Formulation And Evaluation Of Mucoadhesive Polymer Blend Prochlorperazine Maleate Tablet

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Abstract- *The objective of this study was to develop and evaluate a mucoadhesive polymer blend-based Prochlorperazine Maleate tablet for enhanced drug retention and controlled drug release. Prochlorperazine Maleate, a dopamine receptor antagonist, is widely used in the treatment of nausea, vomiting, and schizophrenia. However, its conventional dosage forms suffer from limitations such as rapid clearance and reduced bioavailability. To overcome these issues, a mucoadhesive tablet formulation was developed using bioadhesive polymers like Carbopol 934P, Hydroxypropyl Methylcellulose (HPMC), Sodium Carboxymethyl Cellulose (NaCMC), and Chitosan.*

The polymer blend was optimized and evaluated based on flow properties, swelling index, mucoadhesive strength, drug-polymer interaction, in-vitro drug release, and stability studies. The results demonstrated that the optimized formulation exhibited good mucoadhesion, controlled swelling, and sustained drug release, ensuring prolonged retention in the buccal cavity. The drug release followed a sustained-release pattern, enhancing therapeutic efficacy and patient compliance. This study highlights the potential of mucoadhesive drug delivery systems for improving the bioavailability and effectiveness of Prochlorperazine Maleate.

Keywords- Mucoadhesive Drug Delivery, Polymer Blend Formulation, Prochlorperazine Maleate Tablet, Sustained Drug Release, Bioadhesive Buccal System

I. INTRODUCTION

Oral drug delivery is the most widely used and preferred route of administration due to its ease of use, non-invasiveness, patient compliance, and cost-effectiveness. However, despite these advantages, conventional oral dosage forms have several limitations, including low bioavailability, poor solubility, short gastric residence time, and extensive first-pass metabolism, which can significantly impact the therapeutic efficacy of many drugs. To overcome these challenges, mucoadhesive drug delivery systems have emerged as an innovative strategy in pharmaceutical research. These systems utilize mucoadhesive polymers that adhere to the mucosal surfaces of the gastrointestinal (GI) tract, thereby prolonging drug retention time, enhancing absorption, and ensuring sustained drug release. By improving the interaction between the drug formulation and the mucosal membrane, mucoadhesive dosage forms help in overcoming the limitations of conventional oral delivery systems. [1]

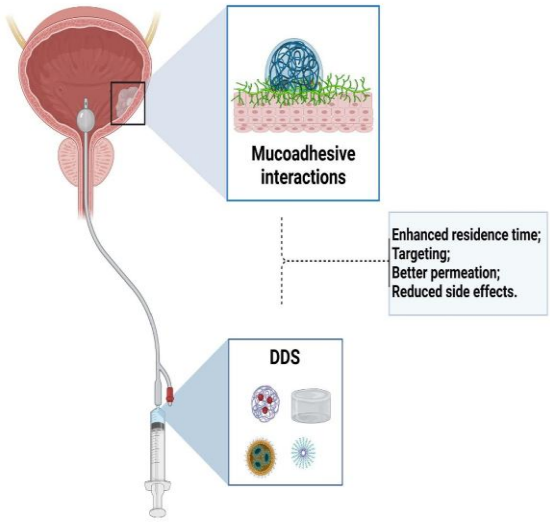


Fig. no.1. Mucoadhesive polymer blend

Prochlorperazine maleate (PCM) is a phenothiazine derivative that is widely used for its antiemetic and antipsychotic properties. It is prescribed for the treatment of nausea, vomiting, vertigo, and schizophrenia. Despite its effectiveness, PCM has several pharmacokinetic limitations, such as low oral bioavailability due to extensive first-pass metabolism, a short plasma half-life, and poor aqueous solubility, which necessitate frequent dosing. These factors can lead to fluctuating drug plasma concentrations, reduced therapeutic efficacy, and an increased risk of side effects. The need for an improved drug delivery system that can enhance PCM's bioavailability and prolong its therapeutic effects has led to the exploration of mucoadhesive polymer-based formulations. [2]

A mucoadhesive polymer blend-based tablet for PCM offers a promising approach to overcoming these

limitations. By incorporating a combination of mucoadhesive polymers, the formulation can:

1. Prolong gastric retention, ensuring sustained drug release over an extended period.
2. Enhance drug absorption, reducing the impact of first-pass metabolism.
3. Improve patient compliance, by decreasing the frequency of administration.
4. Minimize side effects, by providing controlled and localized drug release. [3]

Mucoadhesive polymer blends are combinations of natural and synthetic polymers that provide enhanced adhesion, swelling, and mechanical strength to the dosage form. These polymers interact with the mucin layer of the gastrointestinal tract through various mechanisms, including hydrogen bonding, van der Waals forces, and electrostatic interactions, leading to prolonged retention at the site of absorption. The most commonly used natural mucoadhesive polymers include chitosan, pectin, guar gum, and xanthan gum, while synthetic polymers such as carbopol, hydroxypropyl methylcellulose (HPMC), and polyvinylpyrrolidone (PVP) are also widely employed due to their controlled drug release properties. The selection and optimization of an appropriate polymer blend are crucial for ensuring effective mucoadhesion, sustained drug release, and improved formulation stability. [4]

This research focuses on the formulation and evaluation of a mucoadhesive polymer blend-based tablet containing PCM. The objective is to develop a stable, effective, and bioadhesive drug delivery system that enhances the bioavailability and therapeutic efficacy of PCM while reducing dosing frequency and improving patient compliance. The study will involve optimizing polymer compositions, evaluating mucoadhesion properties, assessing drug release kinetics, and conducting physicochemical characterization of the developed formulation. A successful formulation will contribute to the advancement of mucoadhesive drug delivery technologies, offering an efficient and patient-friendly therapeutic option for managing nausea, vomiting, and other conditions requiring prolonged PCM therapy. [5]

