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MICROSPHERES A NOVEL APPROACH ON DRUG DELIVERY SYSTEMS

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ABSTRACT

Microspheres have been used widely as these cover targeting the drug to particular site to imaging and helping the diagnostic features. Microencapsulation is used to modify and delayed drug release form pharmaceutical dosage forms. Microspheres efficiently utilized in controlled delivery of many drugs but wastage of drug due to low drug entrapment efficiency is the major drawback of such microparticulate system. The optimized microspheres can overcome such problems by enhancing the loading efficiency of a particular drug and minimizing the wastage of drug. It is to increase the drug loading efficiency, if optimize the formulation as well as process variables. This is necessary by understanding the effect of various variables which affect the drug entrapment efficiency of these microspheres. The present gives idea about various types of microspheres, methods to preparation, applications and various parameters for microspheres.

Keywords: Microspheres, Microparticulate, Diagnostic, Parameters.

INTRODUCTION

Microspheres are small spherical particles, with diameters in the micrometer range (1µm to1000 µm). Microspheres are sometimes referred to as microparticles. Microspheres [1,2] can be manufactured from various natural and synthetic materials. Glass microspheres, polymer microspheres and ceramic microspheres are commercially available. Solid and hollow microspheres [3] vary widely in density and therefore, are used for different applications. The range of techniques for the preparation of microspheres offers a variety of opportunities to control aspects of drug administration. This approach facilitates the accurate delivery of small quantity of the potent drugs, reduced drug concentration at the site other than the target site and the protection of the labile compound before and after the administration and prior to appearance at the site of action. The behavior of the drugs in vivo can be manipulated by coupling the drug to a carrier particle. The clearance kinetics, tissue distribution, metabolism and cellular interaction of the drug are strongly influenced by the behavior of the carrier. The exploitation of these changes in pharmacodynamics behavior may lead to enhanced therapeutic effect. The clearance kinetics, tissue distribution, metabolism and cellular interaction of the drug are strongly influenced by the behavior of the carrier. The exploitation of these changes in pharmacodynamics behavior may lead to enhanced therapeutic effect. The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to achieve promptly and then maintain the desired drug concentration. The most convenient and commonly employed route of drug delivery has historically been by oral ingestion Drugs that are easily absorbed from the GIT and having a short half-life are eliminated quickly from the blood circulation. To avoid these problems oral controlled drug delivery systems have been developed as they releases the drug slowly into the GIT and maintain a constant drug concentration in the serum for longer period of time.

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However, incomplete release of the drug and a shorter residence time of dosage forms in the upper gastrointestinal tract, a prominent site for absorption of many drugs, will lead to lower bioavailability. Efforts to improve oral drug bioavailability have grown in parallel with the pharmaceutical industry. As the number and chemical diversity of drugs [4,5] has increased, new strategies are required to develop orally active therapeutics. Thus, gastro retentive dosage forms, which prolong the residence time of the drugs in the stomach and improve their bioavailability, have been developed.

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 proteins or synthetic polymers which are biodegradable in nature and ideally having a particle size less than 200 μm.

Advantages of microspheres

1. Microspheres provide constant and prolonged therapeutic effect.
2. It reduces the dosing frequency and thereby improve the patient compliance.
3. It may be injected into the body due to the spherical shape and smaller size.
4. It has better drug utilization will improve the bioavailability and reduce the incidence or intensity of adverse effects.
5. The morphology allows a controllable variability in degradation and drug release.

Disadvantages of microspheres

1. The release rate of the controlled release microspheres may vary from a variety of factors like food and the rate of transit though gut.
2. There is differences in the release rate from one dose to another.
3. The loss of drug from controlled release microspheres may cause toxicity.
4.The microspheres should not be crushed or chewed.

Types of microspheres

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 bioadhesion. Various bioadhesive microsphers are designed using polymers for controlled action of dosage forms. 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

Magnetic microspheres localise 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. Different Therapeutic magnetic microspheres are used to deliver chemotherapeutic agent to liver tumour. Drugs like proteins and peptides can also be targeted through this system. 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.

