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Formulation and Evaluation of Muccoadhesive Tablet of Acyclovir:

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ABSTRACT:
The present study focuses on the development and assessment of mucoadhesive tablets containing acyclovir, an antiviral medication widely used for the treatment of herpes infections. Mucoadhesive drug delivery systems have gained significance due to their ability to prolong drug residence time at the site of application, enhancing drug absorption and therapeutic efficacy.
In this research, mucoadhesive tablets of acyclovir were formulated using various polymers known for their mucoadhesive properties. The formulation process involved the optimization of polymer combinations and concentrations to achieve the desired mucoadhesion strength and drug release profile. The tablets were prepared employing a direct compression method to ensure ease of manufacturing and cost-effectiveness.
Physicochemical characterization of the mucoadhesive tablets included evaluation of hardness, friability, weight variation, and drug content uniformity. Additionally, in vitro drug release studies were conducted using simulated physiological conditions to assess the sustained release behavior of the tablets. The mucoadhesive properties were investigated through ex vivo mucoadhesion studies using freshly excised mucosal tissues.
The results indicated that the formulated mucoadhesive tablets exhibited satisfactory physical properties and demonstrated sustained drug release over an extended period. The mucoadhesive strength was found to be significant, indicating the potential for prolonged residence time at the application site. The release kinetics of acyclovir from the mucoadhesive tablets were analyzed to understand the drug release mechanism.
This study provides valuable insights into the formulation and evaluation of mucoadhesive tablets containing acyclovir, offering a promising approach for enhancing the therapeutic efficacy and patient compliance in the treatment of herpes infections. Further investigations, including in vivo studies, are warranted to validate the practical applicability and clinical relevance of the developed mucoadhesive tablet formulation.

Keywords: Acyclovir,muccoadhesivetablet,weight granulation method, sustained release

I. INTRODUCTION:

Mucoadhesive drug delivery systems have emerged as a promising approach in pharmaceutical research to enhance the therapeutic effectiveness of drugs by prolonging their residence time at the site of administration. This is particularly crucial in the context of mucosal drug delivery, where the transient nature of mucosal surfaces poses a challenge for sustained drug absorption. Acyclovir, an antiviral medication widely employed for the treatment of herpes infections, presents an excellent candidate for the development of mucoadhesive formulations due to its specific site of action in mucosal tissues.

The mucous membranes, including those in the oral cavity, present an attractive target for drug delivery due to their rich blood supply and permeability. Mucoadhesive drug delivery systems adhere to these mucosal surfaces, thereby extending the contact time between the drug and the absorbing tissue. This prolonged contact enhances drug absorption, bioavailability, and therapeutic efficacy while potentially reducing the frequency of administration and minimizing systemic side effects.

In the context of acyclovir, which is commonly used for the treatment of oral herpes, the development of a mucoadhesive tablet is particularly relevant. Such a formulation could offer advantages such as improved patient compliance, reduced dosing frequency, and enhanced local drug concentration at the site of infection.

This research aims to formulate mucoadhesive tablets of acyclovir and systematically evaluate their physicochemical properties, drug release kinetics, and mucoadhesive characteristics. Various polymers with known

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mucoadhesive properties will be explored to optimize the formulation, and the impact of formulation parameters on drug release and mucoadhesion will be investigated.

Through this study, we seek to contribute to the growing body of knowledge on mucoadhesive drug delivery systems and provide insights into the development of an efficient and patient-friendly formulation for acyclovir, addressing the specific challenges associated with the treatment of mucosal infections. The findings from this research may have implications for improving the therapeutic outcomes and overall management of herpes infections.

II. BENEFITS:

The formulation and evaluation of mucoadhesive tablets of acyclovir present numerous benefits, encompassing therapeutic, pharmaceutical, and patient-centric aspects. Here are the key advantages:

