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A REVIEW ARTICLE ON MUCOADHESIVE MICROSPHERE AS A CONTROLLED DRUG DILIVERY SYSTEM

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ABSTRACT

Microspheres are spherical powders consisting of proteins or synthetic polymers having a particle size ranging from 1-1000 µm. Mucoadhesion is a topic of current interest in the design of drug delivery systems. Mucoadhesive microspheres provide a prolonged residence time at the site of application or absorption and facilitate an intimate contact with the underlying absorption surface and improve or better therapeutic response of the drug. Mucoadhesion while considering drug delivery is having several merits, because of the ideal physiochemical characters of the mucosal membrane. There are various approaches in delivering a therapeutic substance to the target site in a sustained controlled release fashion. Mucoadhesive microspheres deliver the drug to the target site with specificity, if modified, and to maintain the desired concentration at the site of action. Several synthetic and natural polymers are identified as suitable candidates for mucoadhesive formulation. Microspheres received much attention not only for prolonged release, but also for targeting of anticancer drugs.

KEYWORDS: Microspheres, controlled release, Mucoadhesion.

INTRODUCTION

The novel system of drug delivery offering improvement the therapeutic effectiveness of drugs by providing sustained, controlled delivery and targeting the drug to desired site. A number of systems containing various types of polymers were fabricated with drugs into dosage form with the aim of sustaining drug levels and hence drug action is obtained for an extended period of time.[6] However, a lack of understandings of anatomical and physiological barriers imposed impediment on the development of efficient delivery system. The modern era of controlled release technology represents the period in which an attempt at

drug development is emphasized. The drug delivery system should deliver a drug at a rate dictated with side effects like hot flushes, musculoskeletal pain. Taking into account these limitations of delivering by the needs of the body over a specified period of treatment.[5]

In recent years, drug delivery technology is becoming increasingly sophisticated as pharmaceutical scientists across the globe acquire a better understanding of the physicochemical and biological parameters related to the performance of various systems which enhances desirable therapeutic objectives while minimizing side effects. Despite significant advancements in drug delivery, oral route remains the preferred route for administration of several therapeutic agents due to improved patient compliance, ease of administration, flexibility in design of formulation etc. Conventional oral dosage forms such as tablets, capsules etc provide specific drug concentration in systemic circulation without offering any control over drug delivery and also great fluctuations in plasma drug level, as compared to oral controlled drug delivery systems which provide a release profile predominantly controlled by the design of the system itself.[7]

Oral controlled release dosage forms have been extensively used to enhance therapy with better bioavailability. However, developmental process is hindered due to number of physiological activities such as an inability to restrain and locate the delivery system within the desired region of gastrointestinal tract (GIT), fluctuation in gastric emptying and motility.[21] It can be anticipated that, depending upon the physiological state of subject and design of pharmaceutical formulation, the emptying process can last from few minutes to 12 hrs. This variability in turn, may lead to unpredictable time to achieve peak plasma level, since the majority of drugs are preferentially absorbed in upper part of small intestine.[19] Furthermore, the relatively brief gastric emptying time in humans, which normally averages 2-3 hrs through the major absorption zone can result in an incomplete drug release from the dosage form leading to diminished efficacy of administered dose. Thus, control of placement of a drug delivery system in a specific region of the GI tract offers numerous advantages, especially for drugs exhibiting an absorption window in the GI tract or drugs with a stability problem. Overall, the intimate contact of drug delivery system with the absorbing membrane has the potential to maximize drug absorption and may also influence the rate of drug absorption. These considerations have led to the development of oral controlled release dosage forms possessing gastric retention capabilities.[20]