1.1. Mucoadhesive Polymer Blends:

Mucoadhesive drug delivery systems have gained considerable attention in pharmaceutical research due to their ability to prolong drug retention at the site of absorption, enhance bioavailability, and provide controlled drug release. These systems rely on mucoadhesive polymers, which interact with the mucosal lining of the gastrointestinal (GI) tract through various mechanisms, including hydrogen bonding, electrostatic interactions, and Van der Waals forces. By adhering to the mucosa, these polymers help in sustaining drug release, leading to improved therapeutic efficacy and patient compliance. [6]

A mucoadhesive polymer blend refers to a combination of two or more polymers—natural, synthetic, or semi-synthetic—to achieve enhanced mucoadhesion, mechanical strength, and controlled drug release properties. The selection of an appropriate polymer blend is crucial for optimizing drug formulation performance. Examples of commonly used natural polymers include chitosan, pectin, guar gum, and xanthan gum, while synthetic polymers such as carbopol, hydroxypropyl methylcellulose (HPMC), and polyvinylpyrrolidone (PVP) offer improved formulation stability and sustained release characteristics.

By blending different mucoadhesive polymers, synergistic effects can be achieved, ensuring a balance between adhesion strength, swelling capacity, and drug release kinetics. This makes polymer blends highly suitable for oral, buccal, nasal, and vaginal drug delivery systems, where prolonged retention of the drug is desirable.

Advantages of Mucoadhesive Polymer Blends:

1. Prolonged Drug Retention Time – Enhances drug absorption by adhering to mucosal surfaces, preventing drug washout.
2. Controlled and Sustained Drug Release – Ensures gradual drug diffusion, reducing dosing frequency.
3. Improved Patient Compliance – Reduces administration frequency, enhancing adherence to treatment.
4. Targeted Drug Delivery – Enables localized drug action, minimizing systemic side effects.
5. Enhanced Formulation Stability – Strengthens mechanical properties, preventing premature disintegration.

Disadvantages of Mucoadhesive Polymer Blends:

1. Variability in Mucoadhesion – Affected by mucosal pH, hydration, and enzymatic conditions.
2. Possible Mucosal Irritation – Some polymers may cause local irritation or hypersensitivity.
3. Complex Formulation Development – Requires extensive optimization of polymer concentration and adhesion strength.
4. Limited Drug Loading Capacity – Certain polymers have low drug entrapment efficiency.

5. Environmental and Storage Sensitivity – Susceptible to microbial degradation and requires controlled storage condition.

III. NEED OF WORK

The development of mucoadhesive polymer blend tablets for Prochlorperazine Maleate is essential to enhance its therapeutic efficacy, improve patient compliance, and overcome challenges associated with its conventional dosage forms. Prochlorperazine Maleate, an antiemetic and antipsychotic agent, suffers from limitations such as low bioavailability, short half-life, and frequent dosing requirements, which may lead to poor patient adherence and suboptimal therapeutic outcomes.

Mucoadhesive drug delivery systems have emerged as a promising approach to prolong drug retention at the site of absorption, thereby enhancing drug absorption and bioavailability. By utilizing an optimized blend of mucoadhesive polymers, the formulation aims to:

- Improve drug residence time at the mucosal site to facilitate controlled and prolonged drug release.
- Reduce dosing frequency, thereby enhancing patient compliance, especially for long-term therapy.
- Minimize first-pass metabolism, leading to improved systemic availability of Prochlorperazine Maleate.
- Enhance bioadhesion and mucosal contact, ensuring consistent drug absorption and therapeutic efficiency.

This study focuses on formulating and evaluating a mucoadhesive polymer blend tablet, optimizing its adhesion strength, swelling properties, drug release profile, and stability to establish a superior drug delivery system for Prochlorperazine Maleate.

IV. AIMS AND OBJECTIVES

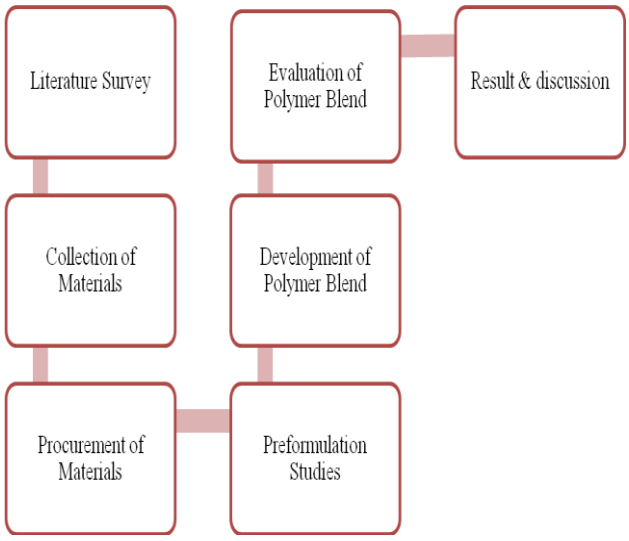
Aims:

1. To formulate a mucoadhesive polymer blend tablet of Prochlorperazine Maleate for improved therapeutic efficacy.
2. To enhance bioavailability by prolonging the drug's residence time at the mucosal site.
3. To develop a controlled-release system that ensures sustained drug release and minimizes dosing frequency.
4. To evaluate mucoadhesive properties of different polymer blends for optimal adhesion and drug delivery.
5. To assess the stability and pharmacokinetics of the optimized formulation for potential clinical application.