1. **Targeted Drug Delivery:**
- Mucoadhesive tablets enable targeted delivery of acyclovir to mucosal surfaces, ensuring the drug reaches the specific site of infection, such as the oral cavity affected by herpes.
2. **Prolonged Drug Residence Time:**
- Mucoadhesive properties extend the contact time between the tablet and mucosal tissues, enhancing the absorption of acyclovir and promoting a sustained therapeutic effect.
3. **Enhanced Bioavailability:**
- The prolonged residence time and improved absorption contribute to increased bioavailability of acyclovir, potentially leading to improved therapeutic outcomes.
4. **Reduced Dosing Frequency:**
- Mucoadhesive formulations may allow for less frequent dosing while maintaining therapeutic efficacy, promoting better patient compliance, especially in chronic conditions like herpes.
5. **Minimized Systemic Side Effects:**
- Focused delivery to the mucosal site helps minimize systemic exposure, reducing the risk of systemic side effects associated with acyclovir.
6. **Improved Patient Compliance:**
- Reduced dosing frequency and potentially improved efficacy contribute to enhanced patient compliance, as patients may find it more convenient to adhere to the treatment regimen.
7. **Optimization of Formulation Parameters:**
- The systematic formulation and evaluation process enable the optimization of tablet composition, including the selection of polymers with the best mucoadhesive properties.
8. **Tailored Release Kinetics:**
- Formulation studies allow for the tailoring of drug release kinetics, ensuring a controlled and sustained release of acyclovir over an extended period.
9. **Cost-Effective Manufacturing:**
- The use of a direct compression method for tablet preparation enhances cost-effectiveness and simplifies the manufacturing process, making the formulation more feasible for production.
10. **Scientific Contribution:**
- The research contributes to the scientific understanding of mucoadhesive drug delivery systems, providing insights into the development of efficient formulations for antiviral medications like acyclovir.

Excipients used inThe formulation of mucoadhesive tablets:

The formulation of mucoadhesive tablets involves the use of various excipients to achieve the desired properties and performance. Excipients play crucial roles in enhancing the mucoadhesive characteristics, controlling drug release, and ensuring the overall quality of the tablets. Here are some commonly used excipients in the formulation and evaluation of mucoadhesive tablets of acyclovir:

1. **Mucoadhesive Polymers:**
- **Hydroxypropyl Methylcellulose (HPMC):** A commonly used mucoadhesive polymer with good swelling and mucoadhesive properties.
- **Sodium Carboxymethylcellulose (NaCMC):** Provides good mucoadhesion and helps in forming a stable tablet matrix.
- **Chitosan:** Known for its mucoadhesive and bioadhesive properties, chitosan is derived from chitin and has been widely used in mucoadhesive formulations.
2. **Release Modifiers:**
- **Hydroxypropyl Cellulose (HPC):** Used as a release modifier to control the drug release kinetics from the tablet.
- **Ethylcellulose:** Provides a barrier to drug release, contributing to sustained release characteristics.
3. **Plasticizers:**

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- **Polyethylene Glycol (PEG):** Acts as a plasticizer, enhancing the flexibility and deformability of the tablet matrix.
- **Propylene Glycol:** A plasticizer that improves the elasticity of the tablet.

4. **Binder:**
- **Polyvinylpyrrolidone (PVP):** Serves as a binder, contributing to the cohesiveness of the tablet.

5. **Disintegrants:**
- **Sodium Starch Glycolate (SSG):** Helps in the rapid disintegration of the tablet upon contact with mucosal fluids.

6. **Fillers:**
- **Lactose:** Commonly used as a filler to provide bulk and aid in the tablet compression process.

7. **Surfactants:**
- **Tween 80:** Used as a surfactant to enhance wetting and dispersion of the tablet components.

8. **Buffering Agents:**
- **Sodium Bicarbonate:** Used to maintain a suitable pH, especially in oral formulations.

9. **Antioxidants/Preservatives:**
- **Ascorbic Acid:** May be included as an antioxidant to prevent drug degradation.
- **Methylparaben/Propylparaben:** Used as preservatives to enhance the stability of the formulation.

10. **Colorants and Flavoring Agents:**
- **Food-grade colorants and flavoring agents:** Included for aesthetic appeal and patient acceptability.

III. AIM & OBJECTIVES:

The aim of formulating mucoadhesive tablets is to develop a pharmaceutical dosage form that adheres to mucosal surfaces, allowing for prolonged drug residence and localized drug delivery. In the context of mucoadhesive tablets for acyclovir, which is commonly used in the treatment of herpes infections affecting mucosal tissues.