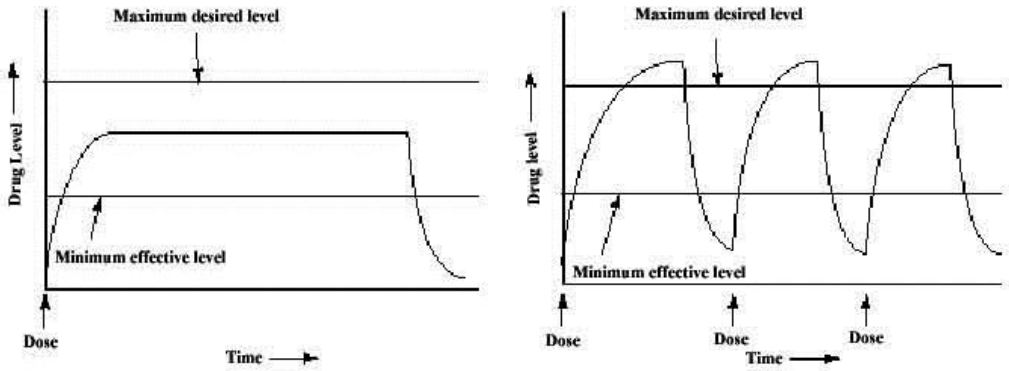
CONTROLLED DRUG DELIVERY SYSTEMS

Oral controlled release (CR) dosage forms (DFs) have been developed over the past three decades due to their considerable therapeutic advantages such as ease of administration, patient compliance and flexibility in formulation. Control of placement of a drug delivery system (DDS) in a specific region of the GI tract offers advantages for a variety of important drugs characterized by a narrow absorption window in the GIT or drugs with a stability problem.[22] Control of placement of a drug delivery system (DDS) in a specific region of the GIT offers advantages for a variety of important drugs characterized by a narrow absorption window in the GIT or drugs with a stability problem the bioavailability of drugs with an absorption window in the upper small intestine is generally limited with conventional pharmaceutical dosage forms. The residence time of such systems and thus, of their drug release into the stomach and upper intestine is often short.

To overcome this restriction and to increase the bioavailability of these drugs, controlled drug delivery systems with a prolonged residence time in the stomach can be used. Incorporation of the drug into a CR-delivery system, which releases its payload in the stomach over a prolonged time period, can lead to significant therapeutic advantages owing to various pharmacokinetic and Pharmacodynamic aspects. Gastro retentive dosage forms (GRDFs) are designed to be retained in the stomach for a prolonged time and release their active ingredients and there by enable sustained and prolonged input of the drug to the upper part of the gastrointestinal (GI) tract. This technology has generated enormous attention over the last few decades owing to its potential application to improve the oral delivery of some important drugs for which prolonged retention in the upper GI tract can greatly improve their oral bioavailability and/or their therapeutic outcome. The challenge to develop efficient gastro retentive dosage forms began near about 20 years ago.[23]

Many attempts have been made to devise an extended release GRDDS where the dosage form is small enough to ingest and then retained in the GI area for a long enough time for the active agent to be dissolved and eventually absorbed. For example, many swelling and expanding systems have been attempted. There are dosage forms that swell and change their size there by mucoadhesive to the surface.[24] The basic rationale for controlled drug delivery is to alter the pharmacokinetic and Pharmacodynamic of pharmacologically active moieties by using novel drug delivery systems or by modifying the molecular structure and/or physiological parameters inherent in a selected route of administration. The term controlled

release implies a predictability and reproducibility in the drug release kinetic, which means that the release of drug from controlled-release drug delivery system proceeds at a rate profile that is not only predictable kinetically, but also reproducible from one unit to another.[25] The drug delivery systems are designed to deliver the drug in such a way that the levels are maintained within the therapeutic window effective for a long period till the system continues to deliver the drug at a particular rate. This minimizes several potential problems characterized by large peaks and troughs in the drug concentration time curve frequent dosing for drugs with short biological half-life, and above all the patient compliance.



