WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 4, 167-191. Review Article ISSN 2277–7105

A REVIEW ON MUCOADHESIVE MICROSPHERES IN GASTRORETENTIVE DRUG DELIVERY SYSTEM

Krishna K. R.[1], Mohith Gowda C. V.[2]*, Parthiban S.[3]

Department of Pharmaceutics, Bharathi College of Pharmacy, Bharathinagara, Mandya, Karnataka-571422, India.

Article Received on 14 Jan. 2026,
Article Revised on 04 Feb. 2026,
Article Published on 15 Feb. 2026,

https://doi.org/10.5281/zenodo.18657628

***Corresponding Author**

Mohith Gowda C. V.

Department of Pharmaceutics, Bharathi College of Pharmacy, Bharathinagara, Mandya, Karnataka-571422, India.

How to cite this Article: Krishna K. R.[1], Mohith Gowda C. V.[2]*, Parthiban S.[3] (2026). A Review on Mucoadhesive Microspheres in Gastroretentive Drug Delivery System. World Journal of Pharmaceutical Research, 15(4), 167–191.

ABSTRACT

Drugs with rapid gastrointestinal absorption and short biological half-lives are quickly eliminated from systemic circulation, necessitating frequent dosing and often compromising patient compliance. Gastroretentive drug delivery systems (GRDDS) have been developed to overcome these limitations by prolonging gastric residence time, thereby improving drug bioavailability and therapeutic efficacy. Microspheres are effective particulate carriers due to their small size and high drug-loading capacity. The incorporation of mucoadhesive properties further enhances their performance by ensuring prolonged contact with the gastrointestinal mucosa, resulting in improved therapeutic outcomes, reduced dosing frequency, minimized drug loss, and better patient compliance. Mucoadhesive microspheres are particularly advantageous for drugs requiring predictable and enhanced bioavailability or intended for local gastrointestinal action. This review provides an overview of GRDDS with emphasis on mucoadhesive microspheres, discussing factors affecting mucoadhesion, commonly used polymers, underlying mechanisms and theories, preparation techniques, and evaluation parameters.

KEYWORDS: Gastroretentive drug delivery systems, microspheres, mucoadhesion, mucoadhesive polymers, bioavailability.

INTRODUCTION

Oral drug delivery is the most desired method of administration compared to other methods; however, it has several drawbacks, such as first-pass hepatic metabolism, gastrointestinal toxicity, and drug degradation by gastrointestinal enzymes.[1]

The increasing interest in the development of oral controlled-release dosage forms is due to their ability to maintain effective drug concentrations in systemic circulation for extended periods of time while providing therapeutic benefits like convenient dosing, improved patient compliance, and increased formulation flexibility.[2]

Microspheres are an innovative drug delivery technology made from various polymers and offer multiple potential applications.[3]

Microspheres are an important component of particulate drug delivery systems due to their small size and high drug-carrying efficiency. They are carrier-based drug delivery systems in which the active pharmaceutical ingredient is encapsulated within an inner core and surrounded by an outer polymeric coating.[4] It is possible to create microspheres with synthetic or natural polymers.[5]

In addition to providing targeted, controlled, or prolonged release, adding mucoadhesive properties to microspheres can enhance drug absorption and bioavailability.[6]

Gastroretentive drug delivery systems are designed to remain in the stomach for extended periods, thereby increasing the gastric residence time of drugs. Prolonged gastric retention enhances bioavailability and reduces drug loss. By retaining the drug within the gastric environment, these systems improve therapeutic efficacy and enable the development of advanced pharmaceutical formulations with improved clinical outcomes. Compared with conventional sustained-release dosage forms, controlled-release gastroretentive systems offer significant advantages.[7]

GASTRO-RETENTIVE DRUG DELIVERY SYSTEM

Drugs that are quickly absorbed from the gastrointestinal tract and have short half-lives are eliminated rapidly from the systemic circulation, which requires frequent dosing. To overcome this limitation, gastroretentive drug delivery systems are designed to maintain therapeutic plasma drug concentrations for extended periods, thereby reducing dosing

frequency. In addition, these systems minimize fluctuations in plasma drug levels by providing controlled and consistent drug release.[8]

APPROACHES OF GRDDS

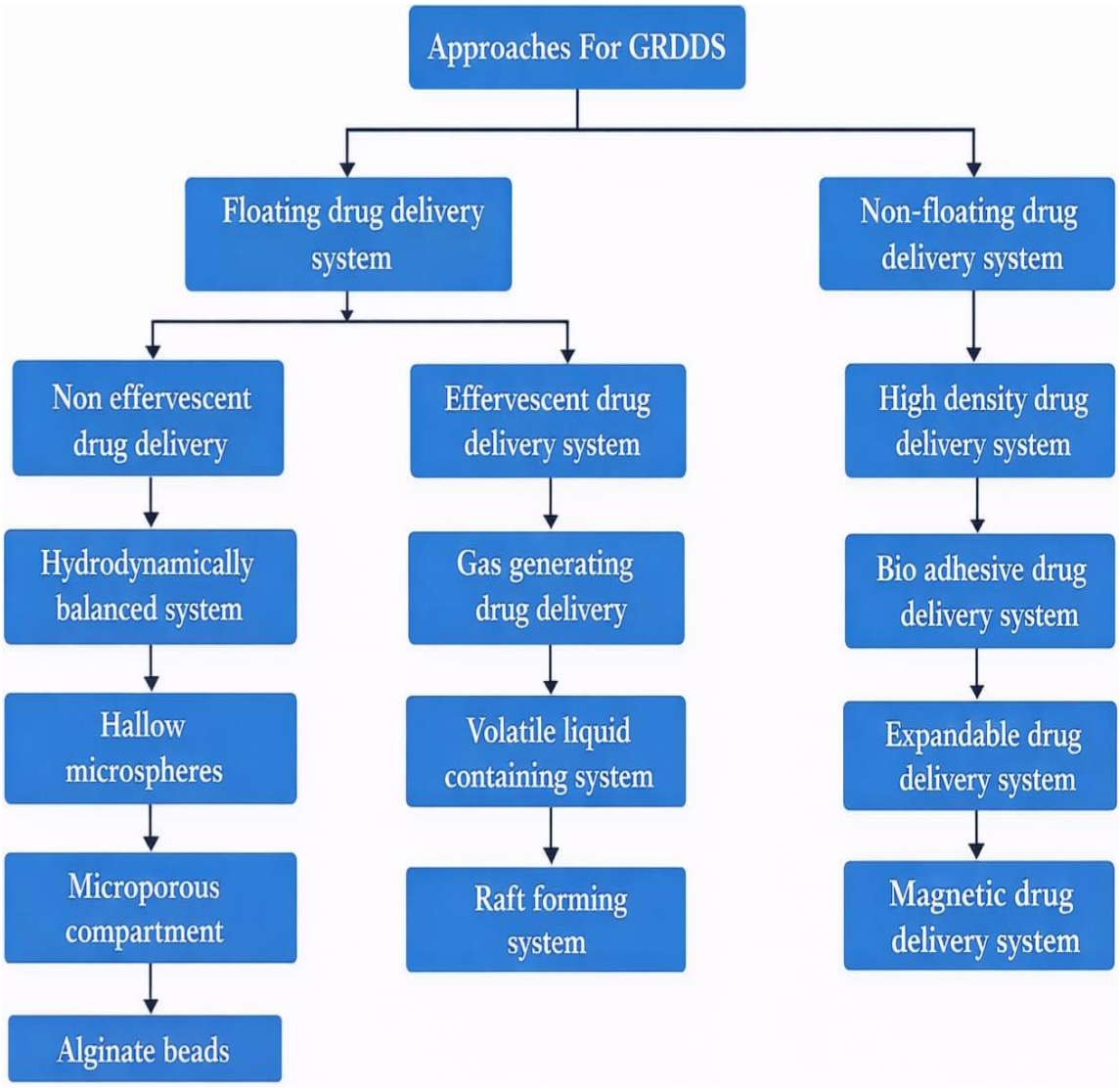

Fig. No.1: Approaches of GRDDS.

