REVIEW ARTICLE

Advances and Challenges in Mucoadhesive Drug Delivery Systems: A Comprehensive Review

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Abstract

Pharmaceutical research has focused a lot of emphasis on the capability of mucoadhesive drug delivery systems to enhance patient compliance and therapeutic effectiveness. This thorough analysis examines the most recent developments as well as the ongoing difficulties in the discipline of mucoadhesive drug delivery. It explores the mechanics of mucoadhesion, emphasizing the complex relationships that exist among mucoadhesive polymers and mucosal surfaces. In addition, it covers the range of uses for mucoadhesive systems in oral, nasal, ocular, and vaginal delivery, among other modes of administration. The analysis sheds light on the design techniques used to maximize mucoadhesive formulations for better bioavailability, prolonged release, and targeted drug delivery. It also discusses the safety profiles and regulatory issues related to mucoadhesive products. The potential of mucoadhesive drug delivery systems to raise treatment effectiveness and patient compliance has attracted a lot of attention in pharmaceutical research. This thorough analysis examines the most recent developments as well as the ongoing difficulties in the discipline. It explores the mechanics of mucoadhesion, emphasizing the complex relationships that exist among mucoadhesive polymers and mucosal surfaces. In addition, it covers the range of uses for mucoadhesive systems in oral, nasal, ocular, and vaginal delivery, among other modes of administration. The analysis sheds light on the design techniques used to maximize mucoadhesive formulations for better bioavailability, prolonged release, and targeted drug delivery. It also discusses the safety profiles and regulatory issues related to mucoadhesive products. Even with the tremendous advancements, several issues including scalability, clinical translation, and formulation stability still need to be resolved. This study assesses mucoadhesive drug delivery systems critically, notes new developments, and suggests possible avenues to go over current obstacles and realize the full promise of these cutting-edge drug delivery platforms.

Key words: Buccal drug delivery, mucoadhesion, mucoadhesive drug delivery system, oral mucosa

INTRODUCTION

Out of all the drug delivery methods, physicians and patients may favor oral medication. Based on what we now know about the physiological and biochemical components of metabolism and absorption. Many medications cannot be delivered by the traditional oral method because they undergo significant pre-systemic clearance in the liver upon ingestion. This often results in a lack of substantial relationship between bioavailability, absorption, and membrane penetrability. The challenges of parenteral administration and the low oral availability of these drugs led to the need to explore alternative routes of administration. Therefore, further absorptive mucous membranes are considered as possible sites of drug administration.[1]

When compared to oral administration, the routes of drug administration through mucosal membranes – the nasal, rectal, vaginal, ocular, and oral mucosa – offer a number of

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benefits for achieving a systemic impact. The oral mucosa is the most suitable transmucosal route with the administration of controlled-release dosage forms because of its relative immobility, smooth muscle covering, and good accessibility.[2] Furthermore, patients find oral medication delivery to be far more acceptable than alternative non-oral transmucosal modes of administration. Increased bioavailability is achieved by straight access into the systemic circulation over the body's own jugular vein, which obviates the initial metabolism within the liver and prevents acid hydrolysis in the gastrointestinal tract. In addition, another advantage of this tea is the rapid regeneration of the cells of the mucous membrane of the cheeks. The mucous membranes of the cheek are an additional advantage of this route.[3] The mucous membrane of the oral cavity has a rich circulation, is well vascularized, and slightly permeable. Oral administration is a viable delivery method for hydrophilic oligonucleotides, polysaccharides, proteins, and conventional tiny drug molecules. Medications were administered both locally and systemically through the oral cavity.[4] The oral membrane and its low permeability, especially compared to the sublingual membrane, as well as its smaller surface area are disadvantages of this drug delivery method.[5] About half of the 170 cm^2 superficial area of the oral membranes are made to composed of the oral membrane along with additional non-keratinized tissues that are used to absorb medicines. The medication is then diluted as a result of constant salivation (0.5–2 L each day).[6] Saliva ingestion may cause the medicine to be lost or disintegrate, which could eventually result in the dose form being accidentally destroyed. One issue with administering drugs orally is that the patient may choke if the dosage gadget is inadvertently swallowed. In addition, it is difficult for the patient to take such a dosage form while eating or drinking.[7]