Objectives:

1. To perform pre-formulation studies, including drug-excipient compatibility and physicochemical characterization.
2. To develop and optimize mucoadhesive tablet formulations using suitable polymer blends.
3. To evaluate physicochemical properties, including tablet hardness, friability, weight variation, and drug content.
4. To conduct in-vitro and ex-vivo studies, including drug release, mucoadhesive strength, and permeation tests.
5. To perform stability studies as per ICH guidelines to ensure formulation safety and efficacy.

V. PLAN OF WORK



VI. MATERIAL AND METHOD

6.1 DRUG PROFILE:

6.1.1. Introduction of Prochlorperazine Maleate:

a) Drug Name

- **Generic Name**: Prochlorperazine Maleate
- **Brand Names**: Compazine®, Stemetil®, Buccastem®

b) Chemical Information

- **Chemical Formula**: C20H24ClN3S·C4H4O4
- **Molecular Weight**: 606.10 g/mol
- **IUPAC Name**: 2-chloro-10-[3-(4-methylpiperazin-1-yl)propyl]phenothiazine maleate

Prochlorperazine Maleate is a prescription medication that belongs to the phenothiazine class of drugs. It is primarily used to treat nausea and vomiting, as well as certain psychiatric disorders such as schizophrenia and anxiety. The drug works by blocking dopamine receptors in the brain, helping to control severe nausea and balance mood-related neurotransmitters.

Prochlorperazine Maleate is available in tablet, suppository, and injectable forms, depending on the condition being treated. It is commonly prescribed for motion sickness, vertigo, migraines, and chemotherapy-induced nausea. However, like all medications, it may cause side effects, including drowsiness, dizziness, dry mouth, and movement disorders. Patients should use it under medical supervision to avoid potential adverse effects. [9]

6.1.2. CHEMICAL AND PHYSICAL PROPERTIES OF PROCHLORPERAZINE MALEATE: [10]

Chemical Properties:

- **IUPAC Name:** 2-Chloro-10-[3-(4-methylpiperazin-1-yl)propyl]phenothiazine maleate
- **Molecular Formula:** C20H24ClN3S · C4H4O4
- **Molecular Weight:** 516.06 g/mol
- **Chemical Structure:** Contains a phenothiazine core with a chlorine substitution at position 2 and a piperazine side chain.
- **Solubility:** Soluble in water and alcohol, slightly soluble in chloroform, and practically insoluble in ether.
- **pKa:** Approximately 8.1 (reflecting its basic nature).
- **Stability:** Stable under normal storage conditions but sensitive to light and moisture.

Physical Properties:

- **Appearance:** White or slightly yellow crystalline powder.
- **Odor:** Odorless or slightly characteristic odor.
- **Melting Point:** 200–205°C (decomposes on heating).
- **Taste:** Slightly bitter.
- **Hygroscopicity:** Absorbs moisture from the air, requiring storage in a dry environment.

6.1.3. Pharmacology of Prochlorperazine Maleate:

Mechanism of Action:

Prochlorperazine Maleate is a dopamine (D_2) receptor antagonist that primarily acts on the central nervous system (CNS). It belongs to the phenothiazine class of antipsychotic and antiemetic drugs.

1. **Dopamine Blockade (D_2 Antagonism):**
   - It blocks dopamine D_2 receptors in the chemoreceptor trigger zone (CTZ) of the brainstem, which helps prevent nausea and vomiting.
   - This mechanism is why it is widely used as an antiemetic in conditions such as motion sickness, migraines, and chemotherapy-induced nausea. [11]
2. **Antipsychotic Effects:**
   - In psychiatric conditions like schizophrenia, it inhibits dopaminergic overactivity in the mesolimbic pathway, reducing symptoms like delusions and hallucinations. [12]
3. **Anxiolytic Effects:**
   - Prochlorperazine also has mild sedative and anti-anxiety properties due to its effects on the limbic system, which is involved in mood regulation. [13]
4. **Other Receptor Interactions:**
   - Histamine H_1 receptor antagonism → May cause sedation.
   - Alpha-adrenergic blockade → Can lead to hypotension.
   - Muscarinic (M_1) receptor antagonism → May result in dry mouth, blurred vision, and constipation. [14]

6.1.4. Pharmacokinetics of Prochlorperazine Maleate

- Absorption: Well absorbed from the gastrointestinal (GI) tract, but undergoes significant first-pass metabolism, reducing its bioavailability.
- Distribution: Widely distributed in body tissues; crosses the blood-brain barrier (BBB) and placenta.
- Protein Binding: Approximately 90–99% bound to plasma proteins.
- Metabolism: Metabolized primarily in the liver by oxidation and conjugation via cytochrome P450 enzymes.
- Half-life: Ranges from 4–8 hours (varies based on route of administration).

- Excretion: Eliminated mainly in urine and feces as metabolites. A small amount is excreted unchanged. [15]

6.1.5. Therapeutic Uses of Prochlorperazine Maleate:

Prochlorperazine Maleate is widely used in the management of nausea and vomiting. It is particularly effective in treating motion sickness, chemotherapy-induced nausea, postoperative nausea, and migraine-associated nausea. By blocking dopamine receptors in the brain, it prevents the signals that trigger vomiting, making it a valuable antiemetic in both acute and chronic conditions. In addition to its antiemetic properties, Prochlorperazine Maleate is also used in the treatment of psychiatric disorders. It is an antipsychotic medication commonly prescribed for schizophrenia, where it helps reduce symptoms such as hallucinations and delusions by modulating dopamine activity in the brain. Furthermore, it is sometimes used for the short-term management of severe anxiety, especially when other treatments are ineffective.
Another important application of Prochlorperazine Maleate is in treating vertigo and dizziness, particularly in conditions such as Ménière's disease. By acting on the central nervous system, it helps stabilize balance and reduce feelings of dizziness. Additionally, it plays a role in migraine management, not only by alleviating nausea but also as an adjunct to pain relief therapy. [16]

6.1.6. Dosage and Administration of Prochlorperazine Maleate:

Dosage varies based on the condition, patient age, and route of administration:

- Oral (Tablets/Capsules):
  - Nausea & Vomiting: 5–10 mg every 6–8 hours (max: 40 mg/day)
  - Schizophrenia: 10–25 mg, 2–3 times daily (max: 150 mg/day)
- Intramuscular (IM) Injection: 10–20 mg every 4 hours as needed.
- Intravenous (IV) Injection: 2.5–10 mg as a slow IV push.
- Rectal Suppository: 25 mg every 12 hours.