(a) **(b)**

Figure 1.1 Drug concentration levels for (a) conventional system; (b) controlled release system

Controlled release drug delivery system has several advantages compared with single unit dosage forms. Recently gastro retentive mucoadhesive microspheres are gaining much more favor among various other dosage forms. Various potential benefits of these multiparticulate systems are presented in the following text:

- Improves patient comfort and compliance by decreasing dose frequency
- Enhances the bioavailability and therapeutic efficacy of drugs with narrow absorption window in the upper part of GIT
- Gastric retention time increases because of buoyancy principle
- Drug releases in a controlled manner for prolonged period of time
- Site-specific drug delivery can be achieved
- Releases drug uniformly and there is no risk of dose dumping
- Avoidance of gastric irritation, because of sustained release effect
- Less inter- and intra-subject variability
- Minimizes the counter activity of the body leading to higher drug efficiency

- Fluctuations in drug concentration are minimized. Therefore, concentration dependent adverse effects can be reduced
- Sustained mode of drug release enables extension of the time over a critical concentration and thus enhances the pharmacological effects and improves the clinical outcomes
- Extend patent protection globalize product, and provide new business opportunities.

MUCOADHESIVE MICROSPHERES

Mucoadhesive microspheres include micro particles of 1-1000 µm range in diameter which comprises of entire mucoadhesive polymer or having an outer coating of it.

Bioavailability of the drugs are enhanced due to their highsurface to volume ratio which provides an intimate contact with the mucus layer, resulting in controlled and sustained release of drug from dosage form and specific targeting of drugs to the absorption site.[27]
The rationale of developing mucoadhesive microspheres are that the formulation will be confined on a biological surface for localized drug delivery and the drug will be released close to the site of action with a consequent enhancement of bioavailability.[28]

A number of different substances both biodegradable as well as non-biodegradable have been investigated for the preparation of microspheres. These materials include polymer of natural origin or synthetic origin and also modified natural substances. Range of microspheres was prepared using both hydrophilic and hydrophobic polymer. Hydrophilic polymers includes gelatin, agar, egg albumin, starch, chitosan, cellulose derivatives; HPMC. Hydrophobic polymer include ethyl cellulose, polylactic acid, PMMA, acrylic acid ester etc.[26]

Mucoadhesive drug delivery is of particular interest for drugs that act locally in the nasal buccal, stomach, The idea of mucoadhesives began with the clear need to localize a drug at certain sites in the GI tract. A number of mucoadhesive-based dosage forms, including sustained- release tablets, semisolid forms, powders, microsphere and/or nanoparticles in the GI tract, have been widely studied. Nonetheless, successful systems that will be retained in the GI tract of humans for a desirable time have not yet been developed.

The primary objectives of mucoadhesive dosage forms are to provide intimate contact of the dosage form with the absorbing surface and to increase the residence time of the dosage form at the absorbing surface to prolong drug action. Due to mucodhesion, certain water-soluble polymers become adhesive on hydration and hence can be used for targeting a drug to a

particular region of the body for extended periods of time. Mucoadhesive drug delivery systems are expected to remain adhesive in a lasting way upon the gastric mucosa and consequently to enhance bioavailability of drugs. The lasting mucosal adhesion of controlled release dosage form might also provide a suitable manner to constantly deliver a drug locally into the stomach and achieve the sustained site-specific therapeutic action.

Advantages of mucoadhesive microspheres.[17-18]

1. Increased prolonged time of drug at the absorption site results in enhanced bioavailability of the drug due to adhesion and intimate contact.
2. Use of specific bio adhesive polymers results in targeting of sites or tissues
3. It offers an excellent route for systemic delivery of drugs with high first-pass metabolism thereby offering greater bioavailability.
4. Maintenance of therapeutic plasma drug concentration

MUCOADHESION

Bio adhesion is defined as a phenomenon in which materials are held for a longer period of time to the mucus membrane by means of interfacial forces. In biological systems, bio adhesion can be classified into 3 types.