IDEAL CHARACTERISTICS OF BUCCAL DRUG DELIVERY SYSTEM

- It is advised to spend a few hours at the attachment location
- The medication must be released in a controlled manner
- Should allow medicine to be released into the mucosa in a single direction
- Should not irritate or cause discomfort to the patient
- It must have lipophilic and hydrophilic balance
- The half-life of the mucoadhesive tablets is about 2–7 h
- The dose range of mucoadhesive tablets is 20 mg–100 mg
- It should make it simple to incorporate the medication and present no obstacles to its release.[3]

BENEFITS OF THE BUCCAL MEDICATION DELIVERY METHOD

- The medication is easily administered, and it may be easier to stop therapy in an emergency
- Prolonged drug release throughout time
- Drugs can be given to traumatized and unconscious patients
- Because the drug bypasses the first pass metabolism, it has a high bioavailability
- Some medications can be delivered buccal since the stomach's acidic environment makes them unstable
- Drugs are absorbed through passive diffusion
- Tight contact with the absorbent membrane surface results in a high absorption rate
- Quick start of action.[3]

FACTORS AFFECTING MUCOADHESION

Several factors affect mucoadhesion, which can be broadly categorized into properties of the mucoadhesive material, the properties of the mucosal surface, and the environmental conditions as shown in Figure 1. Here are the key factors:

1. Properties of the Mucoadhesive Material:
- Molecular Weight: Polymers with higher molecular weight generally show better mucoadhesion due to more significant chain entanglements and stronger interactions with the mucosal surface.
- Flexibility: Flexible polymer chains can better interpenetrate the mucin network on the mucosal surface, enhancing mucoadhesion.
- Hydrophilicity: Hydrophilic polymers can absorb water from the mucosal surface, which helps in swelling and better contact with the mucosa.
- Charge: Ionic polymers can interact more strongly with the mucin (which is also charged) through ionic interactions. Cationic polymers tend to show better mucoadhesion due to their interactions with the negatively charged mucin.
- Degree of Cross-Linking: Polymers with a high degree of cross-linking may have reduced mucoadhesion because they are less flexible and swell less.

2. Properties of the Mucosal Surface:
- Mucin Turnover: High mucin turnover can decrease mucoadhesion since the adhered material may be removed faster.
- Thickness of the Mucus Layer: A thicker mucus layer can provide a more substantial surface for adhesion, but it can also act as a barrier.
- Mucin Composition: Variations in mucin composition and structure can influence mucoadhesive interactions.

3. Environmental Conditions:
- pH: The pH of the environment can affect the ionization state of both the mucoadhesive polymer and the mucosal surface, altering their interactions.
- Hydration: Adequate hydration is crucial for the swelling of the mucoadhesive polymer, which helps in better adhesion.

- Presence of Other Substances: The presence of food, saliva, or other substances can influence mucoadhesion by creating a barrier or changing the properties of the mucosal surface.

4. Biological Factors:
- Mucus Turnover: The rate at which mucus is produced and shed can affect how long a mucoadhesive material remains attached.
- Diseases or Conditions: Certain diseases or conditions can alter the properties of the mucosal surface, affecting mucoadhesion.

By understanding these factors, researchers and developers can design more effective mucoadhesive drug delivery systems and other applications where prolonged adhesion to mucosal surfaces is desired.

CHALLENGES OF MUCOADHESIVE DRUG DELIVERY

Mucoadhesive drug delivery systems offer numerous advantages, such as prolonged residence time at the site of absorption and improved drug bioavailability. However, they also face several challenges as shown in Figure 2 that can affect their efficacy and development:

1. Variability in Mucosal Surfaces (as shown in Figure 3)
- Heterogeneity: Different mucosal surfaces (oral, nasal, gastrointestinal, etc.) have varied structures and compositions, affecting adhesion and drug absorption.
- Mucus Turnover: Rapid turnover of mucus can remove the mucoadhesive formulation before the drug is fully absorbed.

2. Formulation Stability
- Physical and Chemical Stability: Maintaining the stability of the drug and the mucoadhesive polymers during storage and after administration can be challenging.
- pH Sensitivity: Many mucoadhesive polymers are sensitive to pH changes, which can alter their adhesive properties and drug release profile.

3. Drug Loading Capacity
- Limited Capacity: Mucoadhesive systems often have limited drug loading capacities, which can be insufficient for drugs requiring high doses.

4. Irritation and Toxicity
- Local Irritation: Prolonged contact with the mucosa can cause irritation or damage to the mucosal tissue.
- Toxicity: Some mucoadhesive polymers or their degradation products may be toxic or cause adverse reactions.