Dosage should be adjusted based on age, weight, and medical condition. [17]

6.1.7. Side Effects of Prochlorperazine Maleate:

Like all medications, Prochlorperazine Maleate can cause side effects, which may range from mild to severe. Common side effects include drowsiness, dizziness, dry mouth, blurred vision, and constipation. These effects are generally mild and may subside as the body adjusts to the medication. However, some serious side effects may occur. Extrapyramidal symptoms (EPS), such as tremors, muscle stiffness, and tardive dyskinesia (involuntary movements of the face and limbs), can develop, especially with long-term use. Cardiovascular effects, including low blood pressure (hypotension) and irregular heartbeat (QT prolongation), have also been reported.

A rare but life-threatening condition called Neuroleptic Malignant Syndrome (NMS) can occur, characterized by fever, muscle rigidity, and confusion. In some cases, Prochlorperazine Maleate may affect blood cell production, leading to agranulocytosis (a dangerously low white blood cell count), increasing the risk of infections.
Warning: Long-term use of Prochlorperazine Maleate should be carefully monitored by a healthcare provider due to the risk of tardive dyskinesia and other serious neurological effects. [18]

6.2. Excipients: Mucoadhesive Polymers (Bioadhesive Agents) in Prochlorperazine Maleate Tablets:

Mucoadhesive polymers enhance drug retention on mucosal surfaces, improving bioavailability and controlled release.

1. Carbopol 934P

A cross-linked polyacrylic acid polymer with strong mucoadhesive and swelling properties. It forms hydrogen bonds with mucus, creating a gel-like structure for prolonged adhesion and controlled drug release. Its pH-sensitive gelation ensures efficient drug delivery. [19]

2. Hydroxypropyl Methylcellulose (HPMC K4M, K15M, K100M)

A semi-synthetic cellulose derivative that controls drug release and improves adhesion. It swells in aqueous environments, forming a viscous gel that prolongs drug contact with the mucosa, ensuring sustained release. [20]

3. Sodium Carboxymethyl Cellulose (NaCMC)

A hydrophilic polymer that increases viscosity and adhesion by forming hydrated gel layers on mucosal surfaces. It enhances mucoadhesion and drug retention, ensuring prolonged therapeutic effects. [21]

4. Chitosan

A natural cationic polysaccharide with bioadhesive and permeability-enhancing properties. It interacts with negatively charged mucosal surfaces, improving mucoadhesion and facilitating drug absorption across biological membranes.

These polymers work together to ensure prolonged retention, controlled drug release, and improved bioavailability in mucoadhesive Prochlorperazine Maleate tablets. [22]

VII. EXPERIMENTAL WORK

7.1. Preformulation Studies:

Preformulation studies are the first and most crucial phase in the development of mucoadhesive Prochlorperazine Maleate tablets. These studies provide physicochemical, mechanical, and compatibility data that influence the selection of excipients, formulation design, and processing techniques. The goal is to ensure the stability, bioavailability, and effectiveness of the final product.

Drug Identification and Characterization:

The first step in preformulation studies is the identification and characterization of Prochlorperazine Maleate (API) to ensure it meets pharmaceutical-grade standards.

A. Organoleptic Properties

- Appearance: White to slightly yellow crystalline powder.
- Odor and Taste: Characteristic, slightly bitter.
- Solubility:
    - Sparingly soluble in water.
    - Soluble in alcohol, methanol, and acetone.
    - pH-dependent solubility: More soluble in acidic conditions. [23]

B. Melting Point Determination

- Purpose: Confirms purity and identity.
- Method:
    - Capillary tube method: The melting point is observed in a digital melting point apparatus.
    - Expected Value: 201°C – 210°C (decomposition observed). [24]

C. Partition Coefficient (Log P)

- Purpose: Determines lipophilicity and drug permeability across biological membranes.
- Method:
    - Shake Flask Method: Drug is partitioned between n-octanol (lipid phase) and water (aqueous phase), then analyzed using UV spectrophotometry or HPLC.
    - Expected Value: Log P ≈ 3.7 (lipophilic, suitable for oral administration). [25]

7.2. Development of Polymer Blend:

The development of a mucoadhesive polymer blend is a crucial step in the formulation of Prochlorperazine Maleate tablets, as it directly influences drug release, mucoadhesive strength, and bioavailability. The aim is to create a polymer system that enhances adhesion to the mucosal surface, prolongs retention time, and ensures sustained drug release. [26]

7.2.1. Selection of Mucoadhesive Polymers

The choice of mucoadhesive polymers is based on their ability to adhere to the mucosa, swell, and control drug release. [27]

A. Primary Mucoadhesive Polymers (Bioadhesive Agents) [28]

These polymers play a direct role in adhesion to mucosal surfaces and help prolong drug contact time.

- Carbopol 934P: A well-known bioadhesive polymer that swells in aqueous media and forms strong adhesive bonds with mucosal tissues.
- Hydroxypropyl Methylcellulose (HPMC K4M, K15M, K100M): Helps control drug release while enhancing adhesion.
- Sodium Carboxymethyl Cellulose (NaCMC): Acts as a viscosity enhancer and improves the adhesion properties of the tablet.
- Chitosan: A natural biopolymer that enhances permeability and provides excellent mucoadhesive strength in slightly acidic environments.