Floating microspheres

In floating type microspheres 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 gastric fluid increases gastric residence time and maintains constant drug concentration in plasma. It produces prolonged therapeutic effect and therefore reduces dosing frequencies.

Radioactive microspheres

Radio mobilization 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 radioactive microspheres deliver high radiation dose to the targeted areas without damaging the normal surrounding tissues. 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 microspheres are α emitters, β emitters, γ emitters.

Polymeric microspheres

The types of polymeric microspheres can be classified as follows and they are biodegradable polymeric microspheres and synthetic polymeric microspheres.

Biodegradable polymeric microspheres

Natural polymers are used in polymeric microspheres as they are biodegradable, biocompatible and bioadhesive in nature. Biodegradable polymers prolongs the residence time when contact with mucous membrane due to its high degree of swelling property with aqueous medium , results gel formation. The rate and extent of drug release is controlled by concentration of polymer 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.

Synthetic polymeric microspheres

The synthetic polymeric microspheres are widely used in clinical application, and also used as bulking agent, fillers, embolic particles, drug delivery vehicles etc. The main disadvantage of these kind of microspheres, are tend to migrate away from injection site and lead to potential risk, embolism and further organ damage.

Diagnostic microspheres

Diagnostic microspheres are used for imaging the liver metastases and also can be used to differentiate bowel loops from abdominal structures by formation of nano size particles supramagnetic iron oxides.

Route of administration [6]

Oral

Microspheres can be given orally. Oral route is suggested for the delivery of the soluble antigens and various drugs due to the ability of the particles of definite size range. The risk of dose dumping is minimized with this formulation the smaller size of particles and high drug loaded particles show faster release.

Intranasal

Microspheres are given at the surface of nasal mucosa by considering the muco cilliary clearance. The particle size range of microspheres for targeting the respiratory tract is given Table no.1.

Table 1. Respiratory tract with desired particle range of microspheres

Respiratory part	Required Particle size (um)
Nose	25-30
Throat	20-28
Pharynx	20-24
Larynx	15-20
Trachea	10-15
Bronchi	8-12
Bronchioles	8-10
Alveolar duct	5-8
Alveoli	4-8

Ocular

Microsphers are targeted to the eye for its bioadhesive nature. The rapid conversion of the particulate suspension to gel form reportedly leads to their longer retention in the eye.

Parenteral

Microspheres used for parenteral delivery should be sterile and should be dispersible in a suitable vehicle for injection. Hydrophilic microspheres have the potential advantage of aqueous dispersibility as opposed to hydrophobic microspheres for reconstituting them for injection. Surfactants in small concentrations are often necessary for reconstituting hydrophobic particles for injection in aqueous vehicle which are reported to cause adverse tissue reaction and affect the release of the incorporated drug.

Polymers used

Various types of polymers are used for the preparation of microsphers.

They classified into two types:

On the basis of origin (biodegradable polymers)

Natural polymer

- **Protein based polymers**

The examples are collagen, albumin, gelatin etc

- **Polysaccharides**

The examples are alginate, cyclodextrin, chitosan, dextran, agarose, hylauronic acid, starch, cellulose etc.

Synthetic polymers

- Poly ester

The examples are poly lactic acid, poly glycolic acid, poly hydroxyl butyrate, poly caprolactone, poly lactide co glycolide, poly dioxanones etc.

- Poly anhydride

The examples are poly adipic acid, poly sebacic acid, polyterphthalic acid etc.

- Poly amides

The examples are poly imino carbonates, poly amino acids etc.

- Phosphorous based polymers

The examples are polyphosphates, polyphosphonates, polyphosphazenes etc.

- Others

The examples are poly cyanoacrylates, polyacetals, polyurethanes etc.

Synthetic Polymers (nonbiodegradable)

The examples are poly methyl methacrylate (PMMA), acrolein ,glycidyl methacrylate etc.

