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MUCOADHESIVE AND MICROSPHERE: A SHORT REVIEW

Preeti Singh*, Richa Tibrewal

Faculty of Pharmaceutical Sciences, Jayoti Vidyapeeth Women's, University Jaipur, Rajasthan, India.

ABSTRACT:

Microsphere constitutes an important part of novel drug delivery system by virtue of their small size and efficient carrier capacity. Due to their short residence time, bioadhesive characteristics can be coupled to microsphere to develop mucoadhesive microsphere. Bioadhesion defined as state in which two materials, at least one of which is biological in nature, are held together for a prolonged time by the way of interfacial forces. Microsphere are the carrier around drug delivery system in which particle size in ranges from 1-1000 μm range in diameter having a core of drug and entirely outer layers of polymers as coating material. Mucoadhesive microsphere have advantages like efficient absorption and enhanced bioavailability of drugs due to high surface of volume ratio, a much more intimate contact with mucus layer, controlled and sustained release of drug from dosage form and specific targeting of drug to absorption site. This study aim to provide an overview of various aspects of mucoadhesive microsphere based on various polymers, method of preparation of mucoadhesive microsphere, method of evaluation and their applications in drug delivery system.

Keywords: Mucoadhesive, microsphere, bioavailability.

INTRODUCTION:

Microsphere are small spherical particles (typically 1 μm to 1000 μm), sometimes referred to as microparticles. The microsphere can be made up of either natural or synthetic polymers. Drug action can be improved by developing new drug delivery system, such as the mucoadhesive microsphere drug delivery system. These systems remain in close contact with the absorption tissue, the mucous membrane, releasing the drug at the action site leading to a bioavailability increase and both local and systemic effects.

Microsphere constitutes an important part of novel drug delivery system by virtue of their small size and efficient carrier capacity. Due to their short residence time, bioadhesive characteristics can be coupled to microsphere to develop mucoadhesive microsphere. Bioadhesion can be defined as the state in which two materials, at least one of which is biological in nature mucoadhesive microsphere have advantages like efficient absorption and enhanced bioavailability of the drugs due to a high surface to volume ratio, a much more intimate contact with the mucus layer and specific targeting of

Corresponding author: Preeti Singh

drugs to the absorption site. Mucoadhesive microsphere have advantages like efficient absorption and enhanced bioavailability of the drugs due to a high surface to volume ratio, a much more intimate contact with the mucus layer and specific targeting of drugs to the absorption site. Mucoadhesion is a topic of current interest in the design of drug delivery systems. Mucoadhesive micro-spheres exhibit a prolonged residence time at the site of application or absorption and facilitate an intimate contact with the underlying absorption surface and thus contribute to improved and/or better therapeutic performance of drugs.

Advantages of Mucoadhesive Microsphere

1. Provide constant and longer therapeutic effect.

2. Reduces the frequency of daily administration and thereby improve thepatient compliance.

3. Improve the absorption of drug hence improves the bioavailability of drug and reduce the chances of adverse effects.

4. The morphology of microsphere permits a controllable variability in degradation and drug release.

Limitation of Mucoadhesive Microsphere

Some of the disadvantages were found to be as follows

1. The release from the formulations may get modified.

2. The release rate may vary from a variety of factors like food and the rate of transit though gut, mucin turnover rate etc.

3. Differences in the release rate can be found from one dose to another.

4. Any loss of integrity in release pattern of the dosage form may lead to potential toxicity.

5. These kinds of dosage forms cannot be crushed or chewed.

Generally microsphere posses' potentiality to be employed for targeted and controlled/extended release of drug, but incorporating mucoadhesive properties to microsphere will furthermore improve absorption and bioavailability of the drugs. Tailored mucoadhesive microsphere offers the possibilities of localized as well as controlled release of drugs by adherence to any mucosal tissue present in eye, nasal cavity, urinary, and GI tract.

Mucoadhesive

Bioadhesion is a phenomenon in which two materials at least one of which is biological in nature are held together by means of interfacial forces. The term "mucoadhesive" define the adhesion of the polymers with the surface of the mucosal layer. Mucoadhesive polymers have interest around pharmaceutical scientists as a mean in improving drug delivery by the promoting of residence time and contact time of dosage form with in the mucous membranes.

