Review

MICROSPHERE: MORDEN APPROCH OF DRUG CARRIER SYSTEM

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ABSTRACT:

Microspheres are small spherical free flowing powders particles, consisting of proteins or synthetic polymers which are biodegradable in nature with diameters in the micrometer range (typically 1 µm to 1000 µm (1 mm)). Among them microspheric drug delivery system has gained enormous attention due to its wide range of application as it covers targeting the drug to particular site to imaging and helping the diagnostic features. There are various approaches in delivering a therapeutic substance to the target site in a sustained controlled release fashion. One such approach is using microspheres as carriers for drugs. It is the reliable means to deliver the drug to the target site with specificity, if modified, and to maintain the desired concentration at the site of interest without untoward effects.The aim of this article provides a comprehensive review of advantages, methods of preparation, mechanism, routs of administration, different types of microspheres based on natural and synthetic biodegradable polymers and application of microspheres.

KEYWORDS: Microspheres, controlled release, target site, specificity, therapeutic efficacy, novel drug delivery.

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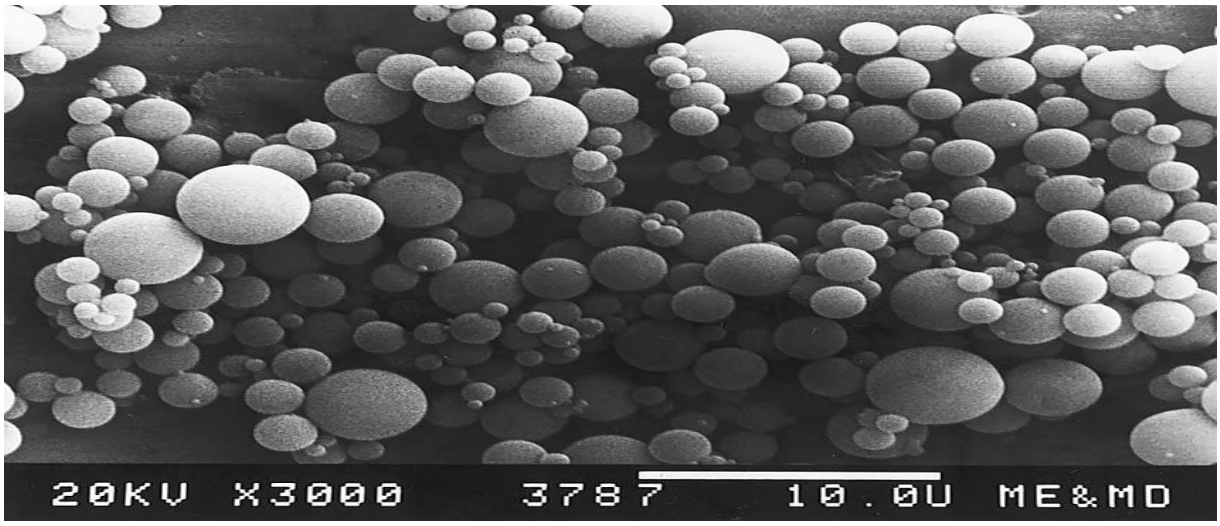
INTRODUCTION

Oral controlled release dosage forms have been developed over the past three decades due to their considerable therapeutic advantages suchas ease of administration, patient compliance and flexibility in formulation. The controlled release drug delivery systems are aimed at controlling the rate of drug delivery, sustaining the duration of therapeutic activity and/or targeting the delivery of the drug to a tissue. Drug release from these systems should be at a desired rate, predictable and reproducible. [1] Among the various approaches for controlled systems, microencapsulation process and microcapsules have gained good acceptance as a process to achieve controlled release and drug targeting. Microspheres carrier systems made from the naturally occurring biodegradable polymers have attracted considerable attention for several years in sustained drug delivery. Recently, dosage forms that can precisely control the release rates and target drugs to a specific body site have made an enormous impact in the formulation and development of novel drug delivery systems. Microspheres form an important part of such novel drug delivery systems. [2] They have varied applications and are prepared using assorted polymers. However, the success of these microspheres is limited owing to their short residence time at the site of absorption