5. Patient Compliance
- Unpleasant Sensations: The presence of a mucoadhesive formulation in the mouth or other mucosal surfaces can be uncomfortable or unpleasant for patients.
- Taste and Odor: An unpleasant taste or odor of the formulation can reduce patient compliance.

6. Environmental Factors
- Hydration: The level of hydration of the mucosal surface can significantly impact the mucoadhesive properties of the formulation.
- Enzymatic Activity: Enzymes present in the mucus or mucosal tissue can degrade the drug or the mucoadhesive polymers.

7. Manufacturing Challenges
- Complexity: The development and manufacturing processes for mucoadhesive formulations can be more complex and costly compared to conventional dosage forms.
- Scalability: Ensuring consistent quality and performance during large-scale production can be difficult.

8. Regulatory Hurdles
- Approval Process: Obtaining regulatory approval can be challenging due to the need for extensive testing to demonstrate safety and efficacy.
- Standardization: Lack of standardized testing methods for evaluating mucoadhesion and drug release profiles can complicate the approval process.

Addressing challenges

To overcome these challenges, ongoing research and innovation are focusing on developing new polymers with better adhesive properties, optimizing drug formulations, and improving patient-friendly delivery systems. Additionally, advancements in understanding mucosal biology and drug-mucosa interactions are critical for the successful development of mucoadhesive drug delivery systems.

An oral medication delivery system's primary partis:

1. Drugs: It is necessary to ascertain if the intended impact is local or systemic, with fast or prolonged discharge, before creating mucoadhesive drug delivery systems. Pharmacokinetic properties are crucial when selecting a drug for designing buccoadhesive drug delivery systems. The drug must have the following features:

- The drug must be taken in a very small, regular single dose
- Drugs with a biological half-life of 2–8 h are well suited for controlled drug dosing
- When administered orally, the Tmax of the drug varies significantly or reaches sophisticated values
- When administered orally, the drug should be absorbed passively
- The molecular weight should be <1000 daltons
- It should be both hydrophilic and lipophilic

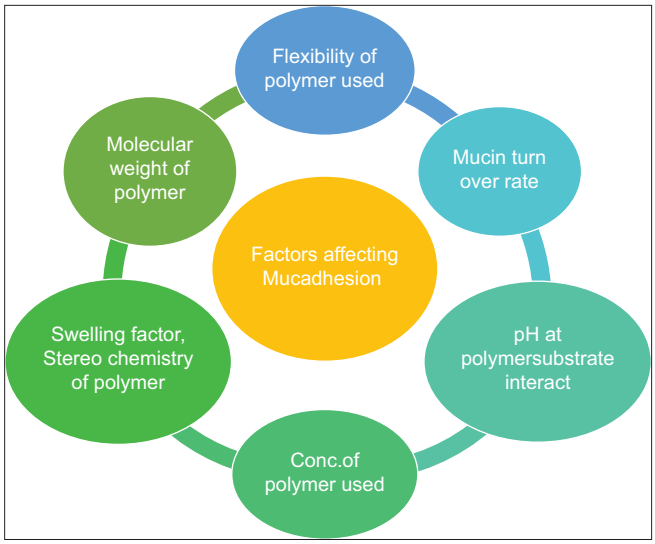

Figure 1: Factors affecting mucoadhesion

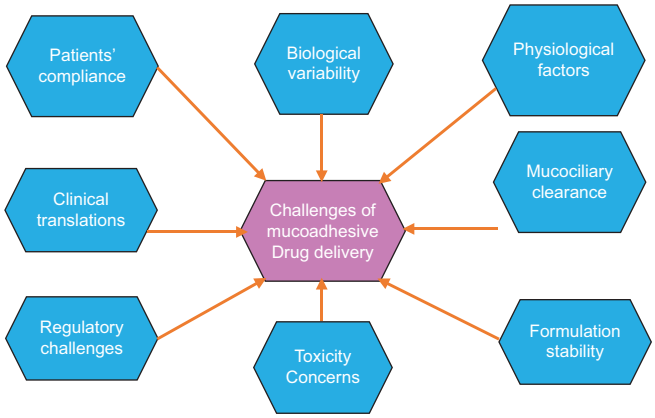

Figure 2: Challenges of mucoadhesive drug delivery

- It should not irritate the oral mucosa and be strong.[8]

2. Bio-adhesive polymer: Making oral formulations begins with the identification and characterization of properbio-adhesive polymers for the design. An important factor in Bucco's adhesive drug delivery is polymeric drug systems. Matrix also makes use of polymer devices, in which the medication is placed in a matrix of polymers that regulates the medication's release time. The most varied class of polymers is by far bio-adhesive polymers and they significantly improve patient health attention and therapy. The medication seeps obsessed by the mucous membrane using a main or rate-controlling layer stratum. A polymer that is bio-adhesive and sticks to the mucin/epithelial surface works well and produces notable enhancement of oral medication administration.

