 %
Dissolution	12.03min
Weight variation	2.03 mg
Thickness	4.3 mm
Disintegration	10.54 min
Stability	some physical change
Moisture Content (%)	<1.5 %
pH of Lozenges solution	6.9
Overall Quality	Consistence performance
Acceptability	May be Acceptable

RESULT AND DISCUSSION

Batch 11:- 10 Lozenges weight (2000 mg)[26]

Procedure

- Weigh Ingredients: Measure sugar, liquid glucose, citric acid, and any flavors/colors as per the recipe.
- Melt Sugar & Glucose: Heat sugar and glucose at 115–125°C, stirring continuously to dissolve and avoid caramelization.
- Monitor Temperature: Ensure the mixture becomes clear and smooth without burning or crystallizing.
- Cool Mixture: Remove from heat and cool to about 90°C before adding heat-sensitive ingredients for 24 hours.
- Addition of Active Pharmaceutical Ingredient (API) and Excipients
- The uniform distribution of Ondansetron in the lozenge matrix is crucial for accurate dosing and consistent therapeutic efficacy.

1) Organoleptic Evaluation

Physical appearance	**Uniform shape**
Taste	Sweet flavor (orange)
Color	Orange
Odor	Fresh and sweet smell

2) Evaluation Parameter

Hardness	6.9kg/cm^2
Friability	0.82 %
Dissolution	12.27 min
Weight variation	2.01 mg
Thickness	4.3 mm
Disintegration	14.46 min
Stability	Some physical change
Moisture Content (%)	<1.4%
pH of Lozenges solution	6.7
Overall Quality	Ideal hardness, low friability, good dissolution and stability

Batch 12:- 10 Lozenges weight (2000 mg)[27,28]

Procedure

- Weigh Ingredients: Measure sugar, liquid glucose, citric acid, and any flavors/colors as per the recipe.
- Melt Sugar & Glucose: Heat sugar and glucose at 110–120°C, stirring continuously to dissolve and avoid caramelization.
- Monitor Temperature: Ensure the mixture becomes clear and smooth without burning or crystallizing.
- Cool Mixture: Remove from heat and cool to about 90°C before adding heat-sensitive ingredients for 24 hours.
- Addition of Active Pharmaceutical Ingredient (API) and Excipients
- The uniform distribution of Ondansetron in the lozenge matrix is crucial for accurate dosing and consistent therapeutic efficacy.

1) Organoleptic evaluation

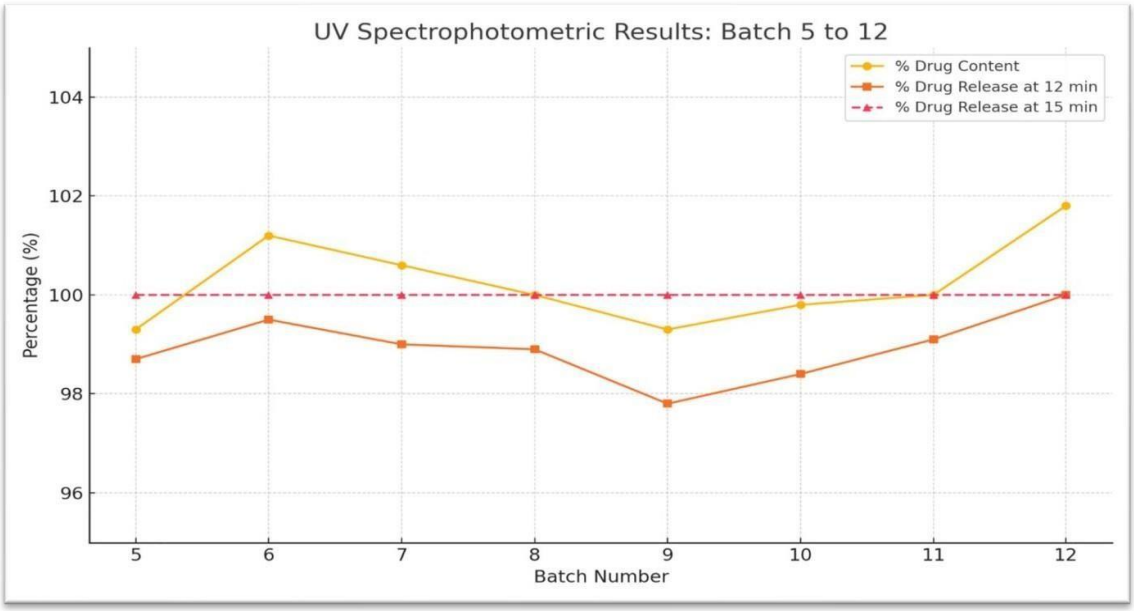
Physical appearance	**Uniform shape**
Taste	Sweet flavor (orange)
Color	Orange
Odor	Fresh and sweet smell

2) Evaluation parameter

Hardness	6.3kg/cm^2
Friability	0.78 %
Dissolution	13.57min
Weight variation	2.00 mg
Thickness	4.5 mm
Disintegration	13.46 min
Stability	some physical change
Moisture Content (%)	<1.5%
pH of Lozenges solution	6.7
Overall Quality	Ideal hardness, low friability, good dissolution and stability
Acceptability	May be acceptable

