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MUCOADHESIVE MICROSPHERES: A NOVEL CARRIER IN DRUG DELIVERY

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ABSTRACT

Carrier technology provides an interesting as well as an intelligent approach for the delivery of drug. It provides delivery of drug by interacting the drug to a carrier particle such as microspheres, nanoparticles, liposomes, etc. Microspheres play an important part of the micro particulate drug delivery system because of their small size and other efficient properties. Mucoadhesive microspheres give better drug absorption because of adherence to the mucosal surface and release the drug for a prolonged period. It is an ideal targeting system with high safety profile. This review article gives the information about mucoadhesion, polymers used in mucoadhesive microspheres, number of available methods of preparation of mucoadhesive microspheres.

KEYWORDS

Microspheres, Mucoadhesion and Bioavailability.

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INTRODUCTION

Oral controlled drug delivery system is the most versatile, convenient and commonly employed route of drug delivery for drugs having less plasma half life and residence time in GIT. Many concepts have been proposed in recent years to provide a dosage form with a longer transit time and therefore a more efficient absorption. Recently the novel dosage forms which may control the release rate and target the active drug molecule to a specific site have attained a best formulation interest. Microspheres are one of the best novel drug delivery system which have several applications and are made up of assorted polymers. The concept of mucoadhesion will more specifically increase gastric retention of drugs[1,2].

Microspheres are small spherical particles (typically 1μm to 1000μm), sometimes referred to as microparticles. The microspheres are often made from natural or synthetic polymers. Generally microspheres possess potentiality to be employed for targeted and controlled/extended release of drug, but incorporating mucoadhesive properties to microspheres will further more improve absorption and bioavailability of the drugs. Mucoadhesive microspheres increase the intimate contact with the mucus layer, and drug targeting to the absorption site. Mucoadhesive microspheres offers the chances of localized as well as controlled release of drugs by adherence to any mucosal tissue present in eye, nasal cavity, urinary, and GItract[1,3].

Advantages

- Provide constant and longer therapeutic effect.
- Microspheres provide controlled, sustained and targeted delivery of the drug.
- Reduces the frequency of daily administration and thereby improve the patient compliance.
- Improve the absorption of drug hence improve the bioavailability of drug and reduce the chances of adverse effects.
- The morphology of microspheres permits a controllable variability in degradation and drug release.
- Microspheres reduce dose dumping.
- Microspheres avoid the first pass metabolism.
- Microspheres also reduce the chances of G.I. irritation[4,5].

Limitations

- The release from the formulations may getmodified.
- The release rate may vary from a variety of factors like food and the rate of transit though gut, mucin turnover rate etc.
- Differences in the release rate can be found from one dose to another.
- Any loss of integrity in release pattern of the dosage form may lead to potential toxicity[4,5].
- These kinds of dosage forms cannot be crushed or chewed.

APPLICATIONS OF MICROSPHERES

Some of the applications of microspheres are mentioned in detail as following

- Microsphere can be used to prepare enteric-coated dosage forms, so that the medicament will be selectively absorbed in the intestine rather than the stomach.
- These are used to protect drugs from environmental hazards such as humidity, light, oxygen or heat.
- Incompatible substances can be separated easily, for example, pharmaceutical eutectics have been achieved by encapsulation.
- Controlled and sustained release dosage forms.
- Volatility can be reduced by microencapsulation.
- Potential danger of handling of toxic or noxious substances can be decreased.
- The hygroscopic properties of many substances may be reduced by microencapsulation.
- Gastric irritation caused by many drugs can be reduced by microencapsulation.
- Microsphere method has also been suggested to prepare intrauterine contraceptive device
- Therapeutic magnetic microspheres are used to deliver chemotherapeutic agent to liver tumor[6,7].

MUCOADHESION

Bioadhesion may be a phenomenon during which two materials a minimum of one of which is biological in nature are held together by means of interfacial forces. The term “mucoadhesion” define the adhesion of the polymers with the surface of the mucosal layer[6].

POLYMERS USED IN THE PREPARATION OF MICROSPHERES

Various polymers were used like natural and synthetic polymers.

Natural Polymer

These polymers are obtained from different sources like Protein, Carbohydrate and chemically modified Carbohydrates.

Eg: Albumin, Gelatin, Collagen, Starch, Agarose, Poly acryl Dexron, Poly acryl Starch.

Synthetic Polymer

Two types were used as synthetic polymers.

Biodegradable Polymers

Polyanhydride, Polyalkyl cyano acrylates, Lactides and Glycolides and copolymer.

Non-Biodegradable Polymers

Acrolein, Glycidyl Methacrylates, and Epoxy Polymer etc[7,8].

METHODS OF PREPARATION

Phase separation coacervation technique

In this method, the drug particles are dispersed uniformly in a polymeric solution and an incompatible polymer is added to the system which makes first polymer to phase separate and engulf the drug particles. Addition of non-solvent results in the solidification of polymer. The process variables are very important since the rate of achieving the coacervates determines the distribution of the polymer film, the particle size and agglomeration of the formed particles.