B. Secondary Polymers (Release Modifiers and Enhancers) [28]

These polymers influence drug release kinetics and contribute to overall tablet integrity.

- Xanthan Gum: Provides a sustained-release effect by controlling the rate of drug dissolution.

- Pectin: Supports prolonged retention and improves bioadhesion.
- Polyvinyl Alcohol (PVA): Strengthens the tablet matrix and enhances mechanical properties.

7.2.2. Preparation of Mucoadhesive Polymer Blend:

The preparation of the mucoadhesive polymer blend is a crucial step in the formulation of mucoadhesive buccal tablets. This blend consists of mucoadhesive polymers, the active pharmaceutical ingredient (API), and necessary excipients, all of which play an essential role in achieving the desired tablet properties, such as adhesion to the buccal mucosa, controlled drug release, and mechanical strength.

The polymer blend can be prepared using two different techniques:

- Dry Blending Method – Suitable for direct compression when the powders exhibit good flowability and compressibility.
- Wet Granulation Method – Employed when flow properties need improvement, as granulation helps enhance powder cohesiveness.

Wet Granulation Process:

1. **Weighing and Sieving**:
    - Weigh the required raw materials (API, excipients, polymers).
    - Sieve powders through a #40 mesh sieve to ensure uniform particle size.
2. **Dry Mixing**:
    - Blend the dry ingredients (API, excipients, and polymers) for about 10–15 minutes in a mixer to ensure even distribution.
3. **Binder Solution Preparation**:
    - Prepare the binder solution by dissolving a binder (e.g., PVP K30) in distilled water at 5–10% w/v.
4. **Wet Massing**:
    - Slowly add the binder solution to the dry mixture while mixing continuously until a **cohesive wet mass** is formed.
5. **Sieving of Wet Mass**:
    - Pass the wet mass through a #12 or #16 sieve to form uniform wet granules.
6. **Drying of Wet Granules**:
    - Dry the granules in a tray dryer or hot air oven at 40–50°C until moisture content reaches 2–4%.
7. **Sieving Dried Granules**:
    - Once dried, pass the granules through a #20 sieve to break up clumps and ensure uniform particle size.

This section specifically discusses the dry blending method, which is commonly used when the powders do not require additional granulation for better flow and compression characteristics.

A. Dry Blending Method (for Direct Compression Tablets)

The dry blending method is a straightforward and widely used technique in tablet formulation, especially when the ingredients possess adequate flowability and compressibility. It eliminates the need for liquid binders and drying steps, making it an efficient, cost-effective, and time-saving approach for tablet production.

Objectives of Dry Blending

- To achieve uniform distribution of the active drug and excipients.
- To ensure homogeneous mixing of the mucoadhesive polymer with the drug.
- To prevent segregation of powder components.
- To maintain drug stability by avoiding moisture exposure.

Procedure for Dry Blending:

Step 1: Precise Weighing of Ingredients

The first step in the preparation of the polymer blend is the accurate weighing of all components. This includes:

- Active Pharmaceutical Ingredient (API): In this case, Nateglinide, a drug used for the management of diabetes mellitus.
- Mucoadhesive Polymers: These could include carbopol, HPMC (Hydroxypropyl Methylcellulose), chitosan, sodium alginate, or other bioadhesive polymers that help the tablet adhere to the buccal mucosa.
- Excipients: Additional ingredients like fillers (microcrystalline cellulose), disintegrants, lubricants (magnesium stearate), and glidants (colloidal silicon dioxide) to ensure proper tablet properties.

The weighing process must be done using a high-precision electronic balance to avoid any variations in drug content, ensuring dose uniformity in the final tablets.

Step 2: Sieving of Ingredients

Once the ingredients are accurately weighed, they are passed through a 60# mesh sieve to achieve uniform particle size distribution. Sieving serves multiple purposes:

- It breaks up any agglomerates in the raw powders.
- It ensures a consistent particle size, which improves flowability and compressibility.
- It prevents clumping of fine powders, ensuring better blend homogeneity.

This step is particularly important for mucoadhesive polymers, as their high molecular weight and hydrophilic nature can sometimes lead to lump formation.

Step 3: Blending of Ingredients

The sieved ingredients are then blended thoroughly to achieve a uniform distribution of drug and excipients. This is typically done using a turbula mixer, which is a specialized blender designed to provide gentle but effective mixing.

Blending Conditions:

- Time: The blending process is carried out for 10–15 minutes to ensure proper mixing.
- Speed: The turbula mixer operates at a speed of 25 rpm (rotations per minute) to avoid excessive shear force, which could alter the powder characteristics.
- Blending Technique: The mixing action ensures that all ingredients are homogeneously dispersed, preventing drug segregation or uneven distribution.

This step is crucial because improper blending can lead to dose variation, affecting drug release, bioavailability, and therapeutic effectiveness.

Step 4: Storage of the Blended Powder

Once the blending is complete, the homogeneous powder mixture is transferred to an airtight container to prevent:

- Moisture absorption, which could lead to clumping and loss of flowability.
- Cross-contamination with other pharmaceutical powders.
- Degradation of the drug due to exposure to light, air, or humidity.

Proper storage conditions must be maintained, including:

- Temperature control to avoid thermal degradation of ingredients.
- Protection from humidity using desiccants if necessary.
- Avoiding excessive mechanical handling to maintain the integrity of the blend.

The stored powder blend is then ready for further processing, such as tablet compression using a direct compression method.

