ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 12, Issue, 06, pp.12053-12056, June, 2020

DOI: https://doi.org/10.24941/ijcr.38954.06.2020

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

REVIEW ARTICLE

A REVIEW ON ADVANCED METHODS AND PREPARATION OF MUCOADHESIVE MICROSPHERE

Nishant kumar*, Hina Chadha and Seema Mahor

Department of Pharmaceutical Sciences, Vishveshwarya Group of Institutions, G B Nagar Dadri, Greater Noida, 203207, U.P. India.

ARTICLE INFO

Article History:
Received 20th March, 2020
Received in revised form
19h April, 2020
Accepted 17th May, 2020
Published online 30th June, 2020

Key Words:
Methods, Mucoadhesive Microspheres, Advanced, Drug Delivery.

ABSTRACT

Carrier technology provides an interesting as well as an intelligent approach for the delivery of the drug. Some general methods of delivery of the drug are by coupling the drug to a carrier particle such as microsphere, nanoparticles, liposome's, etc. Microsphere constitutes an important part of this particulate drug delivery system because of their small size and other efficient properties. Among all these drug delivery system mucoadhesive microsphere are new technology as it provide better drug absorption as they get adhere to the mucosal surface and release are drug for prolonged time the article reviewed about the new technologies and methods for preparation of mucoadhesive microsphere in brief.

Citation: ***Dr. Deepti Diwakar, Dr. Arun Krishnan, Dr. Balakarishnan, R. and Dr. Vijay Ebenezer.*** **2020.** "A Review on advanced methods and preparation of mucoadhesive microsphere", *International Journal of Current Research*, 12, (06), 12053-12056.

INTRODUCTION

Drug action can be improved by developing new drug delivery system, such as the mucoadhesive drug delivery system. These system remain in close contact with the absorption tissue, the mucous membrane, releasing the drug at the action site leading to a bioavailability increase both local and systemic effect (Parmar, 2010) the oral route of drug administration constitutes the most convenient and preferred means of drug delivery to systemic circulation of body. However oral administration of the most drugs in conventional dosage form has short-term due to their inability to restrain and localize the system of gastrointestinal tract. Microspheres constitute an important part of particulate drug delivery system by virtue of their small size and efficient carrier capacity. Microsphere are the carrier linked delivery system in which particle size ranges from 1-1000 μm range in diameter having a core of drug and entirely outer layers of polymer as coating material. However, the success of these Microspheres is limited due to their short residence time at site of absorption. It would, there for be advantageous to have means for providing an intimate contact of the drug delivery system with the absorbing membrane. This can be achieved by coupling bioadhesion Characteristics to microspheres developing "mucoadhesive microspheres",

Corresponding author:* **Nishant kumar,
Department of Pharmaceutical Sciences, Vishveshwarya Group of Ins titutions, G B Nagar Dadri, Greater Noida, 203207, U.P. India.

Mucoadhesive microspheres 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 (Patil , 2006)

Method and preparation of muccoadhesive microsphere

Microspheres can be prepared by using different techniques like (Mathiowitz, 1999a; Zhang, 2009)

- Complex coacervation
- Hot melt microencapsulation
- Single emulsion techniques
- Double emulsion method
- Solvent removal
- Ion tropic Gelatin
- Phase inversion method
- Spray drying.

Complex coacervation: Principle of this method is under suitable condition when solution of two hydrophilic colloids were mixed, results into a separation of liquid precipitate .in this method the coating material phase, prepared by dissolving immiscible polymer in a suitable vehicle and the core material is dispersed in a solution of coating polymer under constant stirring. Microencapsulation was achieved by utilizing one of the methods of phase separation, that is, by changing the ph of

the medium, by adding a salt or an incompatible polymer or a non-solvent to the polymer solution; by including a polymer-polymer interaction. Generally coating is hardened by thermal cross linking or desolation technique, to form a self sustaining microsphere (Ogawa, 1988).

Hot melt microencapsulation

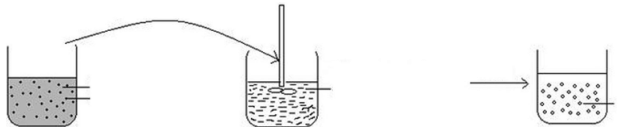

Figure 1. Hot melt microencapsulation

This method was first used by Mathiowitz and Lengerto prepare microspheres of polyanhydride copolymer of poly (bis (P-carboxyphenoxy) propane anhydride) with sebacic acid. In this method, the polymer was first melted and then mixed with solid particles of the drug that had been sieved to less than 50µm. the mixture was suspended in a non miscible solvent (like silicon oil), continuously stirred, and heated to 5 °C above the melting point the polymer. When the emulsion stabilized it was left for cooling until the polymer particles solidified.