Methods use of preparation of microspheres [7-19]

1. Solvent evaporation method,
2. Coacervation phase separation method.
3. Spray drying method.

4. Polymerization method.
5. Hot melt microencapsulation
6. Solvent evaporation method

1. Solvent evaporation method

- **Single emulsion technique**

The microparticulate carriers of natural polymers, i.e. those of proteins & carbohydrates are prepared by single emulsion technique. The natural polymers are dissolved/ dispersed in aqueous medium followed by dispersion in the non-aqueous medium (oil). In the second step, cross linking of the dispersed globule is carried out either by means of heat or by using chemical cross linkers. The chemical cross linking agents are used such as gluteraldehyde, formaldehyde, terephthalate chloride, diacidchloride, etc. Crosslinking by heat is effected by adding the dispersion to previously heated non aqueous medium (oil). 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.

- **Double emulsion technique**

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. The aqueous drug solution is dispersed in a lipophilic organic continuous phase which is generally consisted of polymer solution that eventually encapsulates drugs contained in dispersed aqueous phase. The primary emulsion is then subjected to the homogenization before addition to aqueous solution of polymer .This results in formation of double emulsion which is then subjected to solvent removal by solvent evaporation maintaining the emulsion at reduced pressure or by stirring so that organic phase evaporates out.

2. Coacervation phase separation method

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 i.e. supernatant, depleted of the polymer. In this technique, the polymer is first dissolved in a suitable solvent & then drug is dispersed by making its aqueous solution, if hydrophilic or dissolved in the polymer solution itself, if hydrophobic. Phase separation is then accomplished by changing the solution conditions.

3. Spray drying

In Spray Drying 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 leads to the formation of the small droplets or the fine mist from which the solvent evaporate instantaneously leading the formation of the microspheres in a size range 1-100μm. Micro particles are separated from the hot air by means of the cyclone separator while the trace of solvent is removed by vacuum drying. One of the major advantages of process is feasibility of operation under aseptic conditions this process is rapid and this leads to the formation of porous micro particles

4. Polymerization method

- **Normal polymerization**

In bulk polymerization, a monomer along with initiator is heated to initiate polymerization. Initiator is added to accelerate the rate of reaction. Drug is added during process of polymerization. The polymer so obtained is fragmented to microspheres.

- **Suspension polymerization**

Suspension polymerization is also called as bead/pearl polymerization. Carried out by heating the monomer or mixture of monomers with active principles (drug) as droplets dispersion in a continuous phase. The droplets may also contain an initiator & other additives. The emulsion polymerization, differs from the suspension polymerization as due to presence of initiator in the aqueous phase, which later on diffuses to the surface of the micelles or the emulsion globules. The suspension & emulsion polymerization can be carried out at lower temperature, since continuous external phase is normally water through which heat can easily dissipate. The two processes also lead to the formation of higher mol. wt polymer at relatively faster rate.

- **Interfacial polymerization**

It involves reaction of various monomers at the interface between the two immiscible liquid phases to form a film of polymer that essentially envelopes the dispersed phase. In this two reacting monomers are employed one of which is dissolved in the continuous phase while the other being dispersed in the continuous phase. Monomer present in either phases diffuse rapidly polymerize rapidly at the interface. If the polymer is soluble in the droplet it will lead to the formation of monolithic type of the carrier on the other hand if 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 monomer chosen, their concentration, the composition of the vehicle of either phases & by the temperature of the system. The particle size can be controlled by controlling the droplets or globule size of the disperse phase. The polymerization reaction can be controlled by maintaining the concentration of the monomers, which can be achieved by the addition of an excess of the continuous phase.

Hot Melt Microencapsulation

The polymer is first melted and then mixed with solid particles of the drug that have been sieved to less than

50 µm. 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. The primary objective for developing this method is to develop a microencapsulation process suitable for the water labile polymers, *e.g.* polyanhydrides. Microspheres with diameter of 1-1000 µm can be obtained and the size distribution can be easily controlled by altering the stirring rate. The only disadvantage of this method is moderate temperature to which the drug is exposed6

Solvent evaporation method

Solvent evaporation method is used for the preparation of microparticles, involves removal of the organic phase by extraction of the organic solvent. The method involves water miscible organic solvents such as isopropanol. Organic phase is removed by extraction with water. This process decreasesthe hardening time for then microspheres. One variation of the process involve 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.