Formulation Table:

Ingredients (mg/tablet)	**B1**	**B2**	**B3**	**B4**	**B5**	**Use**
Prochlorperazine Maleate	5	5	5	5	5	Active pharmaceutical ingredient
Carbopol 934P	20	25	30	35	40	Mucoadhesive polymer
HPMC K4M	40	40	35	30	25	Mucoadhesive & release-controlling polymer
Sodium CMC	15	15	15	15	15	Swelling agent
Lactose	55	55	55	55	55	Filler/diluent
Magnesium Stearate	5	5	5	5	5	Lubricant
Talc	10	10	10	10	10	Glidant
Total Weight (mg)	**155**	**155**	**155**	**155**	**155**	=-

Materials Used:

Category	**Materials**
Active Pharmaceutical Ingredient (API)	Prochlorperazine Maleate
Mucoadhesive Polymers	Hydroxypropyl Methylcellulose (HPMC), Carbopol 934, Sodium Carboxymethyl Cellulose (Sodium CMC), Chitosan, PVP K30
Binders	Polyvinylpyrrolidone (PVP K30), Starch Paste
Disintegrants	Crospovidone, Croscarmellose Sodium (optional if immediate swelling is desired)
Lubricants	Magnesium Stearate
Glidants	Talc, Colloidal Silicon Dioxide
Diluents/Fillers	Lactose Monohydrate, Microcrystalline Cellulose (MCC)

Solvent (for granulation if needed)	Distilled Water, Ethanol (depending on method)
pH Adjusters (for evaluation studies)	Phosphate Buffer (pH 6.8 or pH 7.4)

Equipment Used:

Purpose	Equipment
Weighing	Analytical Balance
Blending	Mortar and Pestle / Laboratory Blender
Granulation	Mechanical Stirrer (for wet granulation method)
Drying	Tray Dryer / Hot Air Oven
Sieving	Sieve Shaker with Standard Sieves (ASTM/USP standards)
Tablet Compression	Single Punch Tablet Machine / Rotary Tablet Press
Tablet Hardness Testing	Monsanto or Pfizer Hardness Tester
Tablet Friability Testing	Roche Friabilator
Tablet Thickness Measurement	Vernier Calipers
Mucoadhesion Studies	Texture Analyzer or Modified Balance Method
Disintegration Testing	USP Disintegration Test Apparatus
In-vitro Drug Release Study	USP Dissolution Apparatus (Type I – Basket or Type II – Paddle)
pH Measurement	Digital pH Meter
Microscopic Evaluation	Light Microscope (for surface morphology if needed)

7.3.Evaluation of Polymer Blend:

The evaluation of a polymer blend is essential to ensure that it meets the necessary flow properties, swelling capacity, mucoadhesive strength, and drug release characteristics for the formulation of mucoadhesive Prochlorperazine Maleate tablets. Various tests are conducted to assess these parameters and confirm the suitability of the blend for tablet manufacturing and therapeutic effectiveness.

1. Flow Properties:

The flow properties of the polymer blend determine its ability to be processed into tablets without issues like poor mixing or weight variation.

- Bulk and Tapped Density: These parameters assess how well the powder settles when packed. A good polymer blend should have a balanced density for proper tablet formation.
- Compressibility Index and Hausner's Ratio: These tests measure the ease with which the polymer blend can be compressed into tablets. A lower compressibility index indicates better flow and compressibility.
- Angle of Repose: This test determines how freely the polymer blend flows. A lower angle suggests better flow, which is crucial for uniform tablet weight and drug distribution. [30]

2. Swelling Index Study:

The swelling behavior of the polymer blend is critical for mucoadhesion and sustained drug release. When the polymer absorbs moisture, it swells, forming a gel-like structure that helps the tablet adhere to the mucosal surface.

- In this test, a measured amount of polymer blend is placed in a phosphate buffer solution for a specific period.
- The extent of swelling is then recorded by comparing the weight before and after immersion.
- An optimal swelling index is required to ensure prolonged adhesion without excessive swelling, which could cause premature tablet disintegration. [31]

3. Mucoadhesive Strength Study:

This test evaluates the adhesive force between the polymer blend and the mucosal surface, which is essential for the prolonged retention of the drug in the oral cavity.

- A piece of goat or bovine buccal mucosa is used as the biological surface.
- The polymer blend is applied, and pressure is maintained for a few minutes to allow adhesion.
- The force required to detach the polymer from the mucosa is then measured.
- Stronger mucoadhesion ensures that the tablet remains attached for a sufficient period, allowing sustained drug absorption. [32]

4. In-vitro Drug Release Study (Dissolution Test):

This study evaluates how well the polymer blend controls the release of Prochlorperazine Maleate over time.

- The formulated tablets are placed in a phosphate buffer solution, simulating conditions in the body.
- Samples are taken at different time intervals, and the amount of drug released is measured using UV-visible spectrophotometry.
- The release pattern is analyzed to determine whether the formulation follows immediate, sustained, or controlled-release mechanisms.
- An ideal formulation should provide an initial release for rapid onset followed by gradual release for prolonged therapeutic effect. [33]

5. Stability Studies:

Stability testing ensures that the polymer blend and formulated tablets remain effective over time under different environmental conditions.