1. Type 1, adhesion between two biological phases, for example, platelet aggregation and wound healing.
2. Type 2, adhesion of a biological phase to an artificial substrate, for example tissue, cell adhesion to culture dishes and bio film formation on prosthetic devices and inserts.
3. Type 3, adhesion of an artificial substance to a biological substrate, for example, adhesion of synthetic hydro gels to soft tissues

MECHANISM OF MUCOADHESION.[8]

Mechanism of bio adhesion can be described in two successive steps of formulation:

1. Wetting and Contact stage- Wetting and swelling of polymer to permit intimate contact with biological tissue (Figure 1).
2. Consolidation stage- Interpenetration of bio adhesive polymer chains and entanglement of polymer and mucin chains.

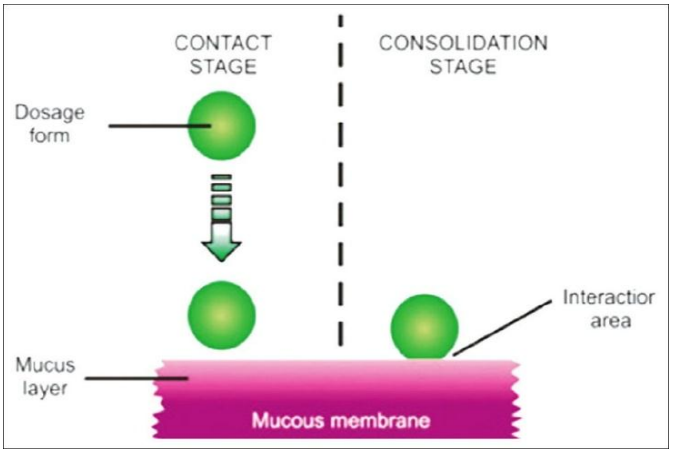


Figure 1: Mechanism of Mucoadhesion

Theories of Mucoadhesion.[9]

Different theories of mucoadhesion include electronic, wetting, adsorption, diffusion, mechanical and fracture theories.

ELECTRONIC THEORY

Electronic theory include transfer of electrons across the adhesive interface and adhering surface which results in formation of the electrical double layer at the interface and a series of attractive forces responsible for maintaining contact between the two layers.

Wetting theory

Wetting theory describes the ability of bio adhesive polymer to spread and develop intimate contact with the mucous membrane. Spreading coefficient of polymer must be positive and Contact angle between polymer and cells must be near to zero.

ADSORPTION THEORY

According to the Adsorption theory, after an initial contact between two surfaces, the materials adhere because of surface forces acting between the chemical

Structures at the two surfaces.

INTERPENETRATION THEORY OR DIFFUSION THEORY

Diffusion theory describes the entanglements of the polymer chains in to mucus network and reaches a sufficient depth within the opposite matrix to allow formation of a semi permanent bond. The exact depth needed for good bio adhesive bonds is estimated to be in the range of 0.2–0.5 μm.

MECHANICAL THEORY

Adhesion arises from an interlocking of liquid adhesive into irregularities on the rough surface which provide an increased surface area available for interaction.

FRACTURE THEORY

This theory relates to the force necessary to separate to surfaces to the adhesive bond strength and it is often used to calculate fracture strength of adhesive bonds.

FORMULATION FACTORS AFFECTING MUCOADHESION.[11-13]

Factors affecting mucoadhesion include:

I. Polymer related factors

II. Environmental related factors

III. Physiological factors

I. Polymer related factors

Hydrophilicity Bioadhesive polymers possess numerous hydrophilic functional groups which allow hydrogen bonding with the substrate, swelling in aqueous media, thereby allowing maximal exposure of potential anchor sites.

Molecular weight- The molecular weight should be optimum for the maximum mucoadhesion. Low-molecular-weight polymers favor the interpenetration of polymer molecules whereas physical entanglements are favoured at higher molecular weights.

Cross-linking density- Cross-link density is inversely proportional to the degree of swelling. Lower the cross-link density, higher the flexibility and hydration rate; larger the surface area of polymer, better the mucoadhesion.

Chain flexibility-Chain flexibility is critical for interpenetration and entanglement of mucoadhesive polymers. Highly cross linked such as water-soluble polymers decrease the mobility of individual polymer chains and reduces bio adhesive strength.