FACTORS AFFECTING GASTRIC RETENTION

The time a dosage form remains in the stomach, known as gastric retention time (GRT), is affected by several factors. These include the formulation's size and density, whether the stomach is empty or full, and dietary components such as fats, specific amino acids, and peptides, which can slow gastric emptying and intestinal movement. Other influences include an individual's position, posture, age, sex, sleep, and health conditions like gastrointestinal disorders or diabetes, all of which can alter gastric motility. Additionally,

certain drugs that act as gastro-kinetic agents, such as metoclopramide and cisapride, may also impact gastric retention.[9]

ADVANTAGES OF GASTRO RETENTIVE DRUG DELIVERY SYSTEMS

- Enhances therapeutic efficacy by maintaining optimal drug concentration at the absorption site.
- Reduces dosing frequency, thereby improving patient compliance.
- Helps in reducing first-pass metabolism, leading to increased bioavailability of the drug.
- Decreases gastric mucosal irritation by releasing the drug slowly and in a controlled manner.[10]
- Gastro retentive drug delivery systems reduce the body's counter-regulatory activity, thereby improving drug efficiency.
- Minimization of fluctuations in drug concentration allows for enhanced and selective receptor activation.[11]
- Allows site-specific delivery of drugs to the stomach.
- Prolonged gastric residence time is advantageous for local therapeutic action in the upper part of the small intestine, such as in the management of peptic ulcer disease.[12]

PHYSIOLOGY OF STOMACH

The stomach plays a vital role in GRDDS; therefore, an adequate understanding of its anatomy and physiology is essential for the successful development of gastroretentive dosage forms. Anatomically, the stomach is divided into two main regions: the proximal stomach, comprising the fundus and body, and the distal stomach, consisting of the antrum and pylorus, as shown in the figure below. The primary functions of the stomach include temporary storage of food, mechanical digestion, and controlled release of gastric contents into the duodenum. The fundus and body mainly serve as reservoirs for undigested food, while the antrum acts as a pump by generating propulsive contractions that facilitate gastric emptying. Gastric motility follows a characteristic pattern known as the migrating myoelectric complex (MMC). Although gastric emptying occurs in both fed and fasted states, the pattern differs significantly between these conditions. In the fasted state, a cyclic sequence of coordinated electrical and motor activity passes through the stomach and small intestine every 90–120 minutes.

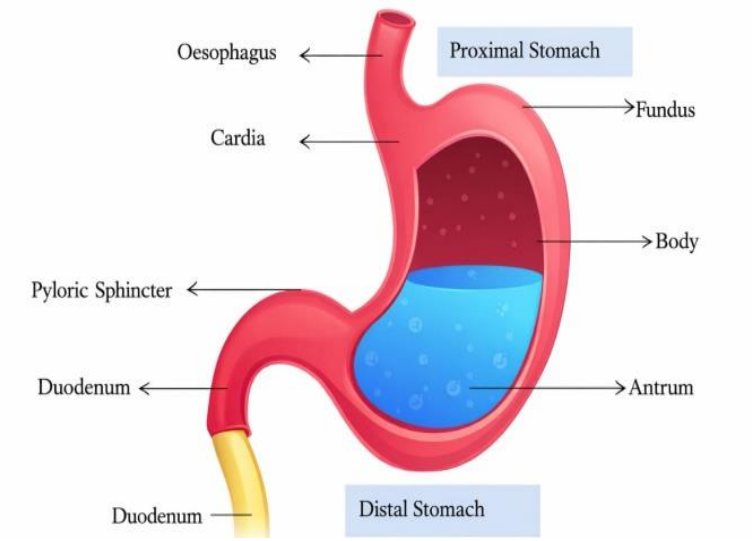

Fig. No. 2: Physiology of Stomach.

Mucoadhesive or bioadhesive drug delivery systems are developed to adhere to the gastric mucosal surface, thereby prolonging the residence time of drugs within the stomach.

In this method, the drug is formulated with a mucoadhesive carrier made from natural or synthetic polymers. Adhesion between the polymeric material and the mucosal surface enables the mucoadhesion process, which generally proceeds through two steps.

(a) Contact stage

(b) Consolidation stage.

Frequently used mucoadhesive polymers include Carbopol, chitosan, sodium alginate, HPMC, polyethylene glycol, and polyacrylic acid. Mucoadhesive polymers help extend the duration of drug residence at the application site by binding drug compounds to mucosal surfaces.[13]

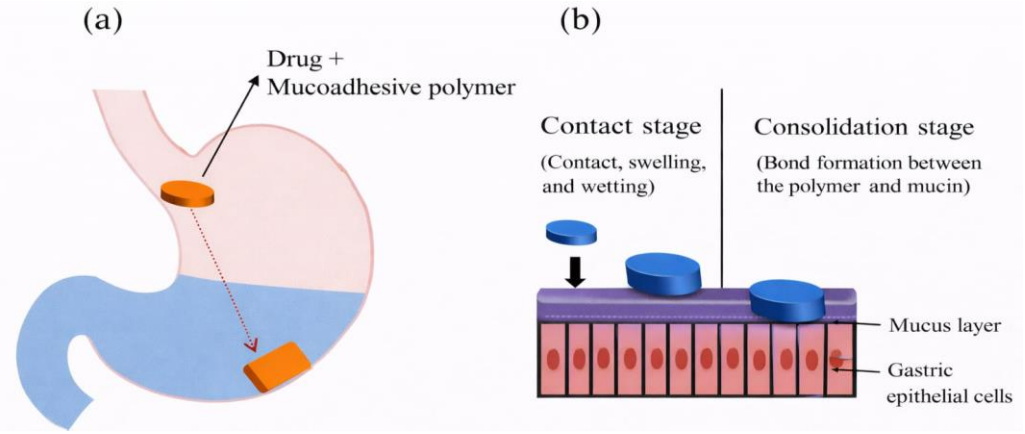

Fig. No. 3: Mechanism of Mucoadhesive Microsphere in Stomach.

MICROSPHERES

Microspheres are tiny spherical particles with diameters ranging from approximately 1 µm to 1000µm. They are also commonly referred to as microparticles.[14]

Microspheres are widely used as drug carriers and represent an effective strategy for sustaining and controlling the release of drugs at specific sites.[15]

Microspheres can be prepared from biodegradable or non-biodegradable materials. These can be injected through 18 or 20-gauge needles. Due to the size of the microspheres, they can be evenly distributed throughout the GI tract. This helps increase the absorption of the drug and reduce the irritation produced by certain drugs on the GI tract. Microspheres, as a controlled drug delivery system, release drugs at a regulated rate, addressing the limitations of conventional delivery systems and improving the therapeutic efficacy of the drug.[16]