The following qualities of the bio-adhesive polymers should be present:

- It should not leave any deposit on the mucosal layer
- It ought to be inoffensive besides harmonious through the organic milieu
- It ought to firmly cling to the mucous membrane
- Ideally, it must create a robust, non-covalent bond through the surface of mucin and epithelial cells.[8]

3. Backing membrane: The backing membrane has a key impact on how bio-adhesive gadgets adhere to the mucous membrane. On buccal bio-adhesive patches, this type of impermeable membrane reduces medication loss and improves patient compliance. Materials such as magnesium stearate, hydroxypropyl methylcellulose (HPMC), hydroxypropylcellulose, carboxy methyl cellulose (CMC), and polycarbophil are often utilized in backing membranes.[9]
4. Penetration enhancers: Penetration accelerators are utilized in buccal preparations to boost the drug's release. They make it simpler for the medication to enter living tissues, aiding in systemic distribution. Sodium lauryl sulfate (SLS), polysorbate 80, etc., are some instances of permeation enhancers that are commonly utilized.[8]

BUCCAL DOSAGE FORMS CLASSIFICATION

- A few of the innovative buccal dosage formulations are classified as shown in Figure 4: they are mainly classified as non-attach delivery systems and muco-adhesive drug delivery systems.

Non-attach delivery systems

- Non-attach delivery system is a drug delivery where the formulation does not attach through the oral mucosa
- These formulations are designed to improve bioavailability and onset of action
- This system is highly used in emergency conditions which is very helpful
- Non-attach delivery is drug delivery where the drug dissolves rapidly within minutes and produces the desired therapeutic activity with a minimal dose.[11]

Fast dissolving tablets

One kind of oral dosage form called buccal fast-dissolving tablets is intended to be inserted obsessed by the buccal cavity – the region of the mouth that lies between the cheek and the gums – where they will dissolve quickly. These tablets do not require water or swallowing because they are designed to dissolve or disintegrate rapidly when they come into proximity to saliva. Benefits of the buccal route of administration include enhanced bioavailability, avoided first-pass metabolism, and quick onset of action.[12]

Microporous hollow fibers

Microporous materials have tiny pores, usually with sizes in the micrometer range. Tubes with a hollow center are known

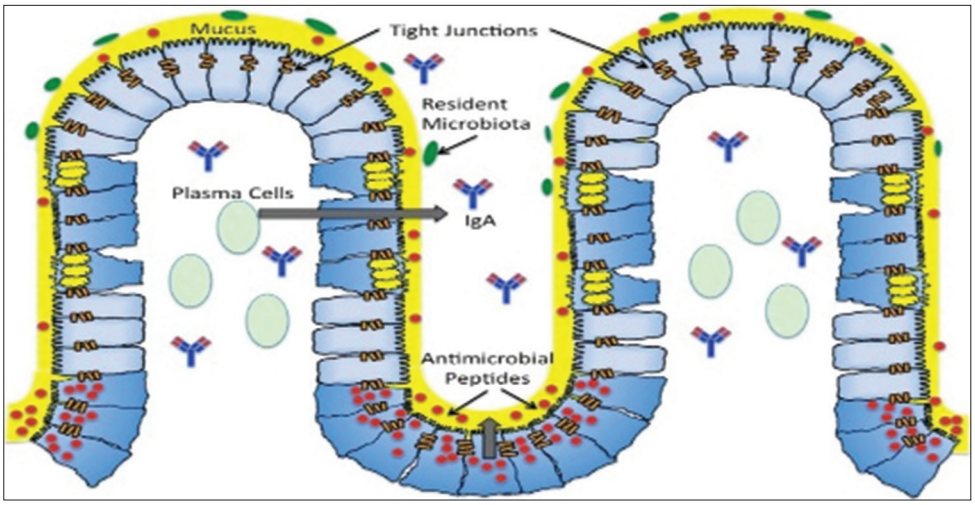

Figure 3: Mucosal surface[10]