II. Environmental factors

pH- pH can influence the charge on the surface of mucus as well as of certain ionisable mucoadhesive polymers. If the local pH is above the pKa of the polymer, it will be largely ionized; if the pH is below the pKa of the polymer, it will be largely unionized.

Initial Contact time-Initial Contact time determines the extent of swelling and interpenetration of the mucoadhesive polymer chains. Moreover, mucoadhesive strength increases as the initial contact time increases.

III. Physiological factors

Mucin turnover- The residence time of mucoadhesive depends on whether the polymer is soluble or insoluble in water and the associated turnover rate of mucin. Mucoadhesion decreases with increase mucin turnover.

Polymer characteristics that are required to obtain adhesion

1. Sufficient quantities of hydrogen-bonding chemical groups (-OH and -COOH).
2. Anionic surface charges.
3. High molecular weight of mucin strands with flexible polymer chains and/or interpenetration of mucin strands into a porous polymer substrate.

Sites for Mucoadhesive Drug Delivery Systems

Buccal cavity

At this site, first-pass metabolism is avoided, and the nonkeratinized epithelium is relatively permeable to drugs. Due to the short residence time, it is selected as one of the most suitable areas for the development of bioadhesive devices that adhere to the buccal mucosa and remain in place for a considerable period of time.

Nasal cavity

Ease of access, avoidance of first-pass metabolism and a relatively permeable and well-vascularised membrane, contribute to make the nasal cavity an attractive site for drug delivery.

Gastrointestinal tract

The gastrointestinal tract has been the subject of intense study for the use of bioadhesive formulations to improve drug bioavailability.

Eye

One major problem for drug administration to the eye is rapid loss of the drug and or vehicle as a result of tear flow, and so it is a target for prolonging the residence time by bioadhesion.

Polymers used in mucoadhesive drug delivery system

Mucoadhesive polymers are water-soluble and water insoluble polymers, which include:

a) Hydrophilic polymers

These polymers swell when come in contact with water and eventually undergo complete dissolution. Systems coated with these polymers show high mucoadhesion (Table 1).

Examples: Hydroxy propyl methyl cellulose, Sodium carboxy methyl cellulose.

b) Hydrogels[14]

These are three-dimensionally cross-linked polymer chains which have the ability to hold water within its porous structure. The water holding capacity of the hydrogels is mainly due to the presence of hydrophilic functional groups.

Examples: Polycarbophil, Carbopol, Polyox.

c) Co-polymers/Interpolymer complex

A block copolymer is formed when the reaction is carried out in a stepwise manner, leading to a structure with long sequences or blocks of one monomer alternating with long of the other.

d) Thiolated polymers (Thiomers)[15]

These are hydrophilic macromolecules exhibiting free thiol groups on the polymeric backbone. **Examples** Cationic thiomers: Chitosan–cysteine. Anionic thiomers: Poly (acrylic acid)–cysteine.

Table 1: List of Mucoadhesive polymers[10]

Criteria	Category	Examples
Source	Natural/semi- synthetic	Chitosan, Agarose, Various gums (guar gum, Xanthan gum, Gellan, Pectin
	Synthetic	Cellulose derivatives like HPC, HPMC; Polyacrylic based polymers
Aqueous solubility	Water-soluble polymers	Carbopol, HPMC, HPC
	Water-insoluble polymer	Chitosan, Ethyl cellulose
Charge	Cationic	Aminodextran, Chitosan
	Anionic	Carboxyl methyl cellulose (CMC), Polyaacrylic acid, (PAA), Sodium alginate, Xanthan gum.
	Non-ionic	HPC, Polyvinyl alcohol, Polyvinyl Pyrrolidone.

HPMC- Hydroxy propyl methyl cellulose, HPC- Hydroxy propyl cellulose.

METHODS OF PREPARATION

Different types of methods are employed for the preparation of the microspheres. These include.