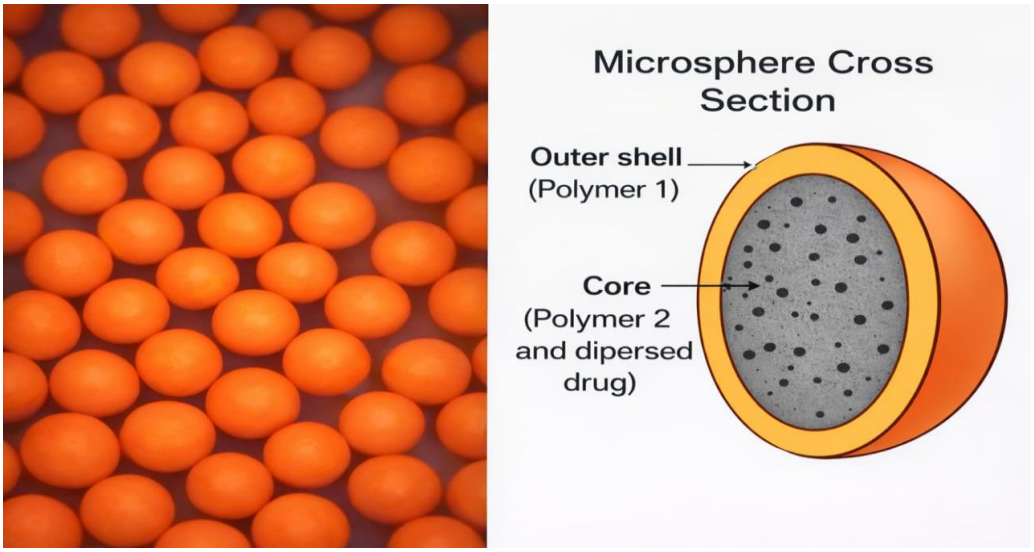

Fig. No. 4: Structure of Microsphere.

TYPES OF MICROSPHERES

1. Bio-adhesive microspheres
2. Magnetic microspheres
3. Floating microspheres
4. Radioactive microspheres
5. Polymeric microspheres
6. Mucoadhesive microspheres

BIO-ADHESIVE MICROSPHERES

The capacity of a drug delivery system to adhere to a biological membrane using the sticky properties of water-soluble polymers is known as bioadhesion. Bioadhesion is the process by which a dose form sticks to mucosal surfaces such as the buccal, ocular, nasal, or rectal membranes.[17]

MAGNETIC MICROSPHERES

An essential drug delivery method for localizing therapeutic medicines at the target site is magnetic microspheres. This method improves targeting efficiency by substituting a lower dose of magnetically guided medication for a large amount of freely circulating medication. These carriers, which are frequently made with polymers like chitosan and dextran, show magnetic responsiveness as a result of the addition of magnetic materials.[18]

FLOATING MICROSPHERE

Floating drug delivery systems are designed with a bulk density lower than that of gastric fluids, allowing them to remain buoyant in the stomach without disrupting normal gastric emptying. As the system floats on gastric contents, the drug is released slowly at a predetermined rate, leading to extended gastric residence time and more consistent plasma drug levels. Furthermore, this approach helps prevent dose dumping, maintains prolonged therapeutic action, and reduces the need for frequent dosing.[19]

RADIOACTIVE MICROSPHERES

Radioactive microspheres enable the localized delivery of high levels of radiation to diseased tissue while minimizing exposure to adjacent healthy organs. After administration, the microspheres become trapped within the fine network of blood vessels supplying the tumor, ensuring that the radioactive dose is concentrated at the target site.[20]

POLYMERIC MICROSPHERES

Polymeric microspheres can be broadly classified into two categories: biodegradable polymeric microspheres and synthetic polymeric microspheres.

BIO-DEGRADABLE POLYMERIC MICROSPHERES

Natural polymers such as starch are frequently employed due to their inherent biodegradability, biocompatibility, and bioadhesive properties. Biodegradable polymers enhance the duration of contact with mucosal membranes owing to their ability to swell

extensively in aqueous environments. Drug release from these systems can be sustainably controlled by modifying polymer concentration and release characteristics. However, a major limitation of biodegradable microspheres is the difficulty in achieving consistent clinical performance and precise regulation of drug release. Nevertheless, they offer a broad range of therapeutic applications in microsphere-based drug delivery systems.

SYNTHETIC POLYMERIC MICROSPHERES

Synthetic polymeric microspheres are frequently employed in medical and pharmaceutical applications, including use as fillers, bulking agents, embolic materials, and drug delivery systems. These microspheres are generally regarded as safe and biocompatible. However, their primary limitation is the possibility of migration away from the injection site, which can lead to complications such as embolism and unintended damage to surrounding or distant organs.[21]

MUCOADHESIVE MICROSPHERES

Mucoadhesive microspheres are microparticles formulated using mucoadhesive polymers, with sizes generally ranging from 1 to 1000 µm. While microspheres are commonly employed for targeted and controlled drug delivery, the inclusion of mucoadhesive properties offers additional advantages. These systems establish close contact with the mucus layer, leading to improved drug absorption and increased bioavailability due to their large surface area relative to volume. Mucoadhesive microspheres allow drugs to be encapsulated within the particles and released directly at the mucosal surface, where adhesion is maintained through mucoadhesive interactions. They can adhere to mucosal tissues of the nasal cavity, gastrointestinal tract, and urinary tract, enabling both localized and systemic drug delivery. Key characteristics of mucoadhesive microspheres such as surface properties, adhesive strength, drug release behavior, and clearance are strongly influenced by the type of mucoadhesive polymer used in their formulation.[22]

ADVANTAGES OF MUCOADHESIVE MICROSPHERES

- Enable controlled and sustained drug release over an extended duration.
- Reduce dosing frequency, thereby improving patient compliance.
- Provide uniform drug release, minimizing fluctuations in plasma drug concentration.
- Require lower drug doses, which helps reduce toxic effects.
- Allow site-specific drug targeting.

- Minimize toxicity to non-target organs.[23]

LIMITATIONS OF MUCOADHESIVE MICROSPHERES

Some of the disadvantages were found to be as follows

- The drug release profile from the formulation may undergo alteration.
- The rate of drug release may be influenced by several factors, including food intake, gastrointestinal transit time, and the rate of mucin turnover.
- Variability in the drug release rate may be observed between different administered doses.
- Any compromise in the integrity of the drug release pattern of the dosage form may result in potential toxicity.
- Such dosage forms are not suitable for crushing or chewing.[24]

MUCOADHESION

The process of two surfaces adhering to one another is known as adhesion. The term "bioadhesion" refers to the biological process of adhesion. This adhesion is referred to as "mucoadhesion" if it happens on mucosal membranes. Additionally, The binding of a natural or artificial polymer to a biological substrate is known as bioadhesion; if the substrate is a mucous membrane, it is referred to as mucoadhesion. Mucoadhesive hydrophilic polymers are added to pharmaceutical formulations along with the active ingredient to provide site-specific drug delivery. To distribute the drug locally, the formulation will be adhered to a biological surface. At the site of action, the active component will be released, improving bioavailability.[25]

MUCUS MEMBRANE

Mucous membranes, or mucosae, are moist tissue surfaces that line the interior of body cavities, including the gastrointestinal and respiratory systems. They are composed of an epithelial layer supported by an underlying connective tissue known as the lamina propria. The epithelial surface is typically kept moist by mucus, which may exist as a gel firmly attached to the mucosal surface or as a soluble or suspended substance within the lumen. Mucus gels are primarily made up of mucin glycoproteins, lipids, inorganic salts, and water, with water constituting more than 95% of their total mass, resulting in a highly hydrated structure. The principal roles of mucus are to protect the underlying tissues and to facilitate lubrication.[26]

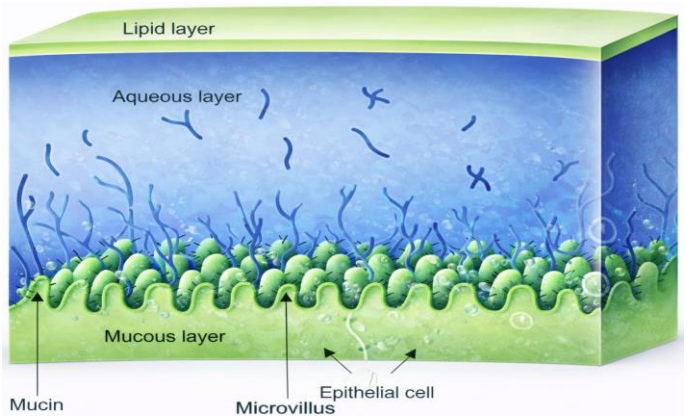

Fig. No. 5: Mucus Membrane.

