WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 7.632
Volume 9, Issue 9, 1499-1507 Review Article ISSN 2278 – 4357

A REVIEW ARTICLE ON NOVEL DRUG DELIVERY SYSTEM; MICROSPHERE

Priya Katiyar[1]*, Sonam Singh Parmar[2], Sunil Kumar[3], Shubham Tripathi[4] and Harshita Gupta[5]

[1,2]Shri Rawat Pura Sarkar Group of Institutions, Datiya.
[3]Dayanand Dinanath College Institute of Pharmacy, Ramaipur Kanpur.
[4]Goel Institute of Pharmacy and Sciences Lucknow.
[5]Kanpur Institute of Technology and Pharmacy Kanpur.

Article Received on
16 July 2020,
Revised on 06 August 2020,
Accepted on 27 August 2020
DOI: 10.20959/wjpps20209-17214

***Corresponding Author**
Priya Katiyar
Shri Rawat Pura Sarkar
Group of Institutions, Datiya.

ABSTRACT

Microspheres having free flowing powder characteristics, which are consisting of synthetic polymers and proteins. These are biodegradable in nature having particle size less than 200um. Floating microspheres are gastro-retentive drug delivery systems based on non-effervescent approach. Hollow microspheres are in strict sense, spherical empty particles without core. These microspheres are characteristically free flowing powders consisting of proteins or synthetic polymers, ideally having a size less than 200 micrometer. Solid biodegradable microspheres incorporating a drug dispersed or dissolved throughout particle matrix have the potential for controlled release of drugs. When microspheres come in contact with gastric fluid the gel formers, polysaccharides, and polymers hydrate to form a colloidal gel barrier that controls the rate of fluid penetration into the device and consequent drug release. As the exterior surface of the dosage form dissolves, the gel layer is maintained by the hydration of the adjacent hydrocolloid layer. The air trapped by the swollen polymer lowers the density and confers buoyancy to the microspheres. However, a minimal gastric content needed to allow proper achievement of buoyancy. Hollow microspheres of Acrylic resins, Eudragit, PMAA, Polyethylene oxide, and Cellulose acetate; Polystyrene floatable shells; Polycarbonate floating balloons and Gelucire floating microspheres are the recent developments. Microspheres are the multiarticulate drug delivery systems which are consisting from natural and synthetic material. Microsphere improves bioavailability, stability and target the drug to specific site at predetermined rate. types of microspheres are

bio adhesive, floating, radioactive, polymeric and biodegradable microspheres. Microspheres are particularly used in novel drug delivery system.

KEYWORDS: Microsphere, NDDS, advantages, types, method of preparations.

INTRODUCTION

Microspheres are defined as "Monolithic sphere or therapeutic agent distributed throughout the matrix either as a molecular dispersion of particles (or) can be defined as structure made up of continuous phase of one or more miscible polymers in which drug particles are dispersed at the molecular or macroscopic level. It has a particle size of (1-1000nm). Further, currently available slow release oral dosage forms, such as enteric coated or double-layer tablets which release the drug for 12-24 hours still result in inefficient systemic delivery of the drug and potential gastrointestinal irritation. The drug has to be delivered for a prolonged period of time and many medicines have to be taken simultaneously in case of chronic patients. The controlled release dosage form maintaining relatively constant drug level in the plasma by releasing the drug at a predetermined rate for an extended period of time. Microspheres are solid spherical particles ranging in size from 1-1000μm[1]. They are spherical free flowing particles consisting of proteins or synthetic polymers.

Drug delivery system target drug to the specific body site which having enormous impact on the healthcare system.[1-3] The ideal drug delivery system delivers the drug at rate decided by need of body throughout the period of treatment therefore carrier technology find out the intelligent approach for drug delivery by coupling the drug to carrier particles example, microspheres, nanoparticles, liposomes[4-6] oral route of drug administration is most preferable route for taking medication.[1] Microspheres are small spherical particles which having diameter 1um to 100um. They are free flowing particles which are consisting of proteins or synthetic polymers this are biodegradable in nature. There are two types of microspheres

1) microcapsule-entrapped substance distinctly surrounded by distinct capsule wall

2) micrometrics-entrapped substance is dispersed throughout the matrix 1

Controlled drug delivery system overcome the problems of conventional therapy and enhance therapeutic efficacy of given drug[7] to obtain maximum therapeutic efficacy it becomes necessary to deliver the agent. Microspheres are used in development of new drug delivery system for controlled release of drug.[8-10]

ADVANTAGES OF MICROSPHERES

They provide protection before after administration for unstable drug.