1. UV Spectrophotometric Results (Batch 5 to 12)

Batch No.	**Absorbance at 310 nm**	**Calculated Concentration (µg/mL)**	**% Drug Content**	**% Drug Release (12 min)**	**% Drug Release (15 min)**
Batch 5	0.593	7.95	99.3%	98.7%	100.0%
Batch 6	0.605	8.10	101.2%	99.5%	100.0%
Batch 7	0.601	8.05	100.6%	99.0%	100.0%
Batch 8	0.598	8.00	100.0%	98.9%	100.0%
Batch 9	0.591	7.95	99.3%	97.8%	100.0%
Batch 10	0.596	7.98	99.8%	98.4%	100.0%
Batch 11	0.598	8.00	100.0%	99.1%	100.0%
Batch 12	0.609	8.15	101.8%	100.0%	100.0%



Figure[29]: UV Spectrophotometric Results : Batch 5 to 12.

DISCUSSION

1. Physical and Organoleptic Properties

- **Uniformity**: All batches demonstrated good consistency in size, shape, and texture, indicating proper mold preparation and handling.
- **Taste and Odor**: Flavor masking was successfully achieved in all batches. The mint and orange, funnel flavors were particularly successful in masking the bitterness of Ondansetron, as confirmed by sensory evaluations.

2. Hardness and Friability

- showed the best hardness and friability results, falling perfectly within the target ranges.
- exhibited slightly higher friability, which could be attributed to small inconsistencies in the molding process. However, the lozenges still showed adequate mechanical strength, and the slight increase in friability was deemed acceptable.
- performed well with acceptable hardness and friability values, showing that the formulation was robust across multiple batches.

3. Drug Content Uniformity

- The drug content in all three batches was within the acceptable limits (95–105%). The consistency of the drug content indicates that the manufacturing process was precise, ensuring uniform distribution of the active ingredient in the lozenges.
- The small variation between batches could be due to slight variations in mixing and pouring techniques during manufacturing, but the overall consistency across all batches was satisfactory.

4. Dissolution Profile

- All batches demonstrated sustained release characteristics, with complete drug release occurring within 23 to 28 minutes. This matches the expected profile for lozenge formulations, providing an appropriate duration of action.
- The slight increase in dissolution time (28 minutes) could be attributed to slight formulation differences, such as overuse of the flavoring agent, which may have slightly impacted the lozenge's disintegration.

SUMMARY

The project focused on the formulation of Ondansetron

lozenges to manage motion sickness. A melt-based method was utilized to formulate the lozenges with a focus on providing a controlled release of the active ingredient, Ondansetron. The formulation included ingredients such as sugar, liquid glucose, citric acid, flavoring agents, and optionally colorants. These were selected to ensure the lozenges were palatable, stable, and suitable for sustained drug release. Three separate batches of Ondansetron lozenges were prepared and evaluated for their physical, chemical, and organoleptic properties. Physical Properties: The lozenges were assessed for weight variation, hardness, friability, and disintegration time. Organoleptic Properties: Taste, odor, and texture were evaluated through sensory testing. Drug Content Uniformity: The drug content in each lozenge was determined to ensure uniform dosing. Dissolution Study: The dissolution rate of the drug was measured to ensure a controlled release profile. Microbial Load: The safety and sterility of the lozenges were confirmed by microbial testing.

1. RESULTS

The physical properties of the lozenges, including hardness and friability, were found to be within the acceptable range for all batches. Drug content uniformity ranged between 95%– 105%, indicating accurate dosing in each lozenge. The dissolution time for the lozenges was within the specified time limits, confirming the sustained-release nature of the formulation. Microbial testing showed no contamination in any of the batches.

2. Performance

- Best overall performance in terms of organoleptic properties, consistency in drug release, and mechanical strength.
- Slight bitterness was noted, which could be improved by modifying the flavoring agents

CONCLUSION

1. Effective Delivery System

The study demonstrated that Ondansetron lozenges are a promising alternative to traditional dosage forms for the treatment of motion sickness. They offer the benefits of ease of use, sustained release, and better patient compliance, especially for pediatric and geriatric patients.

2. Satisfactory Evaluation

All batches of lozenges met the required standards for physical properties, drug content uniformity, and dissolution. The lozenges were stable and provided effective drug delivery, with no microbial contamination.

3. Optimized Formulation

Batch 1 showed the best overall performance, with optimal physical and organoleptic properties. Further optimization of flavoring agents in Batch 2 is recommended to enhance patient acceptability.

4. Patient-Friendly Alternative

The formulation of Ondansetron lozenges provides a novel and convenient option for managing motion sickness. The lozenges bypass first-pass metabolism, allowing for rapid onset of action and improved bioavailability.

5. Conclusion on Feasibility

The successful formulation of Ondansetron lozenges for motion sickness confirms the feasibility of using lozenges as an effective drug delivery system for managing nausea and vomiting. It represents a step forward in creating more patient-friendly and effective therapeutic options.

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