Mucus Membranes

Mucus membranes are the moist surfaces lining walls of various body cavities such as the gastrointestinal and respiratory tracts. Mucus is secreted by the goblet cells. Mucus is present either as a gel layer adherent to the mucosal surface or in suspended form or as a luminal soluble. The major components of all mucus gels are mucin glycoprotein, water, lipids, and inorganic salts. If these materials are then incorporated into pharmaceutical formulations, drug absorption by mucosal cells may be enhanced or the drug will be released at the site for an extended period of time.

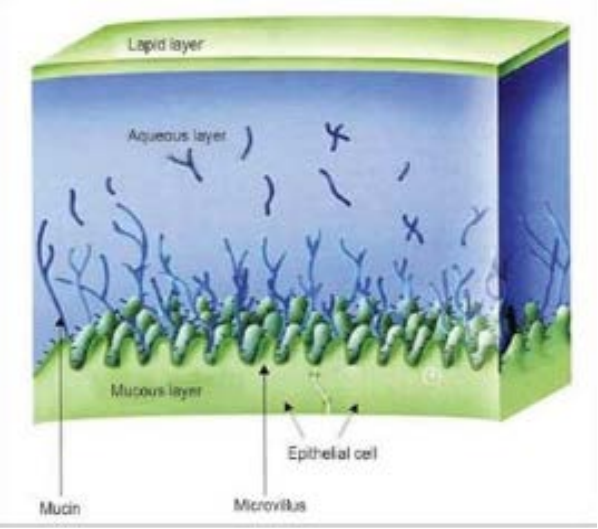

Figure 1: Structure of mucus membrane

EVALUATION OF MUCOADHESIVE MICROSPHERE

Microsphere, in general, have the potential to be used for targeted and controlled release drug delivery; however, coupling of mucoadhesive properties to microsphere has additional advantages like, a much more intimate contact with the mucus layer, efficient absorption and enhanced bioavailability of the drugs due to a high surface to volume ratio. The microspheres are evaluated for the following parameters.

1. Particle Size and Shape

Light microsphere (LM) and scanning electron microsphere (SEM) both can used to determine the size and shape and the outer structure of microsphere. The sizes of prepared microsphere can be measured by optical microsphere using a method of Caliberated stage micrometer for selected samples.

Optical microsphere

Optical microsphere method is use to determine the particle size of microsphere by the using of optical microsphere i.e, (Meizer OPTIK).

2. Percent Swelling Index

This technique is used for the Characterization of sodium alginate microsphere. Different solution (100mL) are taken such as (distilled water, buffer solution of pH (1.2, 4.5, 7.4) are taken. After determination of the original film weight and diameter, the samples were allowed to swell on the surface of agar plate kept in an incubator maintained at 37±0.2°.

The swelling index of the microsphere is calculated by using the formula:-

Swelling index= (mass of swollen microsphere - mass of dry microsphere/mass of dried microsphere) 100.

3. Entrapment Efficiency

The entrapment efficiency of the microsphere or the percent entrapment can be determined by keeping the microsphere into the buffer solution and allowing lysing. The lysate obtained is filtered or centrifuged and then subjected for determination of active constituents as per monograph requirement. The percent entrapment efficiency is calculated using followingequation

(% Entrapment = Actual content/Theoretical content x 100)

4. Surface topography by Scanning Electron Microsphere (SEM).

SEM of the microsphere shows the surface morphology of the microsphere like their shape and size. Scanning electron microsphere (SEM):- Surface morphology of microsphere is determined by the method SEM. In this method microsphere are mounted directly on the SEM sample slub with the help of double sided sticking tape and coated with gold film under reduced pressure. Scanning Electron photomicrographs of drug-loaded microsphere are taken. A small amount of microsphere s spread on gold stub. Afterwards, the stub containing the sample is placed in the Scanning electron microsphere (SEM). A Scanning electron photomicrograph is taken at an acceleration voltage of 20KV and chamber pressure of 0.6 mm Hg.