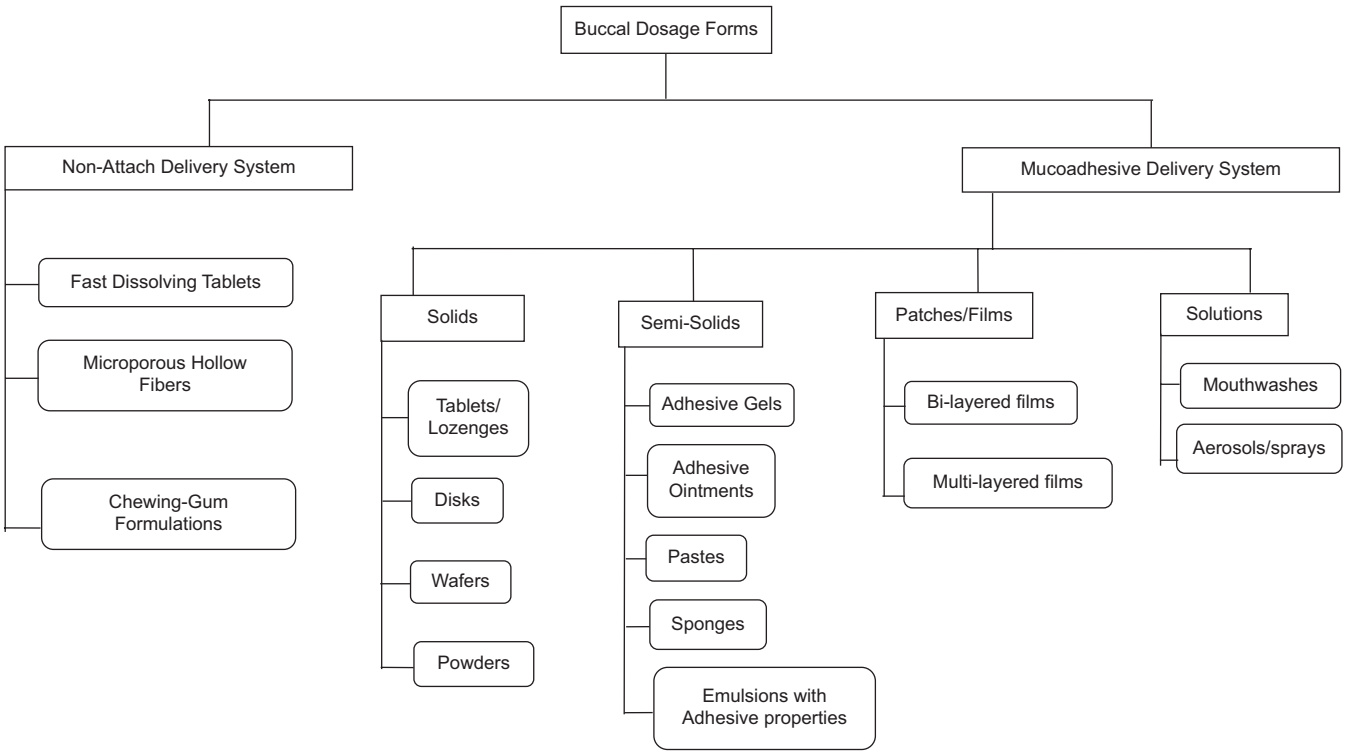

Figure 4: Various types of buccal dosage forms[11]

as hollow fibers. By integrating these two ideas, tubular structures with tiny pores may be referred to as microporous hollow fibers. Insufficient context or specifics make it difficult to offer a thorough explanation of what is meant by "microporous hollow fiber formulations." This may have to be done through drug delivery systems, filtration methods, or other uses where materials have been designed for specific purposes and given particular characteristics.[13]

Chewing gum formulations

The precise mixtures or formulas utilized in the manufacturing of chewing gum are referred to as chewing gum formulations. One common candy that is meant to be chewed rather than swallowed is chewing gum. A gum base, sweeteners, flavors, and occasionally additional compounds, such as colorings or texture modifiers make up its main ingredients. The precise composition may differ among gum product lines and brands. In addition, producers might create formulas with particular qualities, such as flavor retention or benefits for dental health.[14]