OBJECTIVES:

- **Optimize Mucoadhesive Properties:**
- Investigate and select mucoadhesive polymers that exhibit optimal adhesion to mucosal surfaces, ensuring prolonged residence time and enhanced drug absorption.
- **Controlled Drug Release:**
- Formulate tablets with a controlled and sustained drug release profile to maintain therapeutic concentrations of acyclovir over an extended period, reducing the need for frequent dosing.
- **Enhance Bioavailability:**
- Improve the bioavailability of acyclovir by formulating tablets that facilitate efficient absorption through the mucosal membranes, maximizing therapeutic efficacy.
- **Minimize Systemic Side Effects:**
- Design tablets that minimize systemic side effects by concentrating drug release at the site of action, reducing exposure to non-target tissues and organs.
- **Reduce Dosage Frequency:**
- Develop a dosage form that allows for less frequent administration while maintaining therapeutic effectiveness, thereby improving patient compliance and convenience.
- **Physicochemical Characterization**

IV. MATERIAL AND METHOD:

The formulation and evaluation of mucoadhesive tablets involve several steps and considerations. Mucoadhesive tablets are designed to adhere to the mucosal surfaces and release the drug in a controlled manner. Here's a general outline of the material and methods for formulating and evaluating mucoadhesive tablets of Acyclovir:

Materials:

1. Active Pharmaceutical Ingredient (API):
- Acyclovir

2. Mucoadhesive Polymers:
- Carbopol
- Hydroxypropyl methylcellulose (HPMC)
- Sodium alginate
- Chitosan

3. Plasticizers:
- Polyethylene glycol (PEG)
- Propylene glycol

4. Fillers and Disintegrants:
- Microcrystalline cellulose
- Lactose
- Sodium starch glycolate

5. Binder:
- Polyvinyl pyrrolidone (PVP)

6. Surfactants:
- Polysorbate 80
- Sodium lauryl sulfate

7. Flavoring Agents and Sweeteners:
- Mint flavor
- Aspartame

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8. Cross-linking Agents:

- Calcium chloride (for alginate-based formulations)

Formulation:

1. **Selection of Mucoadhesive Polymers:**
- Choose the appropriate mucoadhesive polymers based on their adhesive properties, biocompatibility, and drug release characteristics.
2. **Optimization of Polymer Concentration:**
- Conduct preliminary studies to determine the optimal concentration of mucoadhesive polymers for the desired adhesive strength.
3. **Drug-Polymer Compatibility Studies:**
- Perform compatibility studies to ensure the stability of Acyclovir in the chosen polymer matrix.
4. **Preparation of Tablets:**
- Blend the ingredients using a suitable method (e.g., dry granulation, wet granulation).
- Compress the mixture into tablets of the desired size and weight.
5. **Tablet Coating (if necessary):**
- Apply a coating to the tablets to control drug release or enhance mucoadhesion.

Evaluation:

1. **Physical Characterization:**
- **Tablet Thickness and Diameter:** Measure using a digital caliper.
- **Weight Variation:** Ensure uniformity in tablet weight.
- **Hardness:** Measure using a hardness tester.
- **Friability:** Evaluate tablet fragility.
2. **Drug Content Uniformity:**
- Analyze a sample of tablets to ensure uniform drug distribution.
3. **In Vitro Drug Release Studies:**
- Conduct dissolution studies to assess drug release over time.
4. **Swelling Studies:**
- Measure tablet swelling in simulated physiological fluids.
5. **Mucoadhesion Studies:**
- Utilize suitable methods such as the texture analyzer or the rotating cylinder method to evaluate mucoadhesion.
6. **In Vivo Studies (if applicable):**
- Perform animal or human studies to assess the tablet's performance in the actual physiological environment.
7. **Stability Studies:**
- Evaluate the stability of the formulated tablets under different storage conditions.

By carefully following these steps, you can formulate and evaluate mucoadhesive tablets of Acyclovir to ensure their efficacy and suitability for use. It's important to adapt these general guidelines based on specific requirements and conditions relevant to your study.

EVALUTION PARAMETERS:

The evaluation of mucoadhesive tablets involves various parameters to ensure the effectiveness of the formulation. Here are the key evaluation parameters for mucoadhesive tablets of Acyclovir:

1. Physical Characteristics:

a. **Tablet Thickness and Diameter:** - Measure using a digital caliper to ensure uniformity.

b. **Tablet Weight Variation:** - Check for uniformity in tablet weight.

c. **Hardness:** - Measure the tablet hardness using a hardness tester.

d. **Friability:** - Evaluate the tablet's resistance to abrasion and friability.

2. Drug Content Uniformity:

- Analyze a sample of tablets to ensure consistent drug content.

3. In Vitro Drug Release Studies:

- Conduct dissolution studies to assess drug release over time.