A well designed controlled drug delivery system can overcome some of the problems of conventional therapy and enhance the therapeutic efficacy of a given drug. To obtain maximum therapeutic efficacy, it becomes necessary to deliver the agent to the target tissue in the optimal amount in the right period of time there by causing little toxicity and minimal side effects. There are various approaches in delivering a therapeutic substance to the target site in a sustained controlled release fashion. One such approach is using microspheres as carriers for drugs. Microspheres are characteristically free flowing powders consisting of protiens or synthetic polymers which are biodegradable in nature. Microspheres are solid spherical particles ranging in size from 1-1000µm. They are spherical free flowing particles consisting of proteins or synthetic polymers. The microspheres are free flowing powders consisting of proteins or synthetic polymers, which are biodegradable in nature. There are two types of microspheres; microcapsules and micrometrics, which are described as, Microcapsules are those in which entrapped substance is distinctly surrounded by distinct capsule wall and micrometrics in which entrapped substance is dispersing throughout the microspheres matrix. Solid biodegradable microspheres incorporating a drug dispersed or dissolved through particle matrix have the potential for the controlled release of drug. They are made up of polymeric, waxy, or other protective materials, that is, biodegradable synthetic polymers and modified natural products.



Advantages

1. A highly vascularised sub-epithelial layer allowing for rapid and direct absorption into the systemic circulation, avoiding first-pass hepatic metabolism.
2. A less hostile environment than the gastro-intestinal tract, resulting in reduces drug denaturing.
3. Rapid absorption, higher bioavailability
4. Avoidance of irritation of the gastrointestinal membrane. Reduced risk of overdose.
5. Non-invasive, therefore, reduced risk of infection.
6. Reliable means to deliver the drug to the target site with specificity, if modified, and to maintain the desired concentration at the site of interest without untoward effects.
7. Microspheres received much attention not only for prolonged release, but also for targeting of anticancer drugs to the tumour (3).
8. Blood flow determination: Relatively large microspheres (10-15 µm in diameter) are useful for regional blood flow studies in tissues and organs. In most cases the microspheres are injected at desired locations in the circulatory system and eventually lodge in the capillaries. The microspheres and fluorescent dyes they contain are first extracted from the tissue sample, and then fluorescence is quantitated on a spectrofluorometer or fluorescence microplate reader.

Traditionally, this type of study has been carried out using radio labelled microspheres; however fluorescent microspheres have been shown to be superior in chronic blood flow measurements.

TYPE OF MICROSPHERE

Bioadhesive microspheres

Adhesion can be defined as sticking of drug to the membrane by using the sticking property of the water soluble polymers. Adhesion of drug delivery device to the mucosal membrane such as buccal, ocular, rectal, nasal etc can be termed as bio adhesion. These kinds of microspheres exhibit a prolonged residence time at the site of application and causes intimate contact with the absorption site and produces better therapeutic action.

Magnetic microspheres

This kind of delivery system is very much important which localises the drug to the disease
site. In this larger amount of freely circulating drug can be replaced by smaller amount of magnetically targeted drug. Magnetic carriers receive magnetic responses to a magnetic field from incorporated materials that are used for magnetic microspheres are chitosan, dextran etc.(19) The different type are Therapeutic magnetic microspheres: Are used to deliver chemotherapeutic agent to liver tumour. Drugs like proteins and peptides can also be targeted through this system.(20)

Diagnostic microspheres: Can be used for imaging liver metastases and also can be used to distinguish bowel loops from other abdominal structures by forming nano size particles supramagnetic iron oxides.(21)

Floating microspheres

In floating types the bulk density is less than the gastric fluid and so remains buoyant in stomach without affecting gastric emptying rate. The drug is released slowly at the desired rate, if the system is floating on gasteric contentand increases gastric residence and increases fluctuation in plasma concentration. Moreover it also reduces chances of striking and dose dumping. One another way it produces prolonged therapeutic effect and therefore reduces dosing frequencies. Drug (ketoprofen) given through this form.(22)