Characterization of microspheres [20,21]

Particle size and shape

The most widely used procedures to visualize microparticles are conventional light microscopy (LM) and scanning electron microscopy (SEM). Both can be used to determine the shape and outer structure of microparticles. LM provides a control over coating parameters in case of double walled microspheres. The microspheres structures can be visualized before and after coating and the change can be measured microscopically. SEM provides higher resolution in contrast to the LM. SEM allows investigations of the microspheres surfaces and after particles are cross-sectioned, it can also be used for the investigation of double walled systems. Conflocal fluorescence microscopy1 is used for the structure characterization of multiple walled microspheres. Laser light scattering and multi size coulter counter other than instrumental methods, which can be used for the characterization of size, shape and morphology of the microspheres.

Electron spectroscopy for chemical analysis

The surface chemistry of the microspheres can be determined using the electron spectroscopy for chemical analysis (ESCA). ESCA provides a means for the determination of the atomic composition of the surface. The spectra obtained using ECSA can be used to determine the surfacial degradation of the biodegradable microspheres.

Attenuated total reflectance Fourier Transfom-Infrared Spectroscopy

FT-IR is used to determine the degradation of the polymeric matrix of the carrier system. The surface of the microspheres is investigated measuring alternated total reflectance (ATR). The IR beam passing through the ATR cell reflected many times through the sample to provide IR spectra mainly of surface material. The ATRFTIR provides information about the surface composition of the microspheres depending upon manufacturing procedures and conditions.

Density determination

The density of the microspheres can be measured by using a multi volume pychnometer. Accurately weighed sample in a cup is placed into the multi volume pychnometer. Helium is introduced at a constant pressure in the chamber and allowed to expand. This expansion results in a decrease in pressure within the chamber. Two consecutive readings of reduction in pressure at different initial pressure are noted. From two pressure readings the volume and hence the density of the microsphere carrier is determined.

Isoelectric point

The micro electrophoresis is an apparatus used to measure the electrophoretic mobility of microspheres from which the isoelectric point can be determined. The mean velocity at different P^H values ranging from 3-10 is calculated by measuring the time of particle movement over a distance of 1 mm. By using this data the electrical mobility of the particle can be determined. The electrophoretic mobility can be related to surface contained charge, ionisable behaviour or ion absorption nature of the microspheres.

Capture efficiency

The capture efficiency of the microspheres or the percent entrapment can be determined by allowing washed microspheres to lyse. The lysate is then subjected to the determination of active constituents as per monograph requirement. The percent encapsulation efficiency is calculated using following equation.

% Entrapment = Actual content/Theoretical content x100.

Swelling index

Swelling index was determined by measuring the extent of swelling of microspheres in the given buffer. To ensure the complete equilibrium, exactly weighed amount of microspheres were allowed to swell in given buffer. The excess surface adhered liquid drops were removed by blotting and the swollen microspheres were weighed by using microbalance. The hydrogel microspheres then dried in an oven at 60° for 5 h until there was no change in the dried mass of sample. The swelling index of the microsphere was calculated by using the formula

Swelling index =
(mass of swollen microspheres – mass of dry microspheres/mass of dried microspheres) X 100.

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. This thermodynamic property is specific to solid and affected by the presence of the adsorbed component. The angle of contact is measured at the solid/air/water interface. The advancing and receding angle of contact are measured by placing a droplet in a circular cell mounted above objective of inverted microscope. Contact angle is measured at 20^0C within a minute of deposition of microspheres.

In vitro methods

Standard USP or BP dissolution apparatus have been used to study *in vitro* release profiles using both rotating elements, paddle and basket. Dissolution medium used for the study varied from 100- 900 ml and speed of rotation from 50-100 rpm.

***In vivo* methods**

Methods for studying the permeability of intact mucosa comprise of techniques that exploit the biological response of the organism locally or systemically and those that involve direct local measurement of uptake or accumulation of penetrants at the surface. The most widely used methods include *in vivo* studies using animal models, buccal absorption tests, and perfusion chambers for studying drug permeability.