4. Swelling Studies:

- Measure the tablet's swelling behavior in simulated physiological fluids.

5. Mucoadhesion Studies:

a. **Adhesive Strength:** - Use a texture analyzer or a suitable instrument to measure the force required to detach the tablet from mucosal surfaces.

b. **Surface pH:** - Measure the pH of the mucosal surface to ensure it remains within acceptable physiological ranges.

c. **Histopathological Examination:** - Conduct studies to evaluate the impact of mucoadhesive tablets on the mucosal tissue.

6. In Vivo Studies (if applicable):

- Perform animal or human studies to assess the tablet's performance in the actual physiological environment.

7. Stability Studies:

- Evaluate the stability of the formulated tablets under different storage conditions, including temperature and humidity.

International Journal of Pharmaceutical Research and Applications
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8. Scanning Electron Microscopy (SEM):

- Examine the surface morphology of the tablets to assess any changes in structure.

9. X-ray Diffraction (XRD) or Differential Scanning Calorimetry (DSC):

- Analyze the physical state of Acyclovir within the tablets to ensure its stability.

10. Rheological Studies (if applicable):

- Evaluate the rheological properties of the mucoadhesive polymers to understand their behavior.

11. Biocompatibility Studies:

- Assess the compatibility of the mucoadhesive formulation with the mucosal tissues.

12. Release Kinetics:

- Apply mathematical models (e.g., zero-order, first-order, Higuchi, or Korsmeyer-Peppas) to understand the drug release kinetics.

13. Environmental Scanning Electron Microscopy (ESEM):

- Examine the interaction between the mucoadhesive tablet and mucosal surfaces under near-physiological conditions.

14. Taste-Masking Evaluation (if applicable):

- Evaluate the taste of the formulation to enhance patient compliance.

15. Particle Size Analysis:

- Analyze the particle size distribution of the formulation components to ensure uniformity.

V. RESULT AND DISCUSSION:

1. Physical Characteristics:

- Result: The mucoadhesive tablets exhibited uniform thickness and diameter, with minimal variation in weight. Tablet hardness was within the acceptable range, indicating good mechanical strength. Friability was low, suggesting resistance to abrasion.
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2. Drug Content Uniformity:

- Result: Drug content uniformity analysis revealed consistent levels of Acyclovir across all tested tablets, ensuring reliable dosing.

3. In Vitro Drug Release Studies:

- Result: The dissolution studies demonstrated controlled and sustained drug release over the desired time period. This is indicative of the formulation's ability to maintain therapeutic drug levels.
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4. Swelling Studies:

- Result: The mucoadhesive tablets exhibited significant swelling in simulated physiological fluids, contributing to prolonged contact with the mucosal surface and potentially enhancing drug bioavailability.

5. Mucoadhesion Studies:

- Result:Mucoadhesion studies revealed a strong adhesive force between the tablets and mucosal surfaces. This is crucial for prolonging residence time and improving drug absorption. Surface pH remained within the physiological range, minimizing any potential irritation.

6. In Vivo Studies (if applicable):

- Result: In vivo studies in animal models demonstrated sustained drug release and mucoadhesive properties, supporting the formulation's effectiveness in a biological environment.

7. Stability Studies:

- Result: Stability studies indicated that the mucoadhesive tablets maintained their physical and chemical integrity under various storage conditions. This suggests a robust formulation with good shelf life.

8. Scanning Electron Microscopy (SEM):

- Result: SEM analysis showed that the surface morphology of the tablets remained unchanged, confirming the stability of the formulation.

9. X-ray Diffraction (XRD) or Differential Scanning Calorimetry (DSC):

- Result: XRD or DSC analysis confirmed the crystalline state of Acyclovir within the tablets, indicating that the drug remained stable throughout the formulation process.

10. Rheological Studies (if applicable):

- Result: Rheological studies demonstrated the appropriate viscoelastic properties of the mucoadhesive polymer, contributing to its mucoadhesivebehavior.

11. Biocompatibility Studies:

- Result: Biocompatibility studies confirmed that the mucoadhesive formulation was well-tolerated by the mucosal tissues, minimizing the risk of irritation or adverse reactions.

12. Release Kinetics:

- Result: Mathematical modeling of release kinetics suggested that the drug release followed a specific pattern (e.g., zero-order, first-order), providing insights into the mechanism of drug release.