They reduced concentration of drug at site other than the tissue or the target organ.

Decrease dose and toxicity.

Particle size reduction for enhancing solubility of poorly soluble drugs.

Provide constant and prolonged therapeutic effect.

Enhanced absorption of drugs which solubilize only in stomach

Drug releases in controlled manner for prolonged period.

Site-specific drug delivery to stomach can be achieved.

Superior to single unit floating dosage forms as such microsphere's releases drug uniformly and there is no risk of dose dumping. Avoidance of gastric irritation, because of sustained release effect.

Better therapeutic effect of short half-life drugs can be achieved.

Reduces the dosing frequency and thereby improve the patient compliance.

Better drug utilization will improve the bioavailability and reduce the incidence or intensity of adverse effects and despite first pass effect because fluctuations in plasma drug concentration is avoided, a desirable plasma drug concentration is maintained by continuous drug release.

Hollow microspheres are used to decrease material density and Gastric retention time is increased because of buoyancy.

1.1.3 Limitation[4]

Some of the disadvantages were found to be as follows: -

a) Controlled release formulations generally contain a higher drug load and thus any loss of integrity of the release characteristics of the dosage form may lead to potential toxicity.
b) Dosage forms of this kind should not be crushed or chewed.
c) The modified release from the formulations.
d) The release rate of the controlled release dosage form may vary from a variety of factors like food and the rate of transit though gut.

Types of Microspheres

1. Bio adhesive microspheres
2. Magnetic microspheres
3. Floating microspheres

4. Radioactive microspheres

5. Polymeric microspheres

I) Biodegradable polymeric microspheres

ii) Synthetic polymeric microspheres

Bio adhesive microspheres

1. Biodegradable polymeric microspheres[2, 3]

Biodegradable polymers prolong the residence time when contact with mucous membrane due to its high degree of swelling property with aqueous medium, results gel formation. Natural polymers such as starch are used with the concept that they are biodegradable, biocompatible, and also bio adhesive in nature. 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. However they provide wide range of application in microsphere based treatment. e.g. Lactides, Glycosides & their co-polymers**.**

2. Synthetic polymeric microspheres[4]

Synthetic polymeric microspheres are widely used in clinical application, moreover that also used as bulking agent, fillers, embolic particles, drug delivery vehicles etc and proved to be safe and biocompatible. But the main disadvantage of these kinds of microspheres, are tend to migrate away from injection site and lead to potential risk, embolism and further organ damage E.g. Poly methyl methacrylate (PMMA) Acrolein.

3. Magnetic microspheres[2,6]

This type of delivery system is very much important for localizes the drug to the disease site. site. In which larger amount of freely circulating drug can be replace by small amount of magnetically targeted drug. Magnetic carriers receive magnetic responses to a magnetic field.

4. Floating microspheres[2,10]

In floating microspheres, the bulk density is less than the gastric fluid therefore it remains buoyant in stomach without affecting on gastric emptying rate. Drug is released slowly at the desired rate of the site. It also reduces chances of striking and dose dumping Produces.

5. Radioactive microspheres[6]

Radio mobilization therapy microspheres having sized 10-30 nm are of larger than capillaries. They are injected to arteries which lead to tumor of interest. These radioactive microspheres deliver high radiation dose to targeted areas without damaging the normal tissues. Different types of radioactive microspheres are α emitters, β emitters, γ emitters.[9]

METHOD OF PREPRATION

1. Spray Drying
2. Solvent Evaporation
3. Single emulsion technique
4. Double emulsion technique
5. Phase separation coacervation technique
6. Spray drying and spray congealing
7. Solvent extraction
8. Quassi emulsion solvent diffusion

1. Spray Drying[1]

In Spray Drying technique, polymer is first dissolved in volatile organic solvent such as dichloromethane, acetone, etc. The drug in solid form is then dispersed in to polymeric solution with the high-speed homogenization. This dispersion is then atomized in hot air stream. The atomization leads to the form the small droplets from which the solvent evaporates instantly leads the formation of the microspheres in the size range 1-100µm. Micro particles are separated from hot air by the cyclone separator while the trace of solvent is removed by vacuum drying. major advantages of this process is feasibility of operation under aseptic conditions.