1. Emulsion cross-linking method
2. Solvent evaporation
3. Spray drying
4. Phase separation coacervation technique
5. Orifice-ionic gelation method
6. Hot melt microencapsulation

Emulsion cross-linking method (Emulsion solvent diffusion technique)

Natural polymers are dissolved or dispersed in aqueous medium followed by dispersion in the non-aqueous medium i.e., oil. In the second step, cross-linking of the dispersed globule is carried out either by means of heat or by using the chemical cross- linking agents like glutaraldehyde, formaldehyde. Heat denaturation is not suitable for the thermolabile drugs while the chemical cross-linking suffers disadvantage of excessive exposure of active ingredient to chemicals if added at the time of preparation.[30]

This technique is widely employed by large number of pharmaceutical industries to obtain the controlled release of drug.[31] This approach involves the emulsification of an organic solvent (usually methylene chloride) containing dissolved polymer and dissolved/dispersed drug in an excess amount of aqueous continuous phase, with the aid of an agitator. The concentration of the emulsifier present in the aqueous phase affects the particle size and shape. When the desired emulsion droplet size is formed, the stirring rate is reduced and evaporation of the organic solvent is realized under atmospheric or reduced pressure at an appropriate temperature. Subsequent evaporation of the dispersed phase solvent yield solid polymeric microparticles entrapping the drug. The solid microparticles are recovered from the suspension by filtration, centrifugation, or Lyophilization.[32] For emulsion solvent evaporation, there are basically two systems which include oil-in-water (o/w) and water-in-oil (w/o) type. Mucoadhesive microsphere containing Reloxifene hydrochloride was prepared using emulsion solvent diffusion technique. The drug to polymer ratio was used to prepare in the different formulation. The polymer content was a mixture of Chitosan and hydroxypropylmethylcellulose (HPMC K4M). The drug polymer mixture is dissolved in a mixture of ethanol and dichloromethane was dropped in to 0.75% polyvinyl alcohol solution.

The solution was stirred with a propeller-type agitator at 40° C temperature for 1 hrs at 300 rpm. The formed mucoadhesive microspheres were passed through sieve no:- 12 and washed with water and dried at room temperature in desiccators. The various batches of mucoadhesive microsphere were prepared as follows.

Solvent Evaporation

The processes are carried out in a liquid manufacturing vehicle. The microcapsule coating is dispersed in a volatile solvent which is immiscible with the liquid manufacturing vehicle phase. A core material to be microencapsulated is dissolved or dispersed in the coating polymer solution (Figure 2). With agitation the core material mixture is dispersed in the liquid manufacturing vehicle phase to obtain the appropriate size microcapsule. The mixture is then heated if necessary to evaporate the solvent for polymer of the core material, polymer shrinks around the core.[33]

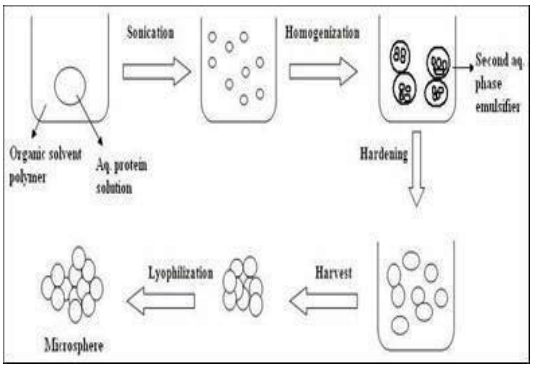


Figure 2: Solvent evaporation method for preparation of Microspheres.[33]

Oil-in-Water emulsion solvent evaporation technique

In this method, the polymer is dissolved in an organic solvent such as dichloromethane, chloroform, or ethyl acetate, either alone or in combination. The drug is either dissolved or dispersed into polymer solution and this solution containing the drug is emulsified into an aqueous phase to make an oil-in water emulsion by using a surfactant or an emulsifying agent. After the formation of a stable emulsion, the organic solvent is evaporated either by increasing the temperature under pressure or by continuous stirring. Solvent removal from embryonic microspheres determines the size and morphology of the microspheres. It has been reported that the rapid removal of solvent from the embryonic microspheres leads to polymer precipitation at the o/w interface. This leads to the formation of cavity in microspheres, thus making them hollow to impart the mucoadhesive properties.[34]