The resulting microspheres were washed with petroleum ether. The main objective for developing this method was to develop a microencapsulation process suitable for the water labile polymers, e.g., polyanhydride. Microspheres with diameter of 1-1000 µm could be obtained and the size distribution could be easily controlled by changing the stirring rate. The major limitation of this method is that it is not suitable for thermo labile substances (Goudanavar, 2010; Alagusundaram, 2009)

Single emulsion technique: Generally, by this technique carriers of natural polymers like protein and carbohydrates are prepared. The natural polymers are dissolved or dispersed in aqueous medium followed by dispersion in non-aqueous medium like oil. Next cross linking of the dispersed globule is carried out. The cross linking can be achieved either by means or heat by using the chemical cross linkers. The chemical cross linking agent used are glutaraldehyde, formaldehyde, Diacid chloride, tetra phthalate chloride etc (Sinha, 2004) that is the first step in next step cross linking is carried out by two methods.

- **Cross linking by heat:** by adding the dispersion into heated oil, but it is unsuitable for the thermo labile drugs.
- **Chemical cross linking agent:** by using agent i.e. formaldehyde, die acid chloride, Glutaraldehyde etc. but it is having a disadvantage of excessive exposure of active ingredient to chemical if added at the time of preparation and then subjected to centrifuge, washing and separation. chitosan solution (in acetic acid) by adding to liquid paraffin containing a surfactant resulting formation of w/o emulsion (Jayaprakash, 2007) metformin hydrochloride microsphere are prepare by using glutaraldehyde 25% solution as cross linking agent (Vyas, 2007; Carino, 2017)

Double emulsion technique: Double emulsion method of microsphere preparation involves the formation of the emulsion of type w/o/w and is best suited for water soluble drugs, peptides, proteins and the vaccines. This method can be used with both the natural as well as synthetic polymers.

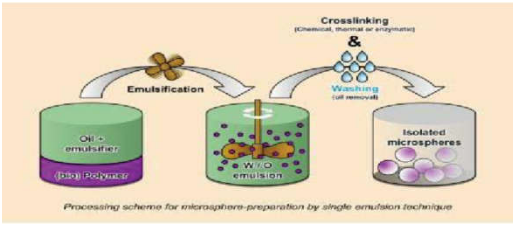

Figure 2. Single emulsion techniques for microspheres preparation

The aqueous protein solution as 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 encapsulation of the protein contained in dispersed aqueous phase. The primary emulsion is subjected then to the homogenization of the sonication before addition before addition to the aqueous solution of the poly vinyl alcohol (PVA). This results in the formation of the double emulsion. The emulsion is then subjected to solvent removal either by solvent evaporation or by solvent extraction. A number of hydrophilic drugs like luteinizing hormone releasing hormone (LH-RH) agonist, vaccines, proteins /peptides and conventional molecules are successfully incorporated into the microspheres using the method of double emulsion solvent evaporation extraction. (Mathiowitz, 1999)

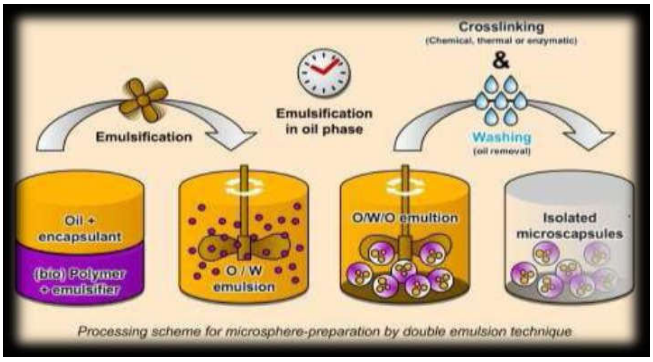

Figure 3. Microspheres preparation Double emulation techniques

Solvent evaporation/ removal: This is non-aqueous method of microencapsulation and is most suitable for water labile polymers such as the poly anhydrides. The method involves dissolving the polymer into volatile organic solvent and the drug is dispersed or dissolved in it, this solution is then suspended in the silicon oil containing span 85 and ethylene chloride under stirring. Then petroleum ether is added and stirred until solvent is extracted into the oil solution .the obtained microsphere were then subjected for vacuum drying (Madhusudan, ?)