MECHANISM OF MUCOADHESION

The mechanism of mucoadhesion is generally described as occurring in two distinct stages.

1. Contact stage.
2. Consolidation stage.

I. The Contact stage, This initial stage involves direct contact between the mucoadhesive formulation and the mucosal membrane. During this phase, the formulation spreads and swells upon hydration, enabling close and intimate interaction with the mucus layer.

II. In the consolidation step, In this phase, the presence of moisture activates the mucoadhesive material. Hydration plasticizes the system, enabling polymer chains to become mobile and interact with the mucosal surface through weak intermolecular forces such as hydrogen bonding and van der Waals interactions.

Essentially, two main theories have been proposed to explain the consolidation step

1. The diffusion theory. 2. The dehydration theory.

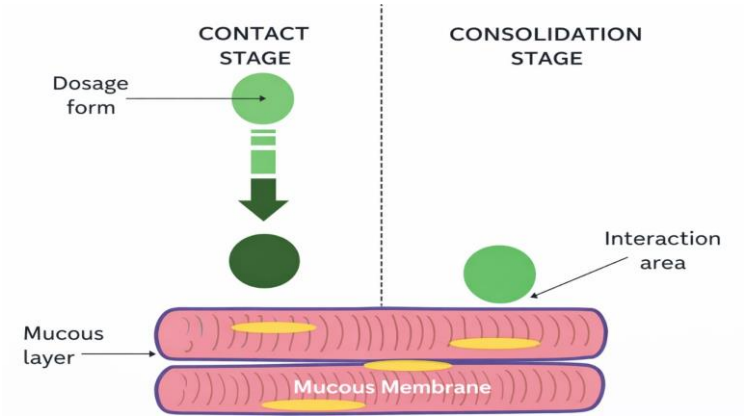

Fig. No. 6: Stages of Mucoadhesion process.

- According to diffusion theory, mucoadhesion occurs through mutual interaction between mucoadhesive polymer chains and mucus glycoproteins via chain interpenetration and the formation of secondary bonds. For effective adhesion, the mucoadhesive system must possess properties that promote both chemical interactions and mechanical interlocking.

- According to dehydration theory, materials that rapidly form gels in aqueous environments can induce dehydration of the mucus layer upon contact, as a result of differences in osmotic pressure.[27]

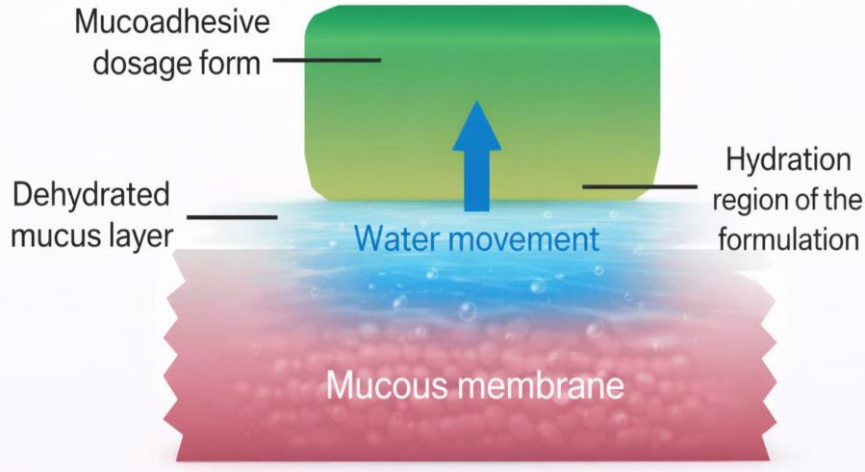

Fig. No. 7: Dehydration theory of mucoadhesion.

THEORIES OF MUCO-ADHESION

Different theories are involved in the mucoadhesion which are as follows

1. The electronic theory
2. The wetting theory
3. The adsorption theory
4. The diffusion theory
5. The mechanical theory
6. The cohesive theory

1. THE ELECTRONIC THEORY

According to the electronic theory, mucoadhesion occurs due to the transfer of electrons between the mucoadhesive material and the mucosal surface, resulting in the formation of an electrical double layer at the interface.

2. THE WETTING THEORY

The wetting theory is mainly applicable to liquid systems and suggests that adhesion is enhanced when a liquid exhibits a low contact angle on a solid surface, indicating better spreading and increased affinity for adhesion.

3. THE ADSORPTION THEORY

This theory proposes that mucoadhesion arises from the adsorption of the mucoadhesive polymer onto the mucosal surface through secondary intermolecular forces such as hydrogen bonding and van der Waals interactions.

4. THE DIFFUSION THEORY

According to diffusion theory, mucoadhesion occurs when polymer chains of the mucoadhesive interpenetrate with the mucin chains of the mucosal surface, leading to the formation of a cohesive network structure.

5. THE MECHANICAL THEORY

The mechanical theory explains mucoadhesion as a result of the penetration of liquid adhesive materials into surface irregularities, pores, or microcracks of the mucosal substrate, creating an interlocking structure.

6. THE COHESIVE THEORY

This theory states that mucoadhesion is primarily due to internal cohesive forces within the adhesive material itself, resulting from intermolecular interactions among similar molecules.[28]

FACTORS AFFECTING MUCOADHESION

1) POLYMER RELATED FACTORS

a) Molecular weight: Polymers with lower molecular weight can penetrate the mucus layer more readily than those with higher molecular weight. In contrast, high molecular weight polymers tend to form greater chain entanglements, which can limit penetration. As a result, smaller polymer chains generally exhibit more effective interpenetration with the mucus layer.

b) Spatial Conformation: The bioadhesive strength of a polymer is influenced by its molecular conformation, such as linear or helical structures. Helical conformations may

conceal functional groups that are essential for adhesion, thereby reducing the overall mucoadhesive effectiveness of the polymer.[29]

c) Flexibility of polymer chain: Polymer chain flexibility is influenced by factors such as viscosity and diffusion coefficient. Increased flexibility enhances the ability of polymer chains to diffuse into the mucus network, thereby improving mucoadhesive interactions.[30]

d) Hydration and swelling: Adequate hydration is essential for mucoadhesive polymers to properly swell and form a macromolecular network of appropriate size. This expansion exposes bioadhesive sites for bonding, creates pores and channels for solute or polymer diffusion, and enhances polymer chain mobility, promoting interpenetration with the mucin layer.[31]

e) Concentration of active polymer: optimal concentration of the active polymer is necessary for effective mucoadhesion. When the polymer concentration is too low, the number of polymer chains capable of penetrating the mucus layer per unit volume is reduced, resulting in weak and inconsistent interactions between the polymer and mucus.