Oil-in-Oil emulsification solvent evaporation technique

This oil-in-oil (sometimes referred as water-in-oil) emulsification process is also known as non aqueous emulsification solvent evaporation. In this technique, drug and polymers are co-dissolved at room temperature into polar solvents such as ethanol, dichloromethane, acetonitrile etc. with vigorous agitation to form uniform drug–polymer dispersion. This solution is slowly poured into the dispersion medium consisting of light/heavy liquid paraffin in the presence of oil soluble surfactant such as Span. The system is stirred using an overhead propeller agitator at 500 revolutions per minute (rpm) and room temperature over a period of 2–3 h to ensure complete evaporation of the solvent. The liquid paraffin is decanted and the microparticles are separated by filtration through a Whatmann filter paper, washed thrice with n-hexane, air dried for 24 h and subsequently stored in desiccator.

Spray Drying.[35]

In Spray Drying, the polymer is first dissolved in a suitable volatile organic solvent. The drug is dispersed in the polymer solution under high-speed homogenization (Figure 3). This dispersion is then atomized in a stream of hot air, leads to the formation of the small droplets from which the solvent evaporate instantaneously leading the formation of the microspheres in a size range 1-100 μm.

Phase separation coacervation technique.[36]

In this method, the drug particles are dispersed in a solution of the polymer and an incompatible polymer is added to the system which makes first polymer to phase separate and engulf the drug particles. Addition of nonsolvent results in the solidification of polymer. The agglomeration must be avoided by stirring the suspension using a suitable speed stirrer.

Orifice-Ionic Gelation Method.[37,38]

Polymer is dispersed in purified water to form a homogeneous polymer mixture. Drug is added to the polymer matrix and mixed thoroughly to form a smooth viscous dispersion which is then sprayed into calcium chloride solution by continuous stirring. Produced droplets are retained in the calcium chloride solution for 15 minutes to complete the curing reaction and to produce rigid spherical microspheres. The resulting microspheres are collected by decantation, and the product is washed repeatedly with purified water and then dried at 45°C for 12 hrs.

Hot Melt Microencapsulation.[39]

The polymer is first melted and then mixed with solid particles of the drug that have been sieved to less than 50µm. The mixture is suspended in a non-miscible solvent (like silicone oil), continuously stirred, and heated to 5°C above the melting point of the polymer. Once the emulsion is stabilized, it is cooled until the polymer particles solidify. The resulting microspheres are washed by decantation with petroleum ether.

Applications of Microspheres.[16]

1. Microspheres in vaccine delivery for treatment of diseases like hepatitis, influenza, and pertusis.
2. Microspheres act as potential carriers for targeting to various organs.
3. Monoclonal antibodies mediated microspheres targeting.
4. Scintiographic imaging of the tumors masses in lungs using labeled human serum albumin microspheres.
5. Used for radio synvectomy of arthritis joint, local radiotherapy, interactivity treatment.

Mucoadhesive drug delivery systems

Mucoadhesive drug delivery systems are among the several approaches that have been developed in order to increase the gastric residence time of the dosage forms. The multiple unit system has been developed to identify the merit over a single unit dosage form because the single unit mucoadhesive systems are more popular but have a disadvantage owing to their "all-or nothing" emptying process, leading to high variability of the gastrointestinal transit time. Still, the multiple unit dosage forms may be better suited because they are claimed to reduce the inter subject variability in absorption and lower the probability of dose dumping. Such a dosage form can be widely distributed throughout the gastrointestinal tract (GIT), which afforded the possibility of a longer lasting retention and more reliable release of the drug from the dosage form. drug delivery systems is one of the important approaches to achieve sufficient drug bioavailability by gastric retention. These delivery systems are desirable for drugs with an absorption window in the stomach or in the upper small intestine. In order to design successful mucoadhesive dosage forms, three major conditions should be met (a) They should release contents slowly to serve as a reservoir. (b) They must have specific gravity lower than gastric contents (1.004 – 1.01 gm/cm3) (c) They must form a cohesive gel barrier.[40]