Radioactive microspheres

Radio emobilisation therapy microspheres sized 10-30 nm are of larger than capillaries and gets tapped in first capillary bed when they come across. They are injected to the arteries that lead to tumour of interest. So all these conditions radcioactive microspheres deliver high radiation
dose to the targeted areas without damaging the normal surrounding tissues.(23)It differs from drug delivery system, as radio activity is not released from microspheres but acts from within a radioisotope typical distance and the different kinds of radioactive microsphers are α emitters, β emitters, γ emitters.(24)

Polymeric microspheres

The diffent types of polymeric microspheres can be classified as followsand they are biodegradable polymeric microspheres and Synthetic polymeric microspheres.

Biodegradable polymeric microspheres Natural polymers such as starch are used with the concept that they are biodegradable, biocompatible, and also bio adhesive in nature.

Biodegradable polymers prolongs the residence time when contact with mucous membrane due to it's high degree of swelling property with aqueous medium , results gel formation. The rate and extent of drug release is controlled by concentration of polymer(24) and the release pattern in a sustained manner. The main drawback is, in clinical use drug

loading efficiency of biodegradable microspheres is complex and is difficult to control the drug release.

However they provide wide range of application in microsphere based treatement.(25)

Synthetic polymeric microspheres

The interest of synthetic polymeric microspheres are widely used in clinical application, moreover that also used as bulking agent, fillers, embolic particles, drug delivery vehicles etc and proved to be safe and biocompatible.(25)But the main disadvantage of these kind of microspheres, are tend to migrate away from injection site and lead to potential risk, embolismand further organ damage.(26)

DIFFERENT TYPES OF METHODS FOR PREPARATION OF MICROSPHERES:

The microspheres can be prepared by using any of the several techniques given below but choice of the technique mainly depends on the nature of the polymer used, the drug, the intended use and the duration of therapy.

1) SINGLE EMULSION TECHNIQUE(4,7):

The micro particulate carriers of natural polymers i.e., those of proteins and carbohydrates are prepared by single emulsion technique. The natural polymers are dissolved or dispersed in aqueous medium followed by dispersion in non-aqueous medium e.g., oil. In the second step of preparation cross-linking of the dispersed globule is carried out. The cross linking can be achieved either by means of heat or by using the chemical crosslinkers. The chemical cross linking agent used include gluteraldehyde, formaldehyde, terephthaloyl chloride, diacid chloride, etc. Croslinking by heat is carried out by adding the dispersion, to previously heated oil. Heat denaturation is however, 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.

2) DOUBLE EMULSION TECHNIQUE(4,5):

Involves the formation of the multiple emulsions or the double emulsion of type w/o/w and is best suited to the water-soluble drugs, peptides, proteins and the vaccines. This method can be used with both the natural as well as the synthetic polymers. The aqueous protein solution is dispersed in a lipophilic organic continuous phase. This protein solution may contain the active constituents. The continuous phase is generally consisted of the polymer solution that eventually encapsulates of the protein contained in dispersed aqueous phase. The primary emulsion is then subjected to the homogenization or the sonication before addition to the aqueous solution of the polyvinyl alcohol (PVA). This results in the formation of the double emulsion. The emulsion is then subjected to the solvent removal either by solvent evaporation or by solvent extraction process. The solvent evaporation is carried out by maintaining emulsion at reduced pressure or by stirring the emulsion so that the organic phase evaporates out. In the latter case, the emulsion is added to the large quantity of water (with or without surfactant) into which organic phase diffuses out. The solid microspheres are subsequently obtained by filtration and washing. A number of hydrophilic drugs like luteinizing hormone releasing hormone (LH-RH) agonist; vaccines, proteins/peptides and conventional molecule are successfully incorporated in to the microspheres using the method of double emulsion solvent evaporation/extraction.