2) ENVIRONMENTAL - RELATED FACTORS

a) pH: pH can influence the surface charge of both mucus and mucoadhesive polymers. Variations in pH affect the dissociation of functional groups on the carbohydrate components and amino acids of the mucin polypeptide backbone, altering the charge density of mucus and potentially impacting the strength of adhesion.

b) Applied strength: The amount of pressure applied to the mucoadhesive at the tissue contact site affects how deeply the polymer chains interpenetrate the mucus. Polymers can become mucoadhesive even without strong intrinsic interactions with mucin if sufficient pressure is maintained for an appropriate duration.

c) Presence of metal ions: The presence of metal ions can bind to charged groups on the polymer or mucus, decreasing the number of sites available for interaction and thereby reducing the mucoadhesive strength.

d) Initial contact time: The strength of bioadhesion is directly related to the initial contact time, as it influences the degree of polymer swelling and interpenetration. In gastric systems, controlling this parameter is challenging.[32]

3) PHYSIOLOGICAL FACTORS

Play a significant role in determining the mucoadhesive behavior of a polymer matrix, particularly the thickness and surface characteristics of the mucosal layer.

a) Mucin turnover: Continuous renewal of mucin limits the residence time of mucoadhesive systems on the mucus layer, regardless of how strong the adhesive interaction may be.

b) Disease state: Pathological conditions such as the common cold, gastric ulcers, and ulcerative colitis can alter the physicochemical properties of mucus, thereby influencing the effectiveness of mucoadhesion.[33]

MUCOADHESIVE MATERIAL

Polymers include hydroxyl, carboxyl, amide, and sulfate moieties, among other hydrophilic functional groups. Hydrogen bonding, hydrophobic interactions, and electrostatic forces are some of the ways in which these groups interact with mucus or epithelial cell membranes. These hydrophilic groups also encourage polymer swelling in wet settings, which exposes more sticky sites.[34]

AN IDEAL POLYMER CHARACTERISTIC FOR A BIOADHESIVE DRUG DELIVERY

- It should be non-irritating to the mucosal membranes.
- The polymer should be capable of forming strong and effective interactions with mucin and epithelial cell surfaces.
- It should allow easy encapsulation of the drug.
- The polymer should not alter the drug release profile.
- It should remain stable and should not degrade during storage or throughout the shelf life of the dosage form.
- The polymer should be cost-effective to ensure economical formulation.[35]

LIST OF MUCOADHESIVE POLYMERS

Some of the commonly employed mucoadhesive polymers are listed below

I. Synthetic Polymers

1. Cellulose derivatives

- Methylcellulose

- Ethylcellulose
- Hydroxy-ethylcellulose
- Hydroxy propyl cellulose
- Hydroxy propyl methylcellulose
- Sodium carboxy methylcellulose

2. Poly(acrylic acid) derivatives

- Carbopol
- Polycarbophil

3. Poly(hydroxyethyl methacrylate)
4. Poly(ethylene oxide)
5. Poly(vinyl pyrrolidone)
6. Poly(vinyl alcohol)

II. Natural Polymers

- Tragacanth
- Sodium alginate
- Karaya gum
- Guar gum
- Xanthan gum
- Lectin
- Soluble starch
- Gelatin
- Pectin
- Chitosan.[36]

PREPARATION OF MUCOADHESIVE MICROSPHERES

Mucoadhesive microspheres can be prepared using any of the following techniques,

- Solvent Evaporation method
- Spray Drying method
- Hot melt microencapsulation method
- Emulsion cross linking method
- Ionotropic gelation method
- Double Emulsion Method.

SOLVENT EVAPORATION METHOD

The process is performed in a liquid manufacturing medium. In this method, the coating polymer is dissolved in a volatile solvent that does not mix with the external liquid phase. The drug or core material intended for microencapsulation is either dissolved or uniformly dispersed in the polymer solution. Upon continuous stirring, this mixture is dispersed into the external phase, producing droplets of the desired microsphere size. If required, the system is heated to remove the solvent. As the solvent evaporates, the polymer solidifies and forms a coating around the core material. When the core substance is dispersed within the polymer solution, the resulting product is a matrix-type microsphere.[37]

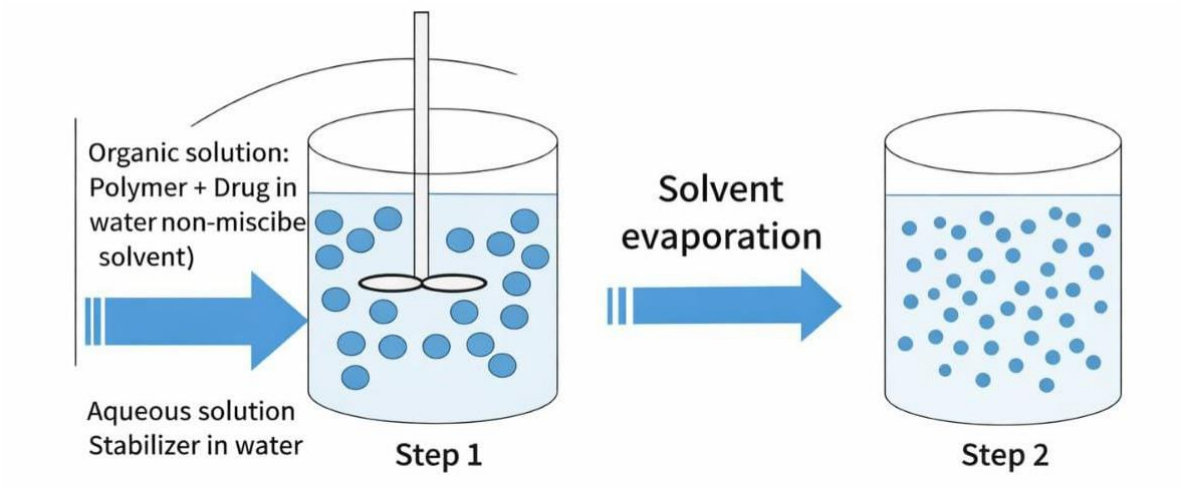

Fig. No. 8: Solvent Evaporation.

SPRAY DRYING METHOD

In this technique, the polymer is initially dissolved in an appropriate volatile organic solvent. The drug is uniformly dispersed into the polymer solution using high-speed homogenization. The resulting mixture is then sprayed into a stream of heated air, where it breaks into fine droplets. Rapid evaporation of the solvent from these droplets results in the formation of microspheres, typically ranging in size from 1 to 100 µm.