Mucoadhesive drug delivery system

The idea of muco-adhesion has drawn a lot of attention in pharmaceutical technology since the beginning of the 1980s. Adhesion refers to the connection formed when

a pressure-sensitive adhesive comes into contact with a surface. Mucoadhesive drug delivery techniques extend the dosage form's time of stay at the place of use or absorption area. They enhance the therapeutic efficiency of the medicine by enabling close contact between the dose form and the absorption area behind it. Many mucoadhesive drug delivery methods have been created subsequently in a variety of dosage forms, including solids, semi-solids, patches, films, and liquids, for both systemic and regional effects.[8]

Solids

Pharmaceutical formulations called mucoadhesive solid dosage forms are made to stick to the mucosal surfaces of the body, including those in the mouth, buccal, nasal, gastrointestinal, vaginal, and rectal areas. Combining the words "mucus" and "adhesive," the term "mucoadhesive" highlights the formulations' capacity to stick to mucous membranes. The common mechanism involves hydration, swelling, wetting, and association with mucin, the glycoprotein component of mucus, which is involved in adhesion to mucosal surfaces. Van der Waals pressures, chain entanglement, and electrostatic interactions between the mucoadhesive polymer and mucosal elements promote adhesion.

The following are typical components found in mucoadhesive solid dosage forms, polymeric muco-adhesives, plasticizers, fillers, excipients, binding agents, disintegrants, surfactants, anti-oxidants, and preservatives. Solid dosage forms include tablets, lozenges, wafers, disks, and powders.[15]

Semi-solids

The advantage of semisolid dosage forms, such as gels, ointments, pastes, and sponges, is that they are easily dispensed across the oral mucosa. On the other hand, these may not provide as exact a pharmaceutical dose as pills, patches, or films. Mucoadhesive mixtures are being used to solve unsatisfactory gel persistence at the placing area. Certain mucoadhesive polymers, including sodium CMC and carbopol, undergo a phase shift from liquid to semisolid. This change makes the substance more viscous, which permits a regulated and extended release of the drug. Hydrogel is an additional effective dosage form for buccal medication administration.[16]

Patches/films

A mucoadhesive area for mucosal adhesion, an impassable supporting layer, and a medication-containing storage layer that allows the medication to leave in a controlled manner make up patches that are laminated. In the latter technique, the mixture of elements is mixed uniformly and compressed to the necessary thickness, followed by the appropriate size and structure of patches punched or carved out. During the application period, an impenetrable supporting layer can be used to minimize instrument displacement and disintegration, regulate medicine discharge direction, and avoid medication waste.[15]

Solutions

Mucoadhesive solutions are liquid formulations developed to adhere to and prolong address with mucosal surfaces in the body. The aforementioned solutions are formulated alongside particular mucoadhesive polymers that boost their capacity to adhere to mucosal tissues, such as those noticed in the oral, nasal, ocular, or vaginal regions. Solutions include mouthwashes, aerosols, and sprays.[11]

Mucoadhesive tablets

One kind of medication dosage form called a mucoadhesive tablet is made to stick to mucous membranes, such as those in the gastrointestinal system, mouth, or other mucosal surfaces of the body. The term "mucoadhesive" refers to the capacity of such tablets to stick to the film of mucus covering the oral cavity.

The mucus layer's component mucin is favored by certain polymers or bio-adhesive agents used in the formulation of these tablets. The capacity of the mucoadhesive properties to prolong the tablet's living duration at the intended site could prove advantageous for drug delivery. This prolonged interaction with the mucosal surface improves drug absorption and might heighten the therapeutic effect.[9]

Common ingredients of mucoadhesive tablets

The Common ingredients used in mucoadhesive tablets include polymeric mucoadhesive materials such as HPMC and sodium carboxymethylcellulose; Bioadhesives like chitosan and alginate; Plasticizers like polyethylene glycols and glycerol; Binding agents like starches; Disintegrants like crospovidone and sodium starch glycolate; Surfactants like SLS; Fillers such as microcrystalline cellulose, lactose, and mannitol, etc.[9]

Pre-formulation studies

The drug-excipient compliance of the pure medication then the solid combination of medication and various excipients utilized in the production of sublingual tablet products was examined using Fourier transform infrared spectroscopy.[17]

Angle of repose

To establish the movement assets, the angle of repose was calculated. This refers to the biggest angle that can happen among a horizontal, powdery pile, and an autonomous surface.[17]