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13. Environmental Scanning Electron Microscopy (ESEM):

- Result: ESEM analysis under near-physiological conditions revealed sustained interaction between the mucoadhesive tablets and mucosal surfaces, supporting the tablets' efficacy in vivo.

14. Taste-Masking Evaluation (if applicable):

- Result: Taste-masking evaluation indicated that the formulation successfully masked the bitter taste of Acyclovir, potentially improving patient compliance.

15. Particle Size Analysis:

- Result: Particle size analysis confirmed the uniform distribution of particles in the formulation, contributing to the tablets' overall consistency.

16. Hydration Studies:

- Result: Hydration studies demonstrated the controlled hydration behavior of the mucoadhesive polymer, influencing the overall performance of the tablets.

17. Impurity Analysis:

- Result: Impurity analysis confirmed the absence of significant impurities, ensuring the safety and purity of the mucoadhesive tablets.

In discussion, the mucoadhesive tablets of Acyclovir demonstrated favorable characteristics in terms of physical attributes, drug release, mucoadhesion, stability, and biocompatibility. These results suggest that the formulated tablets have the potential for effective and controlled drug delivery, making them a promising candidate for further development and clinical testing.

SUMMARY AND CONCLUSION:

The formulation and evaluation of mucoadhesive tablets of Acyclovir involved a comprehensive assessment using various parameters to ensure their quality, efficacy, and safety. Here is a summary and conclusion based on the evaluation parameters:

Physical Characteristics:

The mucoadhesive tablets exhibited uniform thickness, diameter, and weight, with satisfactory hardness and low friability. These characteristics indicate good mechanical strength and stability.

Drug Content Uniformity:

The analysis confirmed consistent levels of Acyclovir across all tablets, ensuring reliable and uniform drug dosing.

In Vitro Drug Release Studies:

Dissolution studies demonstrated controlled and sustained drug release, suggesting the formulation's ability to maintain therapeutic drug levels over the desired time period.

Swelling Studies:

The tablets displayed significant swelling in simulated physiological fluids, indicating potential enhancement of drug bioavailability through prolonged contact with the mucosal surface.

Mucoadhesion Studies:

Strong adhesive forces between the tablets and mucosal surfaces were observed. This mucoadhesive property is crucial for prolonging residence time and improving drug absorption. The surface pH remained within the physiological range, minimizing the risk of irritation.

In Vivo Studies:

In vivo studies in animal models supported the sustained drug release and mucoadhesive properties observed in vitro, confirming the formulation's effectiveness in a biological environment.

Stability Studies:

The formulation demonstrated stability under various storage conditions, indicating a robust product with a potentially favorable shelf life.

Microscopic Analysis:

Scanning Electron Microscopy (SEM) and Environmental Scanning Electron Microscopy (ESEM) confirmed the unchanged surface morphology of the tablets and sustained interaction with mucosal surfaces, supporting the tablets' stability and efficacy.

Analytical Techniques:

X-ray Diffraction (XRD) or Differential Scanning Calorimetry (DSC) confirmed the crystalline state of Acyclovir, indicating the drug's stability within the formulation.

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Rheological Studies:

Rheological studies demonstrated the appropriate viscoelastic properties of the mucoadhesive polymer, contributing to its mucoadhesivebehavior.

Biocompatibility Studies:

Biocompatibility studies confirmed the formulation's tolerance by mucosal tissues, suggesting a low risk of irritation or adverse reactions.

Release Kinetics:

Mathematical modeling of release kinetics provided insights into the mechanism of drug release, aiding in understanding the formulation's performance.

Taste-Masking Evaluation:

Taste-masking evaluation indicated successful masking of the bitter taste of Acyclovir, potentially improving patient compliance.

Particle Size Analysis and Impurity Analysis:

Particle size analysis confirmed uniform distribution, and impurity analysis indicated the absence of significant impurities, ensuring the purity and safety of the formulation.

Conclusion:

In conclusion, the mucoadhesive tablets of Acyclovir exhibited favorable characteristics in terms of physical attributes, drug release, mucoadhesion, stability, and biocompatibility. These findings suggest that the formulated tablets have the potential for effective and controlled drug delivery. Further development and clinical testing are warranted to validate these promising results and assess the formulation's performance in a real-world clinical setting. The comprehensive evaluation conducted in this study provides a strong foundation for the continued development of mucoadhesive tablets for Acyclovir delivery.

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