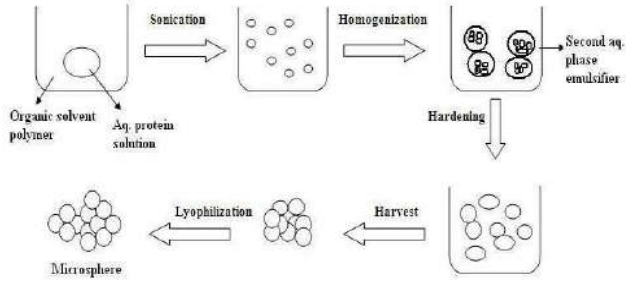

Figure 4. Solvent removal/ Evaporation method Microspheres preparation

Ionotropic gelation technique: sodium alginate and the mucoadhesive polymer are dispersed in purofied water (50 ml) to form a homogeneous polymer mixture. Drug is added to the polymer matrix and mixed throughly to form smooth viscous dispersion. Resulting dispersion ps then sprayed into calcium chloride (10% w/v) solution by continuous stirring. Produced droplets are retained in the calcium chloride solution for 15 minutes to complete the curing reaction and the thus separated is washed repeatedly with purified water to remove excess calcium impurity deposited on the surface of microsphere and then dried at 45 °C for 12 hrs (Patil, 2012)

Mechanism: Microsphere prepared by ionotropic gelatin technique mechanism involves electrostatic interaction between amine groups of polymer and negatively charged group of polyanion such as tripolyphosphate. Chemical reaction between sodium alginate and calcium chloride to form calcium alginate was utilized for microsphere formation. As calcium ions are being released by ion exchange with sodium ion in the medium, electrostatic repulsion between the carboxylate anions further accelerates the swelling and erosion of alginate gels. On account of short time release in alkaline media , alginate was not found to be an ideal sustained release wall material for microencapsulation (Chickering, 1999)

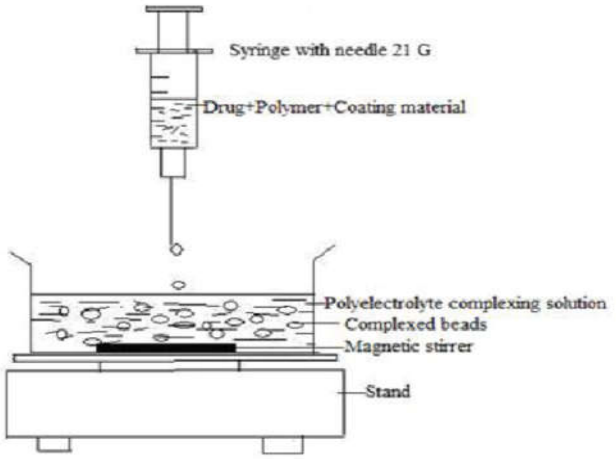

Figure 5. By Ion tropic gelation method for Microspheres preparation

Phase inversion method: The method involves addition of drug into dilute polymeric solution, in ethylene chloride; and resultant mixture is poured into an unstirred bath of strong non-solvent, petroleum ether, in a ratio of 1:100. Microspheres produced are then clarified, washed with petroleum ether and air dried (Costa and Margarida Cardoso, 2006).

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. The 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 microsphere in a size range 1-100 µm. 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 condition. This process is rapid and this leads to the formation of porous micro particles (Koff, 1963).

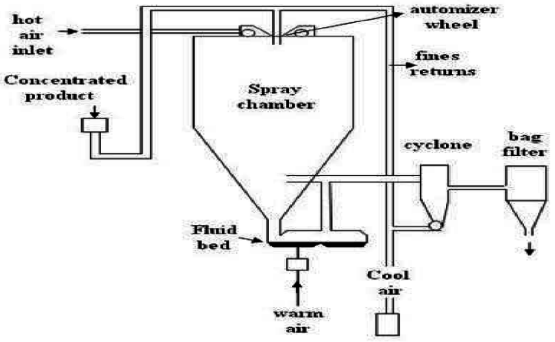

Figure 6. Spray drying method for Microsphere preparation

Canclusion

A new approach investigated to over ride normal gastric emptying is the use of mucoadhesive microspheres for gastro-retention. Based on this approach mucoadhesive microspheres in gastro-retentive delivery system present the promising area for continued research. This delivery system offers the advantages of controlled release with an enhanced bioavailability. The degree of success of this approach lies on the thorough understanding of mucoadhesive polymers, methodologies for preparation and evaluation techniques for mucoadhesive microspheres.