3) **POLYMERIZATION TECHNIQUES**(4,5):

The polymerization techniques used for the preparation of the microspheres are mainly classified as:

1) Normal polymerization
2) Interfacial polymerization

1.Normal polymerization:

1) Bulk polymerization:

A monomer or a mixture of monomer along with the initiator is usually heated to initiate the polymerization and carry out the process. The catalyst or the initiator is added to the reaction mixture to facilitate or accelerate the rate of the reaction. The polymer so obtained may be molded or fragmented as microspheres. For loading of drug, adsorptive drug loading or adding drug during the process of polymerization may be adopted.

2) The suspension polymerization:

It is carried out by heating the monomer or mixture of monomers with active principles (drugs) as droplets dispersion in a continuous aqueous phase. The droplets may also contain an initiator and other additives.

3) The emulsion polymerization:

However, differs from the suspension polymerization as due to presence of the initiator in the aqueous phase, which later on diffuses to the surface of the micelles or the emulsion globules.

2. Interfacial polymerization(6)

In Interfacial polymerization technique two reacting monomers are employed; one of which is dissolved in the continuous phase while the other being dispersed in the continuous phase. The continuous phase is generally aqueous in nature through which the second monomer is emulsified. The monomers present in either phase diffuse rapidly and polymerize rapidly at the interface. Two conditions arise depending upon the solubility of formed polymer in the emulsion droplet. If the polymer is soluble in the droplet it will lead to the formation of the monolithic type of the carrier on the hand if the polymer is insoluble in the monomer droplet, the formed carrier is of capsular (reservoir) type.

The degree of polymerization can be controlled by the reactivity of the monomer chosen, their concentration, and the composition of the vehicle of either phases and by the temperature of the system. Controlling the droplets or globules size of the dispersed phase can control the particle size. The polymerization reaction can be controlled by maintaining the concentration of the monomers, which can be achieved by addition of an excess of the continuous phase. The interfacial polymerization is not widely used in the preparation of the microparticles because of certain drawbacks, which are associated with the process such as:

- Toxicity associated with the unreacted monomer
- High permeability of the film
- High degradation of the drug during the polymerization
- Fragility of microcapsules
- Non-biodegradability of the microparticles

4) PHASE SEPERATION AND COACERVATION:

Phase separation method is specially designed for preparing the reservoir type of the system, i.e. to encapsulate water soluble drugs e.g. peptides, proteins, however, some of the preparations are of matrix type particularly, when the drug is hydrophobic in nature e.g. steroids. In matrix type device, the drug or the protein is soluble in the polymer phase. The process is based on the principle of decreasing the solubility of the polymer in the organic phase to affect the formation of the polymer rich phase called the coacervates. The coacervation can be brought about by addition of the third component to the system which results in the formation of the two phases, one rich in the polymer, while the other one. In this technique, the polymer is first dissolved in a suitable solvent and then making its aqueous solution disperses drug. Phase separation is then accomplished by changing the solution conditions by using any of the method mentioned above. The process is carried out under continuous stirring to control the size of the microparticles. The process variables are very important since the rate of achieving the coacervate determines the distribution of the polymer film, the particle size and agglomeration of the formed particles. The agglomeration must be avoided by stirring the

suspension using a suitable speed stirrer as the process of microsphere formation begins the polymerize globules start to stick and form the agglomerates. Thus the process variable critical as they control the kinetic of the formed particles since there is no defined state of equilibrium attainment.

5) SPRAY DRYING AND CONGEALING (4,5):
Spray drying and spray congealing methods are based on the drying of the mist of the polymer and drug in the air. Depending upon the removal of the solvent or the cooling of the solution, the two processes are named spray drying and spray congealing respectively. The polymer is first dissolved in a suitable volatile organic solvent such as dichloromethane, acetone, etc. The drug in the solid form is then dispersed in the polymer solution under high- speed homogenization. This dispersion is then atomized in a stream of hot air. The atomization lead to the formation of small droplets or the fine mist from which the solvent evaporates leading to the formation of microspheres in a size range 1-100µm. Microparticles are separated from the hot air by means of the cyclone separator while the traces of solvent are removed by vacuum drying.