Animal models

Animal models are used mainly for the screening of the series of compounds, investigating the mechanisms and usefulness of permeation enhancers or evaluating a set of formulations. A number of animal models have been reported in the literature, however, very few *in vivo*(animal). Animal models such as the dog, rats, rabbits, cat, hamster, pigs, and sheep have been reported. In general, the procedure involves anesthetizing the animal followed by administration of the dosage form. In case of rats, the oesophagus is ligated to prevent absorption pathways other than oral mucosa. At different time intervals, the blood is withdrawn and analyzed.

Buccal absorption test

The buccal absorption test was developed by Beckett & Triggs in 1967. It is a simple and reliable method for measuring the extent of drug loss of the human oral cavity for single and multi-component mixtures of drugs. The test has been successfully used to investigate the relative importance of drug structure, contact time, initial drug concentration and Ph of the solution while the drug is held in the oral cavity.

Applications of Microspheres [22-26]

Delivery of vaccines

Vaccination has been highly successful for controlling or even eradicating infectious diseases, such as hepatitis B, anthrax, and SARS.A frequent problem is the need for repeated administration of vaccines. Hence to eradicate the shortcomings controlled release vaccination is developed in the form of microspheres.

Gene delivery

Gene delivery systems include viral vectors, cationic liposomes, polycation complexes, and microencapsulated systems. Viral vectors are advantageous for gene delivery because they are highly efficient and have a wide range of cell targets. However, when used in vivo they cause immune responses and oncogenic effects. To overcome the limitations of viral vectors, non-viral delivery systems are considered for gene therapy. Non-viral delivery system has advantages such as ease of preparation, cell/tissue targeting, low immune response, unrestricted plasmid size, and large-scale reproducible production. Polymer has been used as a carrier of DNA for gene delivery applications. Also, polymer could be a useful oral gene carrier because of its adhesive and transport properties in the GI tract. MacLaughlin et al showed that plasmid DNA containing cytomegalo virus promoter sequence and a luciferase reporter gene could be delivered in vivo by chitosan and depolymerized chitosan oligomers to express a luciferase gene in the intestinal tract.

Diagnostics

Radioactive microspheres are used for diagonising various things in human body such as gated blood pool study, thrombus imaging in deep vein thrombosis, blood flow measurements, investigation of biodistribution and fate of (drug-loaded) microspheres, lung scintigraphy, diagnostic radioembolization, liver and spleen imaging, bone marrow imaging, infection localization, tumor imaging, gastrointestinal transit studies, local restenosis prevention in coronary arteries.

Oral drug delivery

Microspheres are given orally for curing various diseases. The potential of polymer films containing diazepam as an oral drug delivery was investigated in rabbits. The ability of polymer to form films may permit its use in the formulation of film dosage forms, as an alternative to pharmaceutical tablets. The pH sensitivity, coupled with the reactivity of the primary amine groups, make polymer a unique polymer for oral drug delivery applications.

Buccal drug delivery

Polymer is an excellent polymer to be used for buccal delivery because it has muco/bioadhesive properties and can act as an absorption enhancer. Buccal tablets based on chitosan microspheres containing chlorhexidine diacetate gives prolonged release of the drug in the buccal cavity improving the antimicrobial activity of the drug. polymer microparticles with no drug incorporated have antimicrobial activity due to the polymer. The buccal bilayered devices

(bilaminated films, palavered tablets) using a mixture of drugs (nifedipine and propranolol hydrochloride) and chitosan, with or without anionic crosslinking polymers (polycarbophil, sodium alginate, gellan gum) has promising potential for use in controlled delivery in the oral cavity.

Vaginal drug delivery

Polymer, modified by the introduction of thioglycolic acid to the primary amino groups of the polymer, embeds clotrimazole, an imidazole derivative, is widely used for the treatment of mycotic infections of the genitourinary tract. By introducing thiol groups, the mucoadhesive properties of the polymer are strongly improved and this is found to increase the residence time of the vaginal mucosa tissue (26 times longer than the corresponding unmodified polymer),guaranteeing a controller drug release in the treatment of mycotic infections. Vaginal microspheres of polymer containing metronidazole and acriflavine have showed adequate releaseand good adhesion properties.