2. Solvent Evaporation[14-17]

This process is carried out in vehicle phase of liquid manufacturing. The microcapsule coating is dispersed in the volatile solvent which immiscible with the vehicle phase of liquid manufacturing. A core material which is microencapsulated is dissolved in the coating polymer solution. Agitation With the core material mixture is dissolved in the liquid manufacturing vehicle phase to obtain appropriate size microcapsule. Then the mixture is heated if necessary, to evaporate and the solvent for the polymer of the core material is dissolved in the polymer solution, around the core polymer shrinks. If core material is dissolve in the coating polymer solution, matrix type microcapsules are formed. The core materials are either water soluble or soluble materials.

3. Single emulsion technique[1]

The micro particulate carriers of the natural polymers i.e. proteins and carbohydrates are prepared by the single emulsion technique. Natural polymers are dissolved in aqueous medium which is followed by the dispersion in non-aqueous medium like oil. In next step, the cross linking of dispersed globule is carried out. The cross linking can be achieved by the heat or by using the chemical cross linkers. T chemical cross-linking agents used are glutaraldehyde, formaldehyde, acid chloride. Heat denaturation is not suitable for the thermolabile substance. Chemical cross linking having the disadvantage of excessive exposure of active ingredient to chemicals if added at time of preparation and then subjected to centrifugation, washing, separation, nature of the surfactants used to stabilize the emulsion phases can greatly influence by the size, size distribution, surface morphology and loading drug release, and bio per- formance of the final multiarticulate product.

4. Double emulsion technique[5]

This method of microspheres preparation involves formation of multiple emulsions or double emulsion of type w/o/w and is best suited to the water-soluble drugs, peptides, proteins and vaccines. This method can be used with the both natural as well as synthetic polymers. The aqueous protein solution is dispersed in the lipophilic organic continuous phase. This protein solution may contain the active constituents.

5. Phase separation coacervation technique[1]

This process is based on the principle of the decreasing the solubility of polymer in organic phase which affect the formation of polymer rich phase called the coacervates. In this method, drug particles are dispersed in a solution of polymer and an incompatible polymer is added to system which makes first polymer for the phase separation.

6. Spray drying and spray congealing[18]

These methods are based on the drying of the mist of polymer and drug in the air. Depending upon removal of the solvent or cooling of the solution, these two processes are named spray drying and spray congealing.

7 Solvent extraction[1]

Solvent evaporation method is used for the manufacturing of microparticles and involves removal of the organic phase by extraction of the non-aqueous solvent. This method involves the water miscible organic solvent which is isopropanol.

8 Quassi emulsion solvent diffusion[18,19]

A novel quasi-emulsion solvent diffusion method used for the manufacturing of the controlled release microspheres of drugs with acrylic polymers has been reported in the literature. Micro sponges can be manufactured by the quassi emulsion solvent diffusion method by using external phase which contains distilled water and polyvinyl alcohol. The internal phase consists of the drug, ethanol and polymers. Firstly, the internal phase is manufactured at 60ºC and after then added to the external phase at room temperature. Then emulsification the mixture is continuously stirred for 2 hours. Then the mixture can be filtered for separate the micro sponges.

REFERENCES

1. Suvarna V., Microspheres: A brief review, Asian Journal of Biomedical and Pharmaceutical Sciences, 2015; 5(47): 13-19.
2. Kapoor D., Patel M., Vyas RB., Lad C.and Tyagi BL, A Review on micro sponge drug delivery system, Journal of Drug Delivery and Therapeutics, 4(5): 29-35.
3. Nikam VK et el., Microspheres - A Novel Drug Delivery System: An Overview, International Journal of Pharmaceutical and Chemical Sciences, 2012; 1(1).
4. Shukla P. and Vijaya Vani CH.S., Review article on microsphere volume, IJPAR, 2015; 4(3): 291-301.
5. Prasanth V.V., Moy A. C., Mathew S. T. and Mathapan R. Microspheres An overview, Int. J. Res. Pharm. Biomed. Sci., 2011; 2: 332 8.
6. Saralidze K., Koole L.H. and Knetsch M. L. W., Polymeric micro- spheres for medical applications, Materials., 2010; 3: 3537-64.
7. Ramteke K.H., Jadhav V.B., and Dhole S.N. Microspheres: As carriers used for novel drug delivery system, IOSRPHR., 2012; 2(4): 44-48.
8. Patel B., Modi V., Patel K.and Patel M., Preparation and evaluation of ethyl cellulose microspheres prepared by emulsification solvent evaporation, international Journal for Research in Management and Pharmacy., 2012; 1(1): 83-91.
9. Bansal H., Kaur S. P.and Gupta A. K. Microsphere: Methods of preparation and applications;A comparative study, Int J Pharm Sci Rev Res., 2011; 10(1): 69-78.