6) SOLVENT EXTRACTION:
This method is used for the preparation of microparticles, involves the removal of the organic phase by extraction of the organic solvent. The method involves water miscible organic solvent such as isopropanol; organic phase is removed by extraction with water. The process decreases the hardening time for the microspheres. One variation of the process involves direct addition of the drug or protein to polymer organic solution. The rate of solvent removal by extraction method depends on the temperature of water, ratio of emulsion volume to the water and the solubility profile of the polymer.

7) QUASSI EMULSION SOLVENT DIFFUSION(6)
A novel quasi-emulsion solvent diffusion method to prepare the controlled release microspheres of drugs with acrylic polymers has been reported in the literature. Microsponges can be prepared by a quasi-emulsion solvent diffusion method using an external phase containing distilled water and polyvinyl alcohol (PVA). The internal phase is consisting of drug, ethyl alcohol and polymer is added at an amount of 20% of the polymer in order to facilitate the plasticity. At first, the internal phase is prepared at 60ºC and added to the external phase at room temperature. After emulsification, the mixture is continuously stirred for 2 hours. Then the mixture can be filtered to separate the microsponges. The product is then washed and dried by vacuum oven at 40ºC for 24 hours. Example: - Ibuprofen.

Materials used Microspheres used usually are polymers. They are classified into two types:

1. Synthetic Polymers
Synthetic polymers are divided into two types**.**

a. Non-biodegradable polymers
Poly methyl methacrylate (PMMA) (8)
Acrolein (9)
Glycidyl methacrylate
Epoxy polymers

b. Biodegradable polymers
Lactides, Glycolides & their co polymers (10)
Poly alkyl cyano acrylates
Poly anhydrides

2. Natural polymers obtained from different sources like proteins, carbohydrates and chemically modified carbohydrates**.**

Proteins:
Albumin(11), Gelatin(12), and Collagen

Carbohydrates:
Agarose, Carrageenan, Chitosan, Starch(13)
Chemically modified carbohydrates: Poly dextran, Poly starch**.**

In case of non-biodegradable drug carriers, when administered parenterally, the carrier remaining in the body after the drug is completely released poses possibility of carrier toxicity over a long period of time.

Synthetic polymers
Poly alkyl cyano acrylates is a potential drug carrier for parenteral as well as other ophthalmic, oral preparations. Poly lactic acid is a suitable carrier for

sustained release of narcotic antagonist, anti cancer agents such as cisplatin, cyclo phosphamide, and doxorubicin (14).

Sustained release preparations for anti malarial drug as well as for many other drugs have been formulated by using of co-polymer of poly lactic acid and poly glycolic acid.

Poly anhydride microspheres (40µm) have been investigated to extend the precorneal residence time for ocular delivery.

Poly adipic anhydride is used to encapsulate timolol maleate for ocular delivery. Poly acrolein microspheres are functional type of microspheres. They donot require any activation step since the surfacial free CHO groups over the poly acrolein can react with NH2group of protein to form Schiff's base.

Natural polymers

Albumin6 is a widely distributed natural protein .It is considered as a potential carrier of drug or protiens (for either their site specific localization or their local application into anatomical discrete sites). It is being widely used for the targeted drug for the targeted drug delivery to the tumour cells.

Gelatin7 microspheres can be used as efficient carrier system capable of delivering the drug or biological response modifiers such as interferon to phagocytes.

Starch8 belongs to carbohydrate class. It consists of principle glucopyranose unit, which on hydrolysis yields D-glucose. It being a poly saccharide consists of a large number of free OH groups. By means of these free OH groups a large number of active ingredients can be incorporated within as well as active on surface of microspheres.

Chitosan13 is a deacylated product of chitin. The effect of chitosan has been considered because of its charge. It is insoluble at neutral and alkaline Ph values, but forms salts with inorganic and organic salts. Upon dissolution, the amino groups of chitosan get protonated, and the resultant polymer becomes positively charged.

Evaluation of Mucoadhesive Microspheres

Particle size and shape

The particle size of the prepared microspheres can be measured by the optical microscopy method using a calibrated stage micrometer for randomly selected samples of all the formulations.