Emulsion cross linking method

In this method drug is dissolved in aqueous gelatin solution which is already heated for 1 hr at 40ºC. The solution is added drop wise to liquid paraffin while stirring the mixture at 1500rpm for 10 min at 35ºC, results in w/o emulsion then further stir continuously for 10 min at 15ºC. Thus the produced microspheres are washed respectively three times with acetone and isopropyl alcohol which then air dried for 3hrs.

Solvent Evaporation

The polymer is dispersed in an organic solvent and the drug is either dissolved /dispersed in the polymer solution. The solution containing the drug is then emulsified into an aqueous phase containing suitable additives (surfactants/polymer) to form oil in water emulsion. After the formation of emulsion, the organic solvent is evaporated either by increasing the temperature under pressure or by continuous stirring. The solvent removal leads to polymer precipitation at the oil/water interphase of droplets, forming cavity.

Spray Drying

In spray drying the polymer is initially 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.

Wet Inversion Technique

Chitosan solution in acetic acid was dropped in to an aqueous solution of counter ion sodium tripolyposphate through a nozzle. Microspheres formed were allowed to stand for 1 hr and cross linked with 5% ethylene glycol diglysidyl ether. Microspheres were then washed and freeze dried. By changing the pH of the coagulation medium could modify the pore structure of microspheres.

Hot Melt Microencapsulation

The polymer is initially melted and then mixed with solid particles of the drug that have been sieved to less than 50µm. The mixture is then 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 gets solidified. The resulting microspheres are washed by decantation with petroleum ether[8-10].

EVALUATION OF MUCOADHESIVE MICROSPHERES

The microspheres are assessed for the accompanying parameters.

Molecule Size and Shape

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

Surface Characterization of the Mucoadhesive Microspheres

Information from the Scanning electron microscopy, checking microscopy and the electron microscopy gives knowledge to the surface morphology of microspheres and the morphological changes created through corruption of polymer[11-13].

Surface Charge Study

From photon connection spectroscopy information the surface charge (zeta capability) of the mucoadhesive microspheres can be resolved. The surface charge can be controlled by relating estimated electrophoretic versatility into zeta potential with in constructed programming in view of the Helmholtz-Smoluchowski condition. Zeta potential is a pointer of molecule surface charge, which can be utilized to anticipate furthermore, control the glue quality, security, and the instruments of mucoadhesion. Procedure of mucoadhesion includes associations between the bodily fluid and mucoadhesive polymers, and is affected by their structure including their charge. Estimation of zeta capability of microspheres and bodily fluid predicts electrostatic cooperations during mucoadhesion.

Entrapment Efficiency

The Entrapment productivity of the microspheres or the percent Entrapment can be dictated by keeping the microspheres into the cradle arrangement and permitting lysing. The lysate got is sifted or centrifuged and after that oppressed for assurance of dynamic constituents according to monograph prerequisite. The percent Entrapment productivity is determined utilizing following condition:

% Entrapment = Actual substance/Theoretical substance x 100

Swelling Index

Swelling list represent the capacity of the mucoadhesive microspheres to get expand at the engrossing surface by retaining liquids accessible at the site of ingestion, which is an essential necessity for inception of mucoadhesion. The percent growing worth can be resolved utilizing following condition.

Percent swelling = DT - D0/D0 × 100

Where, D0 = weight of dried microspheres,

DT = weight of expand microspheres

***In-Vitro* Release Study**

Standard IP/BP/USP disintegration mechanical assembly is utilized to think about *in-vitro* discharge profile in the disintegration media that is like the liquid present at the ingestion site according to monograph, utilizing pivoting bin or oar type disintegration contraption.

***Ex-Vivo* Mucoadhesion Study**

The mucoadhesive property of the microspheres is assessed on goat's intestinal mucosa by utilizing phosphate cradle, according to monograph. Gauged microspheres are spread onto wet flushed tissue example and quickly from that point the slides are clung to the arm of a USP tablet breaking down test machine with appropriate support at 37ºC. The heaviness of microspheres drained out at various interims is estimated[14,15].

CONCLUSION

Mucoadhesive microspheres have emerged as a promising drug carrier system in pharmaceutical industry. Controlled and delayed drug release is possible using mucoadhesive microspheres, and GI mucosa is a viable target for these. Such systems offer increased residence time, safety, and protection for drugs, increased plasma concentration versatility. Mucoadhesive microspheres are one of the most ideal systems for the most preferred drug intake mode, i.e., oral, and to realize the dream of delivering otherwise orally in efficient drugs as well as drugs currently delivered through invasion only. Hence, it is concluded that mucoadhesive microspheres are the effective drug delivery systems for safe and prolong delivery of the drug.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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