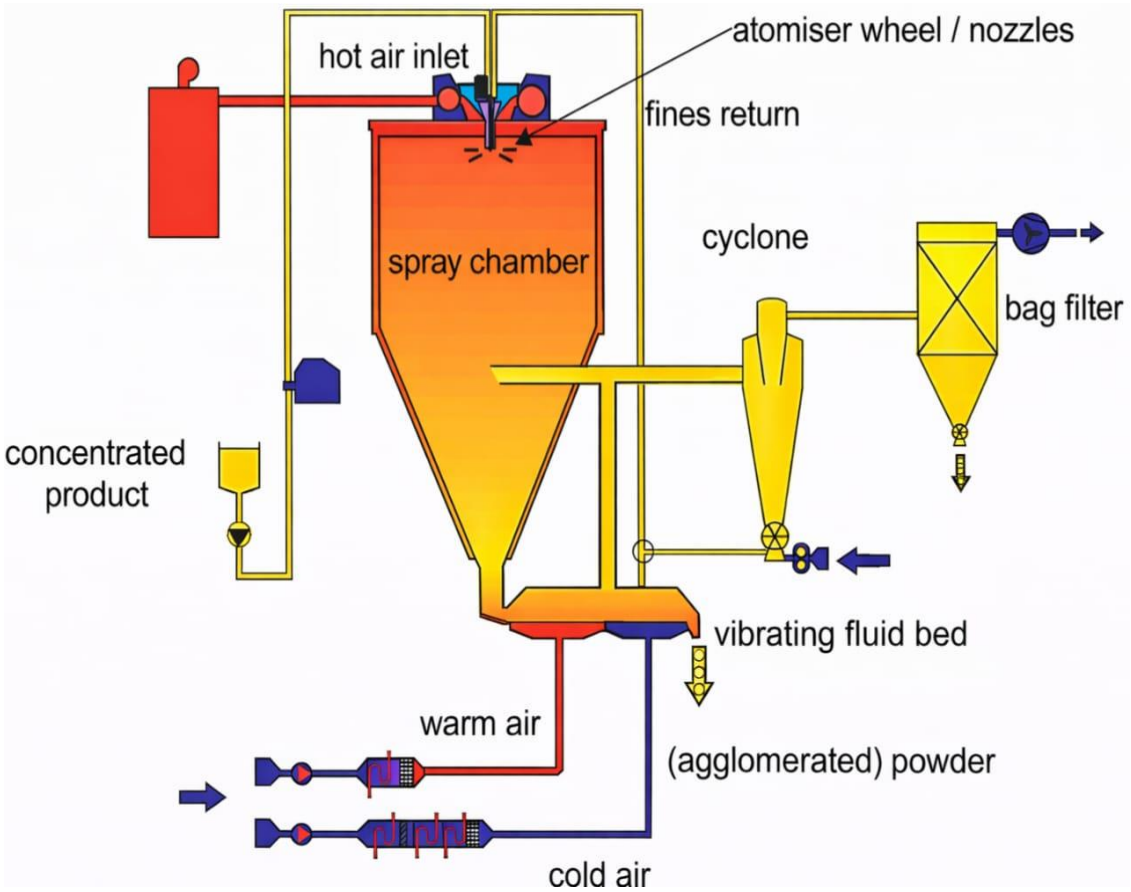

Fig. No. 9: Spray Drying.

HOT MELT MICROENCAPSULATION METHOD

After the polymer has been melted, solid drug particles that have been sieved to a size of less than 50 μm are combined with it. The combination is heated to 5°C over the polymer's melting point while being suspended in a non-miscible solvent (such as silicone oil) and constantly agitated. After stabilizing the emulsion, the polymer particles are allowed to solidify by cooling it. Petroleum ether is used to cleanse the resultant microspheres by decantation process. By varying the stirring speed, it is easy to adjust the particle size distribution and produce microcapsules with a diameter of 1 to 1000 μ.[38]

EMULSION CROSS LINKING METHOD

Using this technique, the polymer aqueous solution was emulsified in the oily phase to create a water-in-oil (w/o) emulsion. Appropriate surfactant, such as span 80 or dioctyl sodium sulphosuccinate, was used to stabilize aqueous droplets. By hardening the droplets with a suitable cross-linker, such as gluteraldehyde, the stable emulsion was cross-linked. To get rid of any remaining oil, microspheres were filtered and repeatedly cleaned with

petroleum ether or hexane. After being cleaned with water to get rid of the cross linkers, they were allowed to dry for a full day at room temperature.[39]

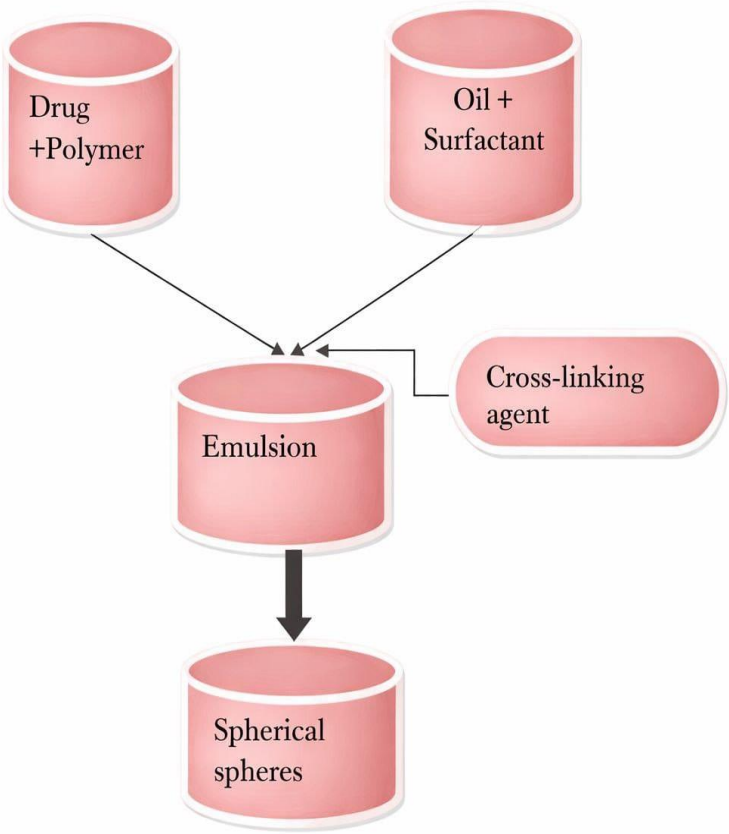

Fig. No. 10: Emulsion cross linking method.

IONOTROPIC GELATION METHOD

A homogenous polymer mixture is created by dispersing the mucoadhesive polymer and sodium alginate in 50 ml of filtered water. To create a smooth, viscous dispersion, the drug is introduced to the polymer matrix and thoroughly mixed. The resulting dispersion is then continuously stirred and by using needle to produce microdroplets that fall into a 10% w/v calcium chloride solution. To finish the curing process and create stiff, spherical microspheres, the generated droplets are kept in the calcium chloride solution for 15 minutes. The resulting microspheres are collected by decantation, and after being separated, they are periodically cleaned with purified water to get rid of any excess calcium impurities that may have accumulated on their surface. They are then dried for 12 hours at 45°C.

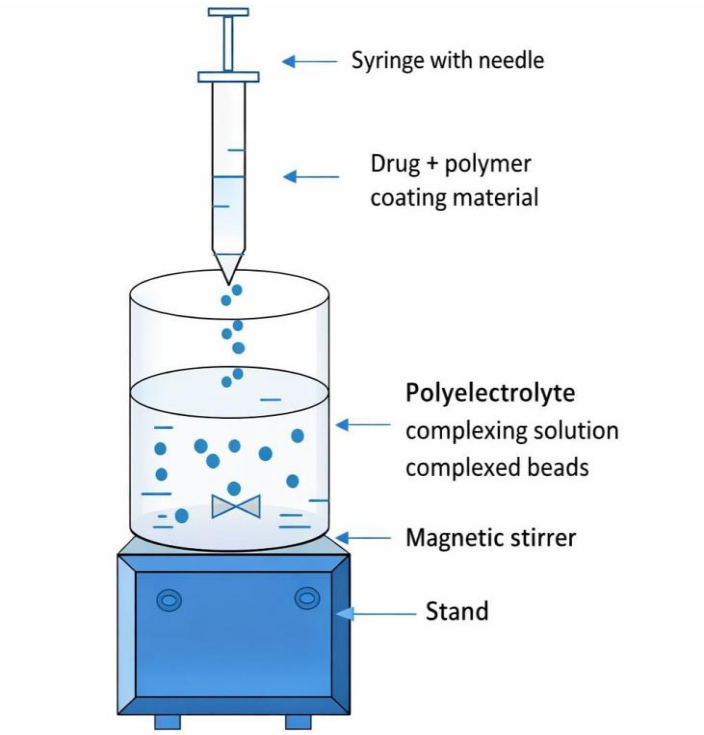

Fig. No. 11: Ionotropic gelation method.