5. Stability studies.

By placing the microsphere in screw capped glass container and stored them at following conditions:-

1. Ambient humid condition
2. Room temperature (27+/-2 0C)
3. Oven temperature (40+/-2 0C)
4. Refrigerator (5 0C -80C).

It is carried out of a 60 days and the drug content of the microsphere is analyzed.

6. Moisture content

For the determination of moisture content, 3 cm ×3 cm piece of film was weighed and kept in a desiccator containing calcium chloride at 40°C for 24 h. Films were removed from the desiccator and weighed until a constant weight was obtained. The percentage of the moisture content was calculated as the difference between initial and final weights with respect to the initial weight.

7. In-Vitro Release Study

Standard IP/BP/USP dissolution apparatus is used to study in-vitro release profile in the dissolution media that is similar to the fluid present at the absorption site as per monograph, using rotating

basket or paddle type dissolution apparatus. One film of each formulation was fixed to the central shaft at just above the basket, using a cyanoacrylate adhesive.

The release study was performed at 37 ± 0.5° with a rotation speed of 50 rpm. The release study was carried out for 6 h. After every hour, 1 ml sample was withdrawn from each station and the same volume was replaced back to the stations. Each withdrawn sample was filtered, diluted suitably and then analyzed spectrophotometrically at 274 nm. The data presented were the mean of three determinations.

8. In vitro mucoadhesive test

The mucoadhesive property of the optimized microsphere prepared by different methods is evaluated by an in vitro mucoadhesive testing method known as the wash-off method. The microsphere remaining at the surface of gastric mucosa is then collected, and the percentage of the remaining microsphere is calculated. A rat stomach mucosa is tied onto the glass slide using a thread. In this method microsphere are spread onto wet rinsed tissue specimen and the prepared slide is hung onto one of the grooves of a USP tablet disintegrating test apparatus.

The formula is using:-

Percent mucoadhesive = (Weight of adhered microsphere /Weight of applied microsphere) ×100

9. In situ Bioadhesivity Studies.

Bioadhesivity testing is done by a novel in situ method. The piece is cut open and the mucosal surface is exposed. A freshly cut 5-6cm piece of small intestine of rat is obtained and clean by washing with isotonic saline solution. The Known weight of microsphere are add evenly on mucosal surface. The intestinal piece is maintain at 80% relative humidity for 30minutes in desiccator. The piece is take out and phosphate buffer pH 6 which is allowed to flow over intestinal piece for about 2 minutes at a rate of 20ml/min. The perfusate is collect and dry to get the particle not adhered. The percent of bioadhesion is estimated by ratio of amount applied to adhere micro matrices.

10. Bulk density

The microsphere fabricated are weighed and transferred to a 10-ml glass graduated cylinder. The cylinder is tapped using an autotrap until the microsphere bed volume is stabilized. The bulk density is estimated by the ratio of microsphere weight to the final volume of the tapped microsphere bed.

CONCLUSION

Novel drug delivery systems achieved a great interest in recent years in the field of modern pharmaceutical formulations. Mucoadhesive microsphere have been proved as a promising tool in delivery of drugs to a particular site in controlled or sustained manner, as they deliver the drug to a particular site for longer duration, the absorption of drug increased and hence, the bioavailability of the drug get increased. In recent years such mucoadhesive microsphere have been developed for oral, buccal, nasal, ocular, rectal and vaginal routes for either systemic or local effects. Therefore, it can be say that in future also mucoadhesive microsphere will play an important role in the development of new pharmaceuticals employing more advanced techniques and materials. The present study indicates a good potential of erodible mucoadhesive buccal films containing glipizide for systemic delivery with an added advantage of circumventing the hepatic first pass metabolism. *In vivo* studies need to be designed and executed to substantiate further *in vitro* - *in vivo* correlation. This delivery system offers advantage of controlled release with enhancement of bioavailability. The objective of this article is reviewing the principles underlying the development and evaluation of mucoadhesive microsphere.

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