Entrapment Efficiency

The percent entrapment efficiency can be determined by allowing washed microspheres to lyse. The percent encapsulation efficiency is calculated using following equation.

% Entrapment = Actual content X 100 Theoretical content

Swelling Index

Swelling index illustrate the ability of the mucoadhesive microspheres to get swelled at the absorbing surface by absorbing fluids available at the site of absorption, which is a primary requirement for initiation of mucoadhesion.

Angle of contact

The angle of contact is measured to determine the wetting property of a micro particulate carrier. It determines the nature of microspheres in terms of hydrophilicity or hydrophobicity. Contact angle is measured at 20º within a minute of deposition of microspheres.

***In-vitro* drug release studies**

An *in-vitro* release profile reveals fundamental information on the structure (e.g., porosity) and behaviour of the formulation on a molecular level, possible interactions between drug and polymer, and their influence on the rate and mechanism of drug release and model release data.

***Ex-vivo* mucoadhesion test**

The *ex-vivo* mucoadhesion tests are important in the development of a controlled release bioadhesive system because they contribute to studies of permeation, release, compatibility, mechanical and physical stability, superficial interaction between formulation and mucous
membrane and strength of the bioadhesive bond.

These tests can simulate a number of administration routes including oral, buccal, periodontal, nasal, gastrointestinal, vaginal and rectal.

Surface topography by Scanning Electron Microscopy(SEM)

SEM uses a focused beam of high-energy electrons to generate a variety of signals at the surface of solid specimens. The signals that derive from electron sample interactions reveal information about the sample including external morphology (texture), chemical composition, and crystalline structure and orientation of materials making up the sample.

1.6.8 Zeta Potential Measurement

The surface charge can be determined by relatin measured electrophoretic mobility into zeta potential with in-built software based on the Helmholtz–Smoluchowski equation. Zeta potential is an indicator of particle surface charge, which can be used to predict and control the adhesive strength, stability, and themechanisms of mucoadhesion.

Drug polymer interaction (FTIR) study

IR spectroscopy can be performed by Fourier transformed infrared spectrophotometer. The pellets of drug and potassium bromide were prepared by compressing the powders at 20 psi for 10 min on KBr-press and the spectra were scanned.

APPLICATION OF MICROSPHERE:

1 Microspheres in vaccine delivery

The prerequisite of a vaccine is protection against the micro organism or its toxic product. An ideal vaccine must fulfill the requirement of efficacy, safety, convenience in application and cost. The aspect of safety and minimization of adverse reaction is a complex issue(28). The aspect of safety and the degree of the production of antibody responses are closely related to mode of application. Biodegradable delivery systems for vaccines that are given by parenteral route may overcome the shortcoming of the conventional vaccines(29). The interest in parenteral (subcutaneous, intramuscular, intradermal) carrier lies since they offer specific advantages including:

1. Improved antigenicity by adjuvant action
2. Modulation of antigen release
3. Stabilization of antigen.

2 Targeting using microparticulate carriers

The concept of targeting, i.e. site specific drug delivery is a well established dogma, which is gaining full attention. The therapeutic efficacy of the drug relies on its access and specific interaction with its candidate receptors. The ability to leave the pool in reproducible, efficient and specific manner is center to drug action mediated by use of a carrier system. Placement of the particles indiscrete anatomical compartment leads to their retention either because of the physical properties of the environment or biophysical interaction of the particles with the cellular content of the target tissue.

3 Monoclonal antibodies mediated microspheres targeting

Monoclonal antibodies targeting microspheres are immunomicrospheres. This targeting is a method used to achieve selective targeting to the specific sites. Monoclonal antibodies are extremely specific molecules. This extreme specificity of monoclonal antibodies (Mabs) can be utilized to target microspheres loaded bioactive molecules to selected sites. Mabs can be directly attached to the microspheres by means of covalent coupling. The free aldehyde groups, amino groups or hydroxyl groups on the surface of the microspheres can be linked to the antibodies. The Mabs can be attached to microspheres by any of the following methods

1. Non specific adsorption
2. Specific adsorption
3. Direct coupling
4. Coupling via reagents

4 Chemoembolisation

Chemoembolisation is an endovascular therapy, which involves the selective arterial embolisation of a tumour together with simultaneous or subsequent local delivery the chemotherapeutic agent. The theoretical advantage is that such embolisations will not only provide vascular occlusion but will bring

about sustained therapeutic levels of chemotherapeutics in the areas of the tumour. Chemoembolisation is an extension of traditional percutaneous embolisation techniques.