DOUBLE EMULSION METHOD

This process creates a primary water-in-oil emulsion by adding an aqueous solution of the medication and polymer to the organic phase while vigorously stirring. In order to obtain multiple emulsions (w/o/w), this emulsion was then added to a significant volume of water containing an emulsifier, such as polyvinyl alcohol or polyvinylpyrrolidone, while being stirred. The stirring was continued until the majority of the organic solvent evaporated, leaving solid microspheres. Afterward, the microspheres are cleaned and dried.[40]

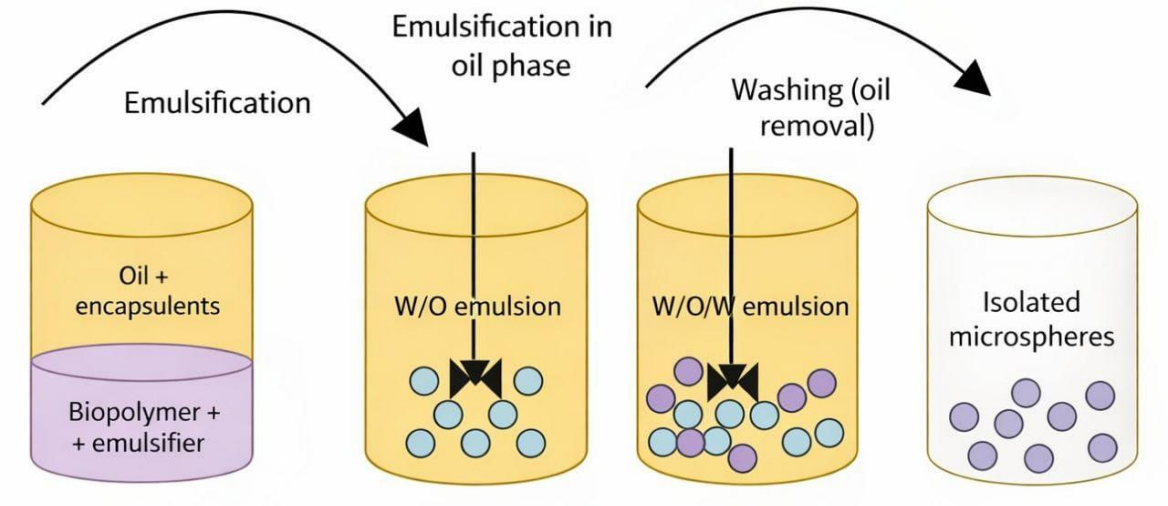

Fig. No. 12: Double emulsion method.

EVALUATION OF MUCOADHESIVE MICROSPHERES

The microspheres are evaluated for the following parameters.

1. PARTICLE SIZE AND SHAPE

Light microscopy (LM) and scanning electron microscopy (SEM) can be used to determine the size, shape, and external structure of microspheres.

2. ENTRAPMENT EFFICIENCY

The microspheres entrapment efficiency, or entrapment percentage, can be found by putting the microspheres in a buffer solution and letting them lyse. In the active components are next examined in accordance with the guidelines in the monograph after the resultant lysate has been filtered or centrifuged. The efficiency of trapping as a percentage is determined by applying the subsequent formula.

% Entrapment = Actual content / Theoretical content x 100

3. SWELLING INDEX

The ability of the mucoadhesive microspheres to swell at the absorbing surface by absorbing fluids present at the site of absorption a crucial need for the start of mucoadhesion is demonstrated by the swelling index. The following formula can be used to calculate the percentage of swelling.

Percent swelling = DT - D0 / D0 × 100

Where,

DT = weight of swelled microspheres

D0 = weight of dried microspheres.[41]

4. SCANNING ELECTRON MICROSCOPY (SEM)

Scanning electron microscopy should be used to investigate the microspheres' surface structure at different magnifications. The surface topography of the samples was examined after they were coated with gold-palladium under vacuum and placed on a scanning electron microscope holder using double-sided adhesive tape. SEM is used to analyze the microspheres internal and external morphology.

5. FTIR STUDIES

To look for potential interactions between the drug and polymers in the location of absorption bands, FTIR experiments should be carried out.[42]

6. SURFACE CHARGE STUDY

Zeta potential is a measure of particle surface charge that can be used to forecast and regulate mucoadhesion mechanisms, stability, and adhesive strength. Mucoadhesive polymers and mucus interact during the mucoadhesion process, which is impacted by the polymers structure and charge. Zeta potential measurements of mucus and microspheres aid in the prediction of electrostatic interactions during mucoadhesion.[43]

7. IN-VITRO MUCOADHESION STUDY

The falling liquid film approach was used to evaluate the in-vitro mucoadhesion investigation of microspheres. About 50 microspheres were applied to a piece of sheep intestinal mucosa that had been fixed on a glass slide. The microspheres were hydrated using a few drops of 0.1N hydrochloric acid. Use a stand to support the intestine at a 50° angle after 5 min. Using flow-controlled tubes (I.V. infusion set), the intestinal mucosa was cleaned at room temperature at a rate of 23 ± 2 ml/min. Rubber bands were used to cover the tissue with the tip of a tube containing buffer solution, allowing the liquid to flow uniformly throughout the mucosa. A beaker is used to collect the washings. Particles that reached the measuring point (2 cm from the initial applied location) and separated were collected in the receiver after 45 minutes, whereas particles that stayed in the applied area were used to measure the bio-adhesion.

The formula was used to determine the percentage mucoadhesion:

$$\%\ Mucoadhesion = \frac{Initial\ no.of\ \ microspheres - No.of\ microspheres\ detached}{Initial\ no.of\ \ microspheres} \times 100$$

8. IN-VITRO DRUG RELEASE STUDIES

USP type-I dissolution assemblies were used to conduct dissolution investigations in pH 1.2 stimulated gastric fluid. In 900 ml of 0.1 N HCI (pH 1.2), which was kept at 37 ± 0.5°C and agitated at 100 rpm, a weighed quantity of microspheres equal to 400 mg of medication was distributed. Aliquots of five milliliters were taken out and filtered every sixty minutes. The necessary dilutions were prepared using 0.1 N HCl, and the drug concentration of the solutions was measured using a UV spectrophotometer at 255 nm against an appropriate blank. This was used to compute the percentage of medication released, which was then displayed versus time.

9. STABILITY STUDY

Stability studies were carried out for a period of three months under different storage conditions, namely 5 °C (ambient), 25 °C ± 60% relative humidity, and 40 °C ± 75% relative humidity, using a programmable environmental stability chamber. The selected formulations were filled into amber-colored glass vials and securely sealed. The samples were stored under the specified conditions and evaluated at predetermined intervals of 0, 30, 60, and 90 days. At each interval, the formulations were assessed for drug entrapment efficiency, percentage mucoadhesion, and in-vitro drug release.[44]

CONCLUSION

Gastroretentive mucoadhesive microspheres represent an advanced and effective approach in oral drug delivery, offering improved gastric retention, enhanced bioavailability, and better therapeutic efficacy. The combination of gastroretentive behavior and mucoadhesion allows prolonged residence in the stomach, sustained drug release, and maintenance of effective plasma drug concentrations. Mucoadhesive microspheres have proven to be a promising tool for delivering drugs to specific sites in a controlled or sustained manner, thereby increasing drug absorption and overall bioavailability. Considering their advantages and flexibility, gastroretentive mucoadhesive microspheres are expected to play an important role in the development of new pharmaceutical formulations using advanced techniques and materials, with great potential for future research.

REFERENCE

1. Begum SA, Sura RS, Phanindra B, et al. Formulation and Evaluation of Mucoadhesive Buccal Tablets of Captopril. Res J Pharm., Dos., Forms. Technol., 2019; 11(3): 162-64.
2. Gavini V, Ragini B, Kaumudi K, Hills V. Mucoadhesive microspheres-a novel approach of drug targeting. World J Pharm Pharm., Sci., 2014; 3(10): 310-35.
3. Lehr CM. Bioadhesion technologies for the delivery of peptide and protein drugs to the gastrointestinal tract. Crit Rev Ther Drug Carrier Syst., 1994; 11(2-3): 119-60.
4. Malvey S, Muthu AK, Balamurugan K, Rao JV, Puchchakayala G, Ravinder E, Kshirasagar N. Mucoadhesive Microsphere Drug Delivery System (MMDDS): A Mini Review. Int J Clin., Exp., Med., Res., 2021; 5(4): 435-44.
5. Reddy LH, Murthy RS. Floating dosage systems in drug delivery. Crit Rev Ther Drug Carrier Syst., 2002; 19(6): 553-85.