Bulk density

Bulk density is the connection between the bulk volume and weight of a powder. A powder material with a predetermined weight has been introduced through a screen, a graduated cylinder, or a volume-measuring instrument and into a container to measure the volume and estimate the bulk density.[18]

Tapped density

An established quantity of powder was placed within a graduated cylinder and the volume V_o was recorded. Before the outcome was collected, the cylinder was tapped 500 times with a density determination instrument affixed. To determine the density, a mechanical tap is used on a measuring cylinder containing the powder material. The cylinder is mechanically tapped after the initial measurement of volume observation, and volume measurements are collected until very little fluctuations in volume are seen.[17]

Compressibility index (CI) and Hausner ratio (HR)

Both the CI and HR will be attained using the bulk density and tapped density data.[19]

Drug excipient compatibility studies

After carefully weighing the active pharmaceutical ingredients (API) into a 100 mL volumetric flask, it disappeared in a minor sum of pH 6.8 phosphate buffer, which was subsequently utilized to build up the volume. Using a pipette, deposit 10 mL of the solution into a different 100 mL volumetric flask. Utilizing the pH 6.8 phosphate buffer, or 100 mg/mL, the volume was computed. 1 mL, 2 mL, 3 mL, 4 mL, and 5 mL of the conventional solution were pipetted into 10 mL volumetric flasks. A phosphate buffer with a pH of 6.8 was used to change the volume. A ultraviolet (UV)-visible spectrophotometer was used to quantify the absorbance of every concentration at 223 nm utilizing a pH 6.8 phosphate buffer by means of a blank.[20]

Formulation methods

For the formulation of mucoadhesive tablets, there are so many methods, some of the main formulation methods are the direct compression method, wet granulation method, dry granulation method, coating tablets, and melt granulation method.[21]

Direct compression method

In the pharmaceutical manufacturing process known as "direct compression," tablets are made without the use of heat or wet granulation by compressing a combination of API and different excipients. Drugs that are sensitive to heat, moisture, or both can benefit most from this approach. Creating a uniform mixture of powders that can be effectively compressed into tablets is the aim of direct compression.[21]

Wet granulation method

A popular method in pharmaceutical manufacturing is wet granulation, which yields granules that are ready to be compressed into tablets. To produce agglomerates or granules, a liquid binder is added to a powder blend. After drying, the granules are compressed into tablets. Wet granulation is used to reduce dustiness and enhance powder flow, homogeneity, and compressibility, among other benefits.[21,22]

Dry granulation method

A pharmaceutical manufacturing technique called "dry granulation" creates granules devoid of liquid solvents or binders. When the formulation's API or other ingredients are heat- or moisture-sensitive, this technique is used. In dry granulation, a powder blend is usually compacted into large agglomerates and then milled to produce the desired size of granules. Tablets can then be formed by compressing these granules. Because dry granulation can maintain the stability of materials that are sensitive to moisture, it is frequently used.[21,22]

Melt granulation method

A melted or molten binder is used in the pharmaceutical manufacturing process known as "melt granulation" to clump powder particles together into granules. This method is applied to enhance a powder blend's all-around tableting features, compressibility, and flow characteristics. Materials requiring changes to their release profiles or with poor flow characteristics are especially well suited for melt granulation.[21]

Evaluation of compressed tablets

Shape and size

It is both dimensionally characterized and controllable. A tablet's thickness is merely variable. The thickness of a tablet can be determined using a micrometer or another tool. Tablet thickness needs to be managed within a standard value deviation of no more than ±5%.[20]

Hardness

The hardness of a tablet, which refers to the amount of strength required to break it down, is measured in kilograms/Newtons. The slight and lightweight hardness tester determines how much strength is required to break down the tablet once the force of a coil spring applies in the opposite direction.[20]

Thickness test

Tablet hardness and thickness are primarily correlated, with the former serving as the initial regulate parameter. A vernier calipers were used to measure the thickness of ten randomly chosen tablets, and the result was recorded in millimeters.[23]

Friability test

The friabilator was set on for one hundred turns every minute, the pre-weighed tablets were placed inside, and subsequently, it was dusted and weighed once more. Conventionally, compressed tablets are usually seen to be suitable if they lose <0.5–1.0% of their original mass.[24]

$$\% \text{ Friability} = (W_1 - W_2)/W_2 \times 100$$

W_1 = Weight of tablets before test; W_2 = Weight of tablets after test

Weight variation test

The mass of twenty different tablets has been identified, and the average among these masses was ascertained. The percentage variance was calculated utilizing the subsequent formula.[25]