Objective & Rationale of the Study

In the present scenario, there is an ever increasing demand for patient compliance dosage forms. One of an important innovation in this direction is the development of gastro retentive mucoadhesive dosage forms. mucoadhesive dosage form is one of the important approaches to achieve gastric retention by maximizing drug bioavailability. This delivery system is desirable for drugs with an absorption window in the stomach. Mucoadhesive dosage systems have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the dosage form is mucoadhesive on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased gastric residence time and better control of fluctuations in plasma drug concentration. Recently, large number of drugs has been formulated as mucoadhesive drug delivery systems with an objective to sustain and control release by restricting the dosage form in the stomach.

These two drawbacks can be overcome by developing a mucoadhesive dosage form so as to remain buoyant in the stomach. Therefore, it is a suitable model candidate for gastroretentive formulation.

CONCLUSION

Mucoadhesive drug delivery system represents frontier and promising avenue of pharmaceutical sciences which involve interdisciplinary scientific advancements in better health care along with varied therapeutic interventions. Significant attempts have been made worldwide to explore these systems according to patient requirements, both in terms of therapeutic efficacy and compliance. Relatively short gastric residence time results in an incomplete drug release from the delivery system leading to a diminished effectiveness of the administered dose. Therefore, an effective control of the placement of a delivery system in a specific region of gastrointestinal tract offers numerous advantages, especially for drugs with specific absorption sites in gastrointestinal tract. These considerations have led to the development of controlled release dosage form that possesses the gastric retention abilities. Prolongation of gastric residence time reduces the inter-subject variability and leads to more predictable effect with increased bioavailability especially for drugs with narrow absorption window in the upper part of gastrointestinal tract. As the total transit time is prolonged, the number of doses in the regimen can be reduced. Retention of drug delivery system in stomach

prolongs overall GI transit time, thereby resulting in improved bioavailability.

Microencapsulation is one of the most fascinating fields in arena of pharmaceutical technology. Microspheres is a monolithic structure made of a continuous phase of one or more polymers in which particulate drug is dispersed throughout the matrix, at either the macroscopic (particulates) or molecular level. Multiparticulate mucoadhesive drug delivery system has relative merits as compared to single unit preparations. The mucoadhesive dosage forms are to provide intimate contact of the dosage form with the absorbing surface and to increase the residence time of the dosage form at the absorbing surface to prolong drug action. Due to mucodhesion, certain water-soluble polymers become adhesive on hydration and hence can be used for targeting a drug to a particular region of the body for extended periods of time. The mucosa lines a number of regions of the body including the gastrointestinal tract. In these systems, dosage of the drug substance is divided on a plurality of subunit typically consisting of thousands of spherical particles. With mucoadhesive microspheres, it is considered that majority of particles will remain above the stomach contents for an extended period of time. This approach reduces the inter subject variability in absorption, lower the probability of dose dumping and bursting associated with the single-unit systems. It has also been described that multiple unit mucoadhesive dosage forms distribute more uniformly within the gastric content, resulting in long lasting effects.

The rationale of present study was to preclude the problem of in vivo instability i.e. instability in the alkaline medium of intestine associated with conventional dosage form by formulating a gastroretentive mucoadhesive microspheres which aimed to increase the gastric retention time, thereby increasing stability and bioavailability. Recently, many drugs have been formulated as mucoadhesive drug delivery systems with an objective to sustain and control the drug release by restricting dosage form in the stomach. Exhaustive and advanced research of recent past has resulted in the development of various mucoadhesive drug delivery systems.

Preformulation studies were carried out to determine physical characteristics of drug, and to establish its compatibility with common excipients. In this study, various parameters were evaluated such as identification of drug using FTIR, melting point determination, solubility analysis, physical state analysis and compatibility studies using FTIR.

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