6. Salamat-Miller N, Chittchang M, Johnston TP. The use of mucoadhesive polymers in buccal drug delivery. Adv., Drug Deliv., Rev. 2005; 57(11): 1666-91.
7. Mule MS, Mr. Kshirsagar RV Gastroretentive mucoadhesive microsphere: a review. Indo Am J Pharm., Res., 2011; 1(6): 483-505.
8. Rathod HJ, Mehta DP, Yadav JS. A review on gastroretentive drug delivery systems. Pharma Tutor., 2016; 4(7): 29-40.
9. Md S, Singh G, Ahuja A, Khar R, Baboota S, Sahni J, Ali J. Mucoadhesive microspheres as a controlled drug delivery system for gastroretention Syst., Rev., Pharm., 2012; 3(1): 4-14.
10. Pant S, Badola A, Kothiyal P. A review on gastroretentive drug delivery system. Indian J Pharm., Biol., Res., 2016; 4(2): 1-10.
11. Jassal M, Nautiyal U, Kundlas J, Singh D. A review: Gastroretentive drug delivery system (grdds). Indian J Pharm., Biol., Res., 2015; 3(1): 82-92.
12. More S, Gavali K, Doke O, Kasgawade P. Gastroretentive drug delivery system. J Drug Deliv., Ther., 2018; 8(4): 24-35.
13. Prajapati VD, Jani GK, Khutliwala TA, Zala BS. Raft forming system An upcoming approach of gastroretentive drug delivery system. J Control Release, 2013; 168(2): 151-65.
14. Kataria S, Middha A, Sandhu P, Bilandi A, Kapoor B. Microsphere: A review. Int J Res Pharm., Chem., 2011; 1(4): 1185-98.
15. Vaibhav R, Satya SS, Roop S, Lal N, Pragya Y. Microspheres: a promising drug carrier. J Drug Deliv., Ther., 2016; 6(3): 18-26.
16. Sharma N, Purwar N, Gupta PC. Microspheres as drug carriers for controlled drug delivery: a review. Int J Pharm., Sci., Res., 2015; 6(11): 4579-87.
17. Singh C, Purohit S, Singh M, Pandey BL. Design and evaluation of microspheres: A Review. J. Drug Deliv., Res., 2013; 2(2): 18-27.
18. Gavali KV, Kengar MD, Chavan KV, Anekar VP, Khan NI. A review on microsphere and it's application. Asian J Pharm Res., 2019; 9(2): 123-29.
19. Midha K, Nagpal M, Arora S. Microspheres: a recent update. Int J Recent Sci Res., 2015; 50(8): 5859-67.
20. Sinha VR, Goyel V, Trehan A. Radioactive microspheres in therapeutics. Die Pharmazie-Int J Pharm., Sci., 2004; 59(6): 419-26.
21. Patel S, Kumhal RP, Dinesh PA, Gorantli CC. A review on microspheres: types, methods.

of preparation, effects of process variables and applications. Am J Pharm Tech Res., 2020; 10(4): 123-40.

22. Patil SB, Sawant KK. Mucoadhesive microspheres: a promising tool in drug delivery. Bentham Science Publishers Ltd .Curr., Drug Deliv., 2008; 5(4): 312-18.
23. Khan M, Ansari VA, Kushwaha P, Kumar A, Akhtar J. Mucoadhesive microspheres for controlled delivery of drugs. Asian J Pharm., Clin., Res., 2015; 8(4): 17-20.
24. Kataria S, Middha A, Sandhu P, Bilandi A, Kapoor B. Microsphere: A review. Int J Res Pharm Chem., 2011; 1(4): 1185-98.
25. Maniyar AH, Patil RM, Kale MT, Jain DK, Baviskar DT. Mucoadhesion: A new polymeric controlled drug delivery. Int J Pharm., Sci., Rev., Res., 2011; 8(1): 54-60.
26. Boddupalli BM, Zulkar MNK, Nath RA, Banji D. Mucoadhesive drug delivery system: An overview. J Adv., Pharm., Tech., Res., 2010; 1(4): 381–87.
27. Mahajan P, Kaur A, Aggarwal G, Harikumar SL. Mucoadhesive drug delivery system: a review. Int J Drug Dev., Res., 2013; 5(1): 11-20.
28. Muthukumaran M, Dhachinamoorthi D, Chandra KB, Sriram NA. Review on polymers used in mucoadhesive drug delivery system. J Pharm Ind., Res., 2011; 1(2): 122-27.
29. Madsen F, Eberth K, Smart JD. A rheological assessment of the nature of interactions between mucoadhesive polymers and a homogenised mucus gel. Biomaterials, 1998; 19(11-12): 1083-92.
30. Phanindra B, Moorthy BK, Muthukumaran M, Recent advances in mucoadhesive/bioadhe sive drug delivery system: A review. Int J Pharma., Med., Biol., Sci., 2013; 2(1): 68-84.
31. Lalge M, Sharma PK, Bhandari A, Garud A, Garud N. Mucoadhesive drug delivery system: a review. Crit., Rev., Pharm., Sci., 2014; 3(3): 17-29.
32. Parmar HK, Pandya KK, Pardasani LJ, Panchal VS, Tandel T. A systematic review on mucoadhesive drug delivery system. World J Pharm., Res., 2017; 6(9): 337-66.
33. Kavitha K, Kumar MR, Singh SJ. Novel mucoadhesive polymers-a review. J Appl Pharm Sci., 2011; 1(8): 37-42.
34. Shaikh R, Singh TR, Garland MJ, Woolfson AD, Donnelly RF. Mucoadhesive drug delivery systems. J. Pharm., Bioallied Sci., 2011; 3(1): 89-100.
35. Vinukonda A, Kunderu R, Gunnam S. A review on mucoadhesive microspheres. Int J Chemtech Res., 2018; 11(9): 277-89.
36. Patil SB, Murthy RS, Mahajan HS, Wagh RD, Gattani SG. Mucoadhesive polymers: Means of improving drug delivery. Pharma., Times., 2006; 38(4): 25-28.

37. Kaurav H, Hari Kumar SL, Kaur A. Mucoadhesive microspheres as carriers in drug delivery: a review. Int., J Drug Dev., Res., 2012; 4(2): 21-34.
38. Swapna S, Balaji A, Shankar MS, Vijendar A. Microspheres as a promising mucoadhesive drug delivery system-review. Int J Pharm Sci., Rev., Res., 2013; 23(2): 8-14.
39. Kumari N, Aggarwal G, Harikumar SL. Mucoadhesive microspheres: A review. J Drug Deliv., Ther., 2014; 4(5): 48-54.
40. Shriwas K, Niranjan SK. A brief review on mucoadhesive microspheres in drug delivery system. World J Pharm., Res., 2019; 8(10): 484-04.
41. Garg A, Upadhyay P. Mucoadhesive microspheres: A short review. Asian J. Pharm. Clin. Res., 2012; 5(3): 24-27.
42. Malvey S, Muthu AK, Balamurugan K, Rao JV, Puchchakayala G, Ravinder E, Kshirasagar N. Mucoadhesive Microsphere Drug Delivery System (MMDDS): A Mini Review. Int J Clin., Exp., Med., Res., 2021; 5(4): 435-44.
43. Bogataj M, Vovk T, Kerec M, Dimnik A, Grabnar I, Mrhar A. The correlation between zeta potential and mucoadhesion strength on pig vesical mucosa. Biol., Pharm., Bull. 2003; 26(5): 743-46.
44. Manivannan R, Rao BL, Reddy VK. Design and Evaluation of Imatinib Mesylate Loaded Microspheres for Stomach Specific Drug Delivery. Br. J. Pharm. Res., 2014; 4(3): 381-96.