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Gastroretentive Mucoadhesive Microsphere as Novel Drug Delivery System

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ABSTRACT

Recently, pharmaceutical experts have become more interested in mucoadhesive polymers as a way to enhance drug delivery by lengthening the duration that the dosage form stays in touch with the mucous membranes and contacts them during that time. Since they stick to the mucosal surface and release the medicine for a longer period of time, mucoadhesive microspheres improve drug absorption. The current research discusses the potential uses of mucoadhesive microspheres as a novel drug delivery system for systemic or local effects through a variety of administration routes, including buccal, oral, nasal, ophthalmic, vaginal, and rectal. The preparation of the mucoadhesive microspheres, as well as their evaluation, was briefly discussed in this paper.

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INTRODUCTION

Oral drug administration has traditionally been the main method of drug delivery. Numerous oral delivery systems have been created during the past 20 years to serve as drug reservoirs from which the active ingredient can be delivered over a predetermined amount of time at a controlled rate.[11]

The best and most preferred techniques for medication drug administration to the body's basic distribution are established by the oral course of medication organization. However, because they are unable to regulate and restrain the gastro-intestinal tract structure, the majority of drugs administered orally in conventional dose forms have temporary limitations. Due of their small size and high effective bearer limit 2, microspheres make up a considerable portion of these particulate medicine drug delivery frameworks.[2] Controlled and predefined rate The optimal sustained and controlled release dosage form should, from a pharmacokinetic perspective, be analogous to an intravenous infusion, which continuously delivers the dosage required to maintain constant plasma levels once the steady state has been attained.[11]

Mechanism of Mucoadhesion

The complicated process of mucoadhesion includes wetting, adsorption, and interpenetration. chain polymers. The following steps are taken to establish mucoadhesion:

Intimate physical contact (wetting or swelling event) between a bioadhesive or mucoadhesive material and a membrane is known as the contact stage.

• Consolidation stage: Infiltration of the bioadhesive/Mucoadhesive into the tissue underneath or into the mucous membranes surface (interpenetration).[7]

Mucoadhesive Microspheres' Benefits

1. Offer a continuous and lasting therapeutic impact.

2. Decreases the number of daily administrations, which enhances patient compliance.

3. Increase drug absorption to increase drug bioavailability and lessen the likelihood of negative effects.

4. The shape of microspheres allows for predictable variations in medication release and breakdown.[3]

Polymers for Mucoadhesion

Swell able networks are present in either water-soluble or water-insoluble mucoadhesive polymers. Ideally, the polymer should have ideal fluidity to allow for mutual adsorption and interpenetration of the polymer and mucus, as well as perfect polarity to ensure that it is suitably wetted by the mucus. When used in controlled release systems, mucoadhesive polymers satisfy the requirements listed below. [4]

Mucoadhesive Microspheres have Some Limitations

The following list of drawbacks was discovered:

1. There may be changes to the formulas' release.

2. A number of variables, including as food intake, intestinal transit times, mucin turnover rates, etc., may affect the release rate.

3. From one dose to the next, there can be variations in the release rate.

4. Potential toxicity may result from a dosage form's release pattern losing its integrity.

5. These dose forms can't be eaten or crushed.[3]

Methods of Prepration of Microsphere

Mucoadhesive microspheres can be prepared by using different techniques like:

1. Complex coacervation

2. Hot melt microencapsulation

3. Single emulsion technique

4. Double emulsion method

5. Solvent removal

6. Ionotropic gelation

7. Phase inversion method

8. Spray drying

Table No. 1: Techniques for preparation of biodegradable microspheres with its advantages and disadvantages

Sr.No	Name of techniques	Outline steps of technique	Advantages	Disadvantages	Ref.
1.	Ionotropic gelation	The drug's dispersion in the polymeric solution. Drug-loaded polymeric solution is dropped into a polyvalent cation aqueous solution.	since hazardous substances or solvents are not employed.	a more porous and permeable product.	8
2.	Solvent evaporation	A volatile solvent that has dissolved the coating substance. In the coating polymer solution, the core material is dissolved or distributed. In a liquid manufacturing vehicle, the mixture for the core coating is continuously stirred.	necessary gentle conditions, like steady stirring and room temperature.	necessary hazardous organic solvents	9, 10
3.	Spray-drying	Preparing the dispersal uniformization of the dispersion In feed dispersion is atomized. the drying out of atomized particles	The finished microsphere has excellent repeatability. Both liquid and solid materials can be enclosed using this technique. Microsphere accumulation can be reduced to a minimum. No biological activity is lost when different proteins are encapsulated	Excellent repeatability of the final microsphere product. Both liquids and solids can be encapsulated using this method. Microsphere accumulation can be	1, 12,13

				reduced. Different proteins can be encapsulated without losing biological activity.	
4.	Coacervation	The final microsphere product has excellent repeatability. Both liquids and solids can be encapsulated using this technique. Microsphere accumulation can be minimized. It is possible to encapsulate different proteins without losing their biological activity.	Coating can be applied to any core material that can be disseminated in a liquid.	the product's aggregation.	10
5.	Spray-congealing	preparing the dispersal uniformization of the dispersion In feed dispersion is atomized.	Encapsulation can be used for chemicals that are not soluble in common solvents, are frozen liquids, or are heat-sensitive.	High coating concentration is necessary.	10