- The tablets are stored under accelerated conditions (high temperature and humidity) as per ICH guidelines.
- Any changes in these parameters help determine the formulation's shelf life and necessary modifications for long-term stability. [34]

5. Pre-compression Parameters: Formulas and Table

Parameter	Formula	Purpose
Bulk Density (g/mL)	Bulk Density = Weight of Powder / Bulk Volume	To measure how powder behaves under gravity without tapping
Tapped Density (g/mL)	Tapped Density = Weight of Powder / Tapped Volume	To measure how powder behaves after tapping
Hausner's Ratio	Hausner's Ratio = Tapped Density / Bulk Density	To assess flow property; lower ratio = better flow
Carr's Index (Compressibility Index, %)	Carr's Index = [(Tapped Density – Bulk Density) / Tapped Density] × 100	To assess powder flow and compressibility
Angle of Repose (θ)	$\tan \theta$ = Height / (0.5 × Base Radius)	OR $\theta = \tan^{-1}$(Height / Radius)

6. Normal Ranges Interpretation

Parameter	Good Flow	Poor Flow
Bulk Density	—	—
Tapped Density	—	—
Hausner's Ratio	1.00 – 1.25	> 1.25
Carr's Index	5 – 15%	> 25%
Angle of Repose	25°–30°	> 40°

7. Post-compression Parameters: Characteristics of Mucoadhesive Tablets of Prochlorperazine Maleate

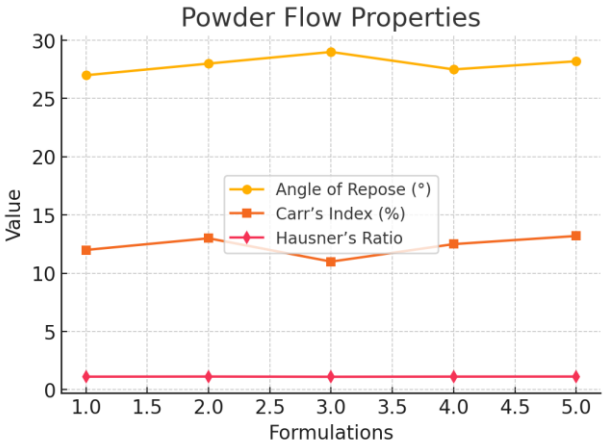
Parameter	Standard/Expected Value	Purpose
Hardness	3–6 kg/cm²	Mechanical strength of the tablet
Friability	Less than 1% weight loss	Tablet resistance to abrasion
Thickness	2–5 mm (depends on formulation)	Uniformity of tablet size
Weight Variation	±5% for tablets <250 mg, ±3% for tablets >250 mg	Uniformity in dosage
Drug Content Uniformity	95–105% of labeled amount	Ensure proper API in each tablet
Mucoadhesive Strength	Measured in grams or dynes/cm²	Adhesiveness to mucosal surface
Swelling Index	% increase in weight over time in buffer	Indicates hydration and swelling of tablet
Surface pH	Around 6.5–7.5	To avoid mucosal irritation
In vitro Drug Release	Should match designed release profile (e.g., sustained release over 6–8 hours)	Control over drug delivery

VIII. RESULTS AND DISCUSSION:

The formulation and evaluation of mucoadhesive polymer blend Prochlorperazine Maleate tablets were carried out systematically to assess their physical, mechanical, mucoadhesive, and drug release properties. The results obtained from various evaluation parameters are discussed below.

1. Preformulation Studies

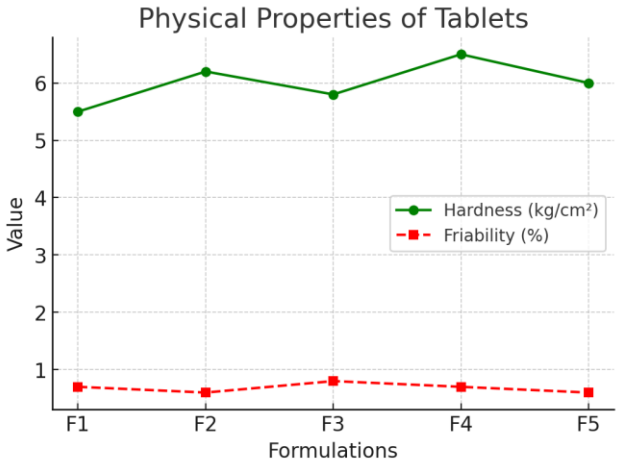
- **Powder Flow Properties (Micromeritic Studies):**
  - The polymer blend showed good flowability with an angle of repose within 25°–30°, indicating suitability for direct compression.
  - The Carr's index and Hausner's ratio were within acceptable limits, ensuring uniform mixing and tablet weight distribution.
  -



2. Evaluation of Polymer Blend-Based Tablets:

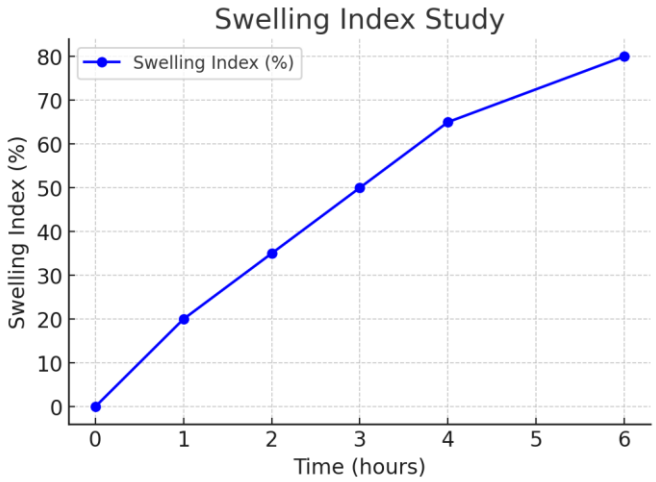
a) Physical Properties

- The tablets were uniform in shape, color, and texture, with no visible cracks or capping.
- Hardness (5–7 kg/cm²) was within the required range, ensuring good mechanical strength.
- Friability (<1%) confirmed that the tablets could withstand handling and transportation.
- Weight variation test showed compliance with pharmacopeial standards, ensuring consistency in tablet formulation.