Acknowledgement

The author declares deep thanks to Vishveshwarya Group of Institutions, G.B. Nagar, Greater Noida, 203207

Conflict of interest: The author declares no conflict of interest.

REFERENCES

Alagusundaram M, Chetty MS, Umashankari K, Badarinath AV, Lavanya C, Ramkanth S. 2009. Microspheres as a novel drug delivery system: A review. *Int J Chem Tech Res.,* 1(3): 526-534.

Carino PG, Jacob JS, Chen CJ, Santos CA, Hertzog BA, Mathiowitz E. 2017. Bioadhesive, bioerodible polymers for increased intestinal uptake. *International Journal of Pharmacy and Pharmaceutical Sciences,* 5(23):21-34

Chickering DE, Santos CA, Mathiowitz E. Adaptation of a microbalance to measure bioadhesive properties of microspheres. In: Mathiowitz E, Chickering DE, Lehr CM, eds. Bioadhesive Drug Delivery Systems: Fundamentals, Novel Approaches and Development. New York: Marcel Dekker; 1999:131-145.

Costa MS and Margarida Cardoso MM. 2006. Effect of uniform sized polymeric microspheres prepared by membrane emulsification technique on controlled release of anthracycline anti-cancer drugs. Desalination, 200: 498–500

Goudanavar PS, Bagali RS, Patil SM. 2010. Design and Characterization of Diclofenac Sodium Microbeads By Ion tropic Gelation Technique, *International Journal of Pharma and Bio Sciences*, 2

Jayaprakash S, Halith S M, Mohamed Firthouse P U, Kulaturanpillai K, Abhijith, Nagarajan M.2009. Preparation and evaluation of biodegradable microspheres of methotrexate. Asian J Pharm, 3; 26-9.

Madhusudan Y R, Jithan AV. Microspheres, Advances in drugdelivery, volume1, Pharma Med Press Pg.no. 309-374.

Mathiowitz E, Chickering DE, Lehr CM, eds. Bioadhesive Drug Delivery Systems: Fundamentals, Novel Approaches and Development. New York: Marcel Dekker; 1999: 459-475

Mathiowitz E, Kreitz MR, Peppas LB. 1999a. Microencapsulation. In: Mathiowitz E, ed. Encyclopedia of Controlled Drug Delivery, Vol. 9. New York: John Willey & Sons; 493-504

Ogawa Y, Yamamoto M, Okada H, Yashiki T, Shimamoto T. 1988. A New technique to efficiently entrap leuprolide acetate into microcapsules of polylactic acid or copoly (lactic/glycolic) acid. Chem Pharm Bull (Tokyo) 36:1095-103.

Parmar H, Bakliwal S, Gujarathi N, Rane B, Pawar S. 2010. Different method of formulation and evaluation of mucoadhesive microsphere. *International Journal of Applied Biology and Pharmaceutical Technology,* 1(3): 1157-1167.

Patil SB, Murthy SR, Mahajan HS, Wagh RD, Gattani SG. 2006. Mucoadhesive polymers: Means of improving drug delivery. Pharma Times. 38: 25-28.

Patil P, Chavanke D, Wagh M. 2012. A review on ionotropic gelation method: novel approach for controlled gastroretentive gelispheres. *International Journal of Pharmacy and Pharmaceutical Sciences* 4(34):27-32

Sinha V R, Singla A K, Wadhawan S, Kaushik R, Kumria R, Bansal K, Dhawan S. 2004. Chitosan microspheres as a potential carrier for drugs, International Journal of Pharmaceutics274; 1–33

U.S. Koff 1963. Patent, March 2, 1963, 3, 080,292.

Vyas SP, Khar RK. Targeted and Controlled drug delivery, 07 edition 2007., 418

Zhang L, Liu Y, Wu Z, Chen H. 2009. Preparation and characterization of coacervate microcapsules for the delivery of antimicrobial oyster peptides. Drug Dev Ind Pharm. 35(3): 369-278.

****