6. Phase inversion method

The procedure entails mixing the drug with a weak non-solvent, petroleum ether, in a 1: 100 ratio before adding the resulting mixture to a dilute polymeric solution in methylene chloride. The created microspheres are subsequently cleared, petroleum ether washed, and air dried.[24,25]

7. Multiple emulsion polymerization technique

To create a multiple emulsion, a primary emulsion (a non-aqueous drug solution in a polymer solution) must first be formed (o/w). [28]

o/w/o emulsion is created by adding a cross-linking agent (glutaraldehyde) to the exterior oily phase and then letting the organic solvent evaporate. This method of preparation is excellent for integrating a drug that is not well soluble in water, increasing the drug's bioavailability. The multiple emulsion approach is used to create microspheres that increase the bioavailability of drugs that are poorly soluble in water, such as ketorolac tromethamine.[28]

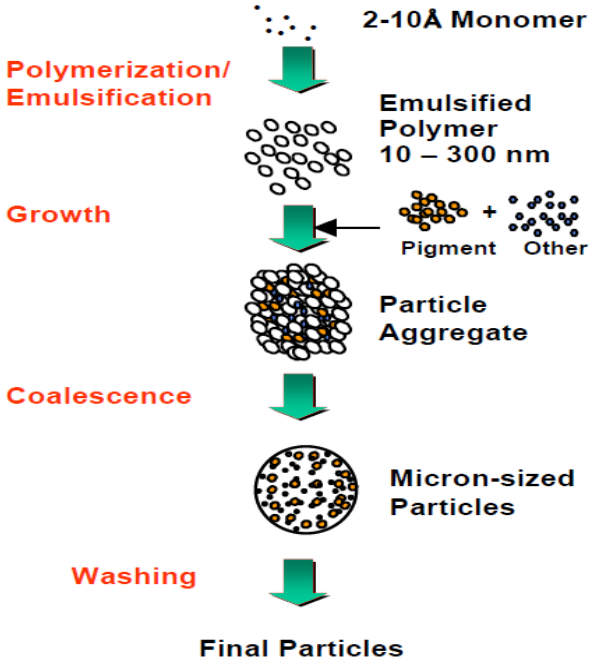

Figure No.1: Microsphere preparation by multiple emulsion method [29]

METHODS OF EVALUATION OF MUCOADHESIVE MICROSPHERES

1. Surface Characterization:

The surface morphology and shape properties of the microspheres can be studied using scanning electron microscopy (SEM), and morphological changes can be observed during polymer degradation.[15,16]

2. Particle Size Determination:

Common techniques include sieving, microscopy, Coulter counter measuring devices, laser light-scattering systems, and laser light diffraction technique can be used to assess particle size.[18]

3. Encapsulation Efficiency:

Two factors can be used to describe the drug content of the microspheres that have been encapsulated. The most typical is the encapsulation efficiency (EE), where EE = D/DT; D is DT minus the amount of unloaded drug. DT stands for the total amount of drug utilized. The loading capacity (LC), on the other hand, is defined as LC = D/SW, where SW is the weight of the spheres. [19]

4. *In-vitro* Release Study:

The *in-vitro* release profile is examined using a standard IP/BP/USP dissolution device in a dissolution medium identical to the fluid using a revolving basket or paddle type dissolution apparatus, present at the absorption location in accordance with the monograph. [20]

5. *Ex-Vivo* Mucoadhesion Study:

According to the monograph, phosphate buffer is used to test the microspheres' mucoadhesive properties on the mucosa of a goat's digestive tract. Weighed microspheres are applied to moist, rinsed tissue samples, and then the slides are immediately suspended from the arm of a USP pill dissolving test apparatus at 37°C with the necessary support. Microsphere weight that is leached off at various times is measured. Equation 34 is used to compute the percentage of mucoadhesion.[21] The adhesion strength increases with an increase in the adhesion number.[28]

$$\% \text{ of mucoadhesion} = \frac{Wa - W1}{Wa} \times 100$$

Where, Wa is the weight of microspheres applied

W1 is the weight of microspheres leached out

6. Surface Charge Study:

The surface charge (zeta potential) of the mucoadhesive microspheres can be calculated from photon correlation spectroscopy data.

By using in-built software based on the Helmholtz-Smoluchowski equation to convert recorded electrophoretic mobility into zeta potential, it is possible to compute the surface charge.[22] Zeta potential, a particle surface charge indicator, can be utilised to forecast and manage the adhesive strength, stability, and mucoadhesion mechanisms. Mucoadhesion is a process that involves interactions between mucus and mucoadhesive polymers and is regulated by these polymers' structure, notably their charge. Electrostatic interactions during mucoadhesion can be predicted with the use of microsphere and mucus zeta potential measurements. [23]

7. Swelling Index

Swelling index show the mucoadhesive microspheres' capacity to swell at the absorbent surface by absorbing fluids present there, which is a prerequisite for the beginning of mucoadhesion.[27]

CONCLUSION

The mucous membrane, the absorption tissue, is in intimate contact with mucoadhesive drug delivery systems, which releases the medication at the site of action and increases bioavailability and local and systemic effects. Mucoadhesive microspheres are unique carrier systems for many drugs, which have been developed for oral, buccal, ocular, nasal, vaginal and rectal routes for either systemic or local effects.

The decision to go for a mucoadhesive or mucopenetrating particulate delivery system depends on various points to be considered. Apart from drug-dependent aspects such as solubility, membrane permeability and mode of action, general delivery aspects such as rapid vs. sustained release properties and the mucosal route of administration have to be taken into account.

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