%Weight variation= (Average weight) – (Individual weight)/(Average weight) × 100

Surface pH test

The electrode has been set onto the formulation's base and allowed to adjust over 1 min afterward allowing it to expand in contact with 1 mL of distilled water for 2 h to test the pH. Three runs of this test were conducted, and the average was ascertained.[26]

Swelling index (SI)

Three distinct tablet compositions underwent testing. Petri plates were filled with 5 mL of phosphate buffer (pH 6.8) along with individually measured tablets (W_1). The tablets were removed from the Petri dishes at intervals of 1, 2, 4, and 8 h, and any remaining base buffer was cautiously smeared away by the filter paper. Next, the larger pills were measured again (W_2), and a formula was used to calculate the SI; the experiments were repeated 3 times, and the average values were recorded.[25]

% of SI = $(W_2–W_1)/W_2 \times 100$

In vitro dissolution studies

6.8 Phosphate buffer was utilized as the dissolution medium in a United States Pharmacopeia apparatus type II (paddle) dissolution test. A sample was taken every 5, 10, 15, 20, and 30 min. A new volume of the medium has been added to replace the evacuated amount to maintain similar sink circumstances. Absorbance was measured from the withdrawn samples using UV-Vis-Spectroscopy. The percentage of drug release was calculated using absorbance detected.[27,28]

Drug content

The tablets were homogenized in 100 mL of phosphate buffer (pH 6.8 or pH 7.4) and filtered individually through a 0.45µ filter. The resulting solution was then accurately diluted using phosphate buffer (pH 6.8 or pH 7.4) and measured spectrophotometrically using a UV spectrophotometer to estimate the medication content.[29]

Ex vivo permeation study

Porcine buccal tissue preparation involved excising the mucosal membrane and eliminating the adipose and connective tissue from a freshly slaughtered pig. The tissue was then equilibrated at 37 ± 1.0°C for 30 min in phosphate buffer pH 6.8. The buccal epithelium was carefully placed in the gap between the two distinct portions within the modified Franz diffusion cell. Tablets having a pH of 6.8 that resembled saliva got stuck to the mucosa on the subject's part. The recipient medium entailed of 20 mL of pH 6.8 phosphate buffer, which was stirred gently to replicate the blood pH of 37 ± 0.5°C. At established intermissions, 2 mL aliquots were taken from the receptor compartment and substituted utilizing a volume of the new buffer. The extracted samples were diluted, filtered, and HPLC-analysed.[30]

Wetting time

This simple method was used to determine the time of watering. The tissue paper was trimmed to 6.5 cm in diameter, and then it was positioned in a petri dish with 6 mL of room-temperature water. Following the placement of the tablet on the tissue paper, the amount of time needed for the tablet to get wet was noted.[31]

Water absorption ratio

A Petri dish with an inner diameter of 6.5 cm and 6 mL of filtered water contained a piece of tissue paper folded twice. The medication was allowed to completely soak over the tissue paper once it had been laid there. Upon draining the moist pill, it was weighed again. The water absorption ratio is computed utilizing the formula below.[32]

(R) R =100 $(W_a–W_b)/W_b$

Where, W_b = Weight of tablet before absorption, W_a = Weight of tablet after absorption

CONCLUSION

The successful construction of new or amended mucoadhesive dosage forms is likely to benefit from the usage of mucoadhesive buccal drug delivery systems, it was found. Mucoadhesion techniques, tool designing, penetration augmentation, and the development of new mucoadhesives are only a few of the uses for mucoadhesive dosage forms. For extended controlled drug delivery, the buccal mucosa provides several benefits. The mucosa contains enough vascular and lymphatic drainage to prevent pre-systemic elimination in the gastrointestinal tract and first-pass metabolism in the liver. Further investigation on buccal drug administration is necessary to distribute oral drugs that are inadequate systemically and to offer a viable and appealing non-invasive method of delivering powerful protein and peptide therapeutic components.

AUTHOR CONTRIBUTIONS

Each author contributed substantially to the conception, design, data acquisition, analysis, and interpretation of the study findings. They collaborated closely in drafting and critically revising the manuscript for intellectual content. Consensus was reached among all authors to submit the manuscript for publication, and they collectively approved the final version. In addition, each author agreed to take responsibility for the integrity of the research in its entirety.

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