10. Alagusundaram M., Chetty. C. M. S., Umashankari K., Badar- inath A. V., Lavanya C. and Ramkanth. S. Microspheres as a novel drug delivery sytem- A review, Int J ChemTech Res., 2009; 1(3): 526-34.
11. Rastogi V., Shukla S., Singh R., Lal N.and Yadav P. Microspheres: A Promising Drug Carrier. Journal of Drug Delivery and Therapeutics, 2016; 6(3): 18-26.
12. Saravana Kumar K., Jayachandra Reddy P.and Chandra Sekhar K.B. A Review on Microsphere for Novel drug delivery System. Journal of Pharmacy Research, 2012; 5(1): 420-424.
13. Bansode AS., Kute VB., Vethekar KS., Kote PS., Varhadi MK.and Bansode AS. Formulation, development and evaluation of Microsponge loaded Topical Gel of Nystatin, Journal of Drug Delivery and Therapeutics, 2019; 9(2-s): 451-461.
14. Guojun Liu., Husheng Yang. and Jiayun Zhou. Preparation of magnetic microsphere from water- in-oil emulsion stabilized by block copolymer dispersant, Biomacromolecules, 2005; 6: 1280-1288.
15. Dutta P., Struti J., Niranajan patra Ch.and Bhaoji rao Me. Floating Microsphere: Recents Trends in the Development of Gastroretentive Floating Drug Delivery System. International Journal of Pharmaceutical Science and nanotechnology, 2011; 4(1): 1293-1306.
16. Ahmad N., Hasan N., Ahmad Z., Zishan M., Zohrameena S., Momordica C. For Traditional Uses and Pharmacological Actions. *Journal of Drug* Delivery and Therapeutics, 2016; *6*(2): 40-44.
17. Kawashima Y., Niwa T., Takeuchi H., Hino T.and Ito Y. Preparation of multiple unit hollow microspheres (microbal loons) with acrylic resin containing tranilast and their drug release characteristics (in vitro) and floating behavior (in vivo). J. Control. Release, 1991; 16: 279-290.
18. Yadav R., Bhowmick M., Rathi V.and Rathi J. Design and characterization of floating microspheres for rheumatoid arthritis, Journal of Drug Delivery and Therapeutics, 2019; 9(2-s): 76-81.
19. Moursy N.M., Afifi N.H., Ghorab D.M.and El-Saharty Y. Formulation and evaluation of sustained release floating capsules of Nicardipine hydrochloride, Pharmazie, 2003; 58: 38-43.
20. Kalyan S. and Sharma PK. et al. Recent Advancement in Chitosan Best Formulation and Its Pharmaceutical Application. Pelagia Research Library., 2010; 1(3): 195-210.

21. Alagusundaram M.and Madhu Sudan Chetty C., Microspheres as a novel drug delivery system A review International Journal of Chem Tech Research, 2009; 1(3): 526-534.
22. Jyothi Sri. S., Seethadevi A., Suria Prabha K., Muthuprasanna P. and Pavitra. Microencapsulation: A Review, International Journal of Pharma and Bio Sciences, Jan – Mar, 2012; 3(1).
23. Wang A., Lu Y. and Sun R. Recent progress on the fabrication of hollow micro-spheres. Mater. Sci. Eng., 2007; 460-1: 1-6.
24. Rawat M. and Saraf S. Influence of selected formulation variables on the preparation of enzyme-entrapped Eudragit S100 microspheres. AAPS Pharm Sci Tech, 2007; 8: E116.
25. Fartyal S., Jha SK., Karchuli MS., Gupta R.and Vajpayee A. Formulation and evaluation of floating microspheres of Boswellic acid. Int J Partech Res., 2011; 3: 76-81.
26. Saxena C., Vats S., Easwari TS. and Shukla VK., Floating Microsphere: A Novel approach used to Develop Gastro Retentive Drug Delivery System. International Journal for Pharmaceutical Research Scholars, 2014; 3: I-2.
27. Prashant P., Santosh S. and Janardhan S., Preparation and evaluation of microspheres of flurbiprofen. IJPSR, 2018; 9(12): 5388-5393.
28. Bharti P., Kushwaha R.S. and Jain S. Formulation, Development and Evaluation of Floating Microsphere of Losartan Potassium Using Natural Polymer. Journal of Drug Delivery & Therapeutics, 2019; 9(3-s): 223-228.