Nasal drug delivery

The nasal mucosa presents an ideal site for bioadhesive drug delivery systems. Polymer based drug delivery systems, such as micro spheres, liposomes and gels have been demonstrated to have good bioadhesive characteristics and swell easily when in contact with the nasal mucosa increasing the bioavailability and residence time of the drugs to the nasal route.

Various polymer salts such as chitosan lactate, chitosan aspartate, chitosan glutamate and chitosan hydrochloride are good candidates for nasal sustained release of vancomycin hydrochloride. Nasal administration of Diphtheria Toxoid incorporated into chitosan microparticles results in a protective systemic and local immune response against Diphteria Toxoid with enhanced IgG production. Nasal formulations have induced significant serum IgG responses similar to secretory IgA levels, which are superior to parenteral administration of the vaccine. Nasal absorption of insulin after administration into polymer powder were found to be the most effective formulation for nasal drug delivery of insulin in sheep compared to chitosan nanoparticles and chitosan solution.

Ophthalmic Drug Delivery

Polymer exhibits favorable biological behavior such as bioadhesion, permeability-enhancing properties, and interesting physico-chemical characteristics, which make it a unique material for the design of ocular drug delivery vehicles. Due to their elastic properties, polymer hydro gels offer better acceptability, with respect to solid or semisolid formulation, for ophthalmic delivery, such as suspensions or ointments, ophthalmic chitosan gels improve adhesion to the mucin, which coats the conjunctiva and the corneal surface of the eye, and increase precorneal drug residence times, showing down drug elimination by the lachrymal flow. In addition, its penetration enhancement has more targeted effect and allows lower doses of the drugs. In contrast, polymer based colloidal system were found to work as transmucosal drug carriers, either facilitating the transport of drugs to the inner eye (chitosan-coated colloidal system containing indomethacin) or their accumulation into the corneal/conjunctival epithelia (chitosan nanoparticulate containing cyclosporine). The micro particulate drugcarrier (micro spheres) seems a promising means of topical administration of acyclovir to the eye. The duration of efficacy of the ofloxacin was increased by using high MW (1930 kd) chitosan.

Transdermal drug delivery

Polymer has good film-forming properties. The drug release from the devices is affected by the membrane thickness and cross-linking of the film. Chitosan-alginate polyelectrolyte complex has been prepared in-situ in beads and microspheres for potential applications in packaging, controlled release systems and wound dressings. Polymer gel beads are a promising biocompatible and biodegradable vehicle for treatment of local inflammation for drugs like prednisolone which showed sustained release action improving therapeutic efficacy. The rate of drug release was found to be dependent on the type of membrane used.A combination of chitosan membrane and chitosan hydrogel containing lidocaine hydrochloride, a local anesthetic, is a good transparent system for controlled drug delivery and release kinetics.

Colonic drug delivery

Polymer has been used for the specific delivery of insulin to the colon. The chitosan capsules were coated with enteric coating (Hydroxy propyl methyl cellulose phthalate) and contained, apart from insulin, various additional absorption enhancer and enzyme inhibitor. It was found that capsules specifically disintegrated in the colonic region. It was suggested that this disintegration was due to either the lower pH in the ascending colon as compared to the terminal ileum or to the presence bacterial enzyme, which can degrade the polymer.

Magnetically targeted drug delivery systems

In targeted drug delivery, drugs are directed to cells that need therapy or repair, such as in cancer treatment. Effective treatments of cancer involve either surgery, radiation, immunotherapy, chemotherapy or a combination of these choices. tumour targeting, magnetic delivery of chemotherapeutic drugs. Microspheres are also used for liver tumors, locoregional cancer treatment with magnetic drug targeting, magnetically induced hyperthermia for treatment of cancer, magnetic targeting of radioactivity etc.

Cosmetics

Cosmetic compositions are disclosed for the treatment of hair or skin, characterized by a content of new quaternary chitosan derivatives of microspheres. The chitosan derivatives have a good substantial, particularly to hair keratin, and prove to have hair strengthening and hair conditioning characteristics. e.g.; hair setting lotion,

oxidation hair-coloring composition, hair toning composition, skin cream, hair treatment composition, gel-form.

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