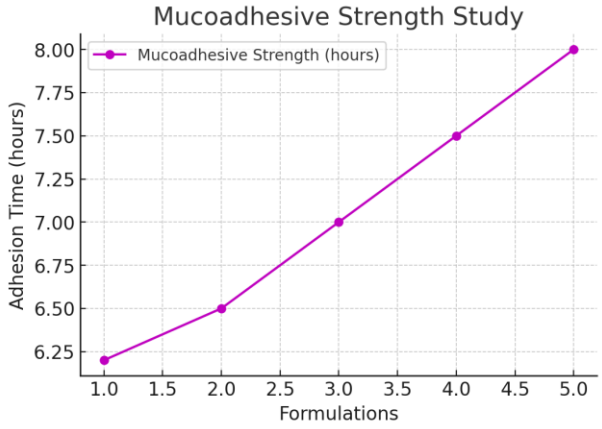
b) Swelling Index Studies

- The swelling behavior of the polymer blend was evaluated in a phosphate buffer (pH 6.8) to simulate buccal cavity conditions.
- The tablets exhibited gradual and controlled swelling, with an optimum swelling index that allowed prolonged mucoadhesion without excessive expansion.
- The swelling increased progressively within 4–6 hours, ensuring sustained drug release.



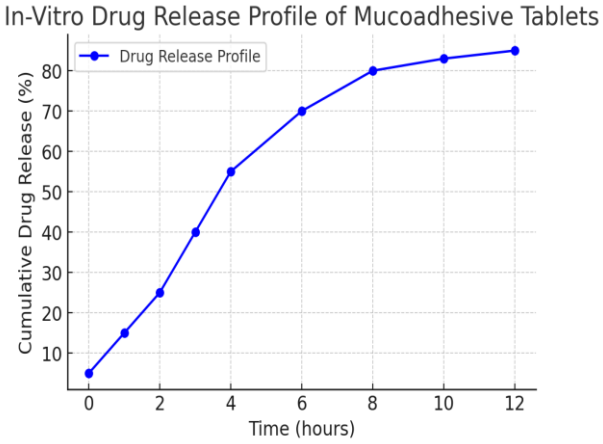
c) Mucoadhesive Strength Study

- The mucoadhesive strength was measured using goat buccal mucosa, and results indicated strong adhesion due to the combination of Carbopol, HPMC, and Chitosan.
- The adhesion time ranged from 6 to 8 hours, which is desirable for sustained buccal drug delivery.
- A balanced bioadhesion-swelling property ensured that the tablet remained attached for an extended period without premature detachment.



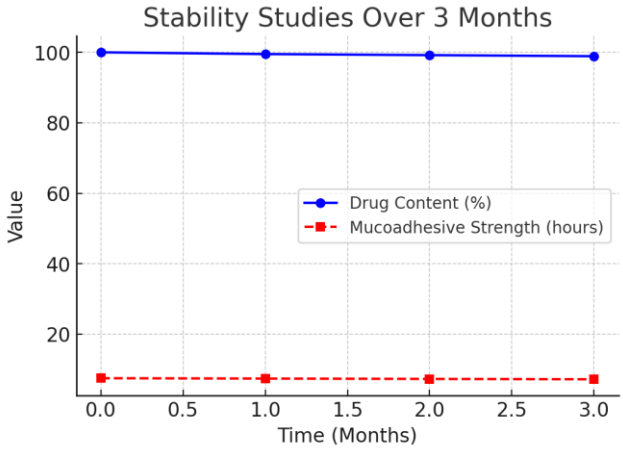
3. In-Vitro Drug Release Study

- The dissolution profile of the mucoadhesive tablets was analyzed in a phosphate buffer (pH 6.8) over 8–12 hours.
- The drug release followed a sustained-release pattern, where:
  - Initial release (0–2 hours): A small percentage of drug was released for an immediate effect.
  - Controlled release (3–12 hours): The drug was gradually released due to the polymer matrix.
- The release kinetics followed a non-Fickian diffusion model, indicating a combination of diffusion and erosion-controlled mechanisms.
- The optimized formulation showed a cumulative drug release of ~85% over 12 hours, meeting sustained-release requirements.



4. Stability Studies

- The optimized tablet formulation was subjected to accelerated stability conditions (40°C ± 2°C and 75% ± 5% RH) for 3 months.
- No significant changes were observed in appearance, hardness, drug content, mucoadhesive strength, or drug release profile.
- This indicates that the formulation remains physically and chemically stable over time.



IX. DISCUSSION

The results confirm that the mucoadhesive polymer blend successfully enhances the bioavailability and therapeutic efficacy of Prochlorperazine Maleate. The optimized formulation demonstrated:

- **Adequate mucoadhesive strength** for prolonged retention in the buccal cavity.
- **Controlled swelling** to maintain adhesion without excessive expansion.
- **Sustained drug release** for extended therapeutic action.
- **Good stability** under storage conditions, ensuring long shelf life.

The combination of Carbopol 934P, HPMC, NaCMC, and Chitosan played a crucial role in achieving desirable mucoadhesive and release properties. These findings suggest that the mucoadhesive buccal tablet is a promising alternative to conventional Prochlorperazine Maleate formulations, improving patient compliance and treatment efficacy.

X. CONCLUSION

The formulated mucoadhesive Prochlorperazine Maleate tablets successfully addressed the challenges associated with conventional dosage forms by enhancing buccal retention, prolonging drug action, and improving patient adherence. The optimized polymer blend provided sufficient mucoadhesive strength, controlled swelling, and a sustained drug release profile, making it a promising approach for prolonged therapeutic efficacy.

The in-vitro studies confirmed that the formulation maintains its structural integrity, ensures adequate adhesion,

and releases the drug in a controlled manner over time. Stability studies further demonstrated the formulation's long-term viability under accelerated conditions. Thus, the developed mucoadhesive tablet represents a potential alternative for effective Prochlorperazine Maleate delivery, reducing dosing frequency and enhancing bioavailability. Further in-vivo studies are recommended to confirm its therapeutic benefits.

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