5 Imagin

The microspheres have been extensively studied and used for the targeting purposes. Various cells, cell lines, tissues and organs can be imaged using radio labelled microspheres. The particle size range of microspheres is an important factor in determining the imaging of particular sites. The particles injected intravenously apart from the portal vein will become entrapped in the capillary bed of the lungs. This phenomenon is exploited for the scintiographic imaging of the tumour masses in lungs using labelled human serum albumin microspheres.

6 Topical porous microspheres

Microsponges are porous microspheres having myriad of interconnected voids of particle size range 5-300 µm. These microsponges having capacity to entrap wide range of active ingredients such as emollients, fragrances, essential oils etc., are used as the topical carries system further, these porous microspheres with active ingredients can be incorporated into formulations such as creams, lotions and powders. Microsponges consist of non collapsible structures with porous surface through which active ingredients are released in a controlled manner(30).

7 Surface modified microspheres

Different approaches have been utilized to change the surface properties of carriers to protect them against phagocytic clearance and to alter their body distribution patterns .The adsorption of the poloxamer on the surface of the polystyrene, polyester or poly methyl methacrylate microspheres renders them more hydrophilic and hence decrease their MPS uptake. Protein microspheres covalently modified by PEG derivatives show decreased immunogenicity and clearance. The most studied surface modifiers are:

1. Antibodies and their fragments
2. Proteins
3. Mono-, oligo- and polysaccharides
4. Chelating compounds (EDTA, DTPA or Desferroxamine)
5. Synthetic soluble polymers

Such modifications are provided surface of microspheres inorder to achieve the targeting to the discrete organs and to avoid rapid clearance from the body.

CONCLUSION:

Microsphere 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 . The microsphere 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.

FUTURE PERSPECTIVES:

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. Mucoadhesive drug delivery systems have been emerged as one of the promising approach for enhancing the bioavailability and controlled delivery of drugs that exhibit a narrow absorption window. By prolonging gastric emptying time of the dosage form, these systems help to provide the drug in an absorbable form at regions of optimal absorption. Future potential in the development of gastroretentive mucoadhesive drug a delivery systems especially mucoadhesive microspheres is very bright and several newer technologies will surely offer numerous applications and opportunities in current health care scenario. Researchers may adopt suitable methodologies to ensure optimum therapeutic potential of various gastroretentive formulations. Further, investigational studies may also concentrate on the designing of more novel and advanced gastroretentive dosage forms with better pharmacological interventions. It is hoped that research with a variety of natural polymers and new preparation methods will lead to the development of more effective mucoadhesive drug delivery systems. Microspheres prepared by these technologies have sufficient buoyancy, better entrapment efficiency and good absorption through GIT. Various drugs which have limited bioavailability, narrow absorption window can be successfully formulated in the form of gastroretentive mucoadhesive microspheres as these dosage forms are well retained in the GIT for sufficient prolonged period of time. These formulations release their active constituent in a controlled manner which reduces the dose and increases the bioavailability. Thus, gastroretentive mucoadhesive microspheres may be developed for most of the drugs like antiulcer, antihypertensive agents, antibiotics etc. in the near future. It is emphasized that further scientific and technological advancements in this area are required to accurately control the drug input rate into the specific site of GI tract for the optimization of the pharmacokinetic and toxicological profiles of medicinal agents. Newer technological aspects in the avenue of microspheres are required to accurately control the therapeutic profile of various potent medicinal agents. Moreover, market size and popularity of these dosage forms will surely expand in near future. It is also anticipitated that newer scientific and technological innovations should be undertaken for the emergence of promising and versatile dosage forms with novel performance and characteristics.

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