ISSN: 0976-3031

Available Online at http://www.recentscientific.com

CODEN: IJRSFP (USA)

International Journal of Recent Scientific Research
Vol. 9, Issue, 5(E), pp. 26787-26790, May, 2018

International Journal of Recent Scientific Research

DOI: 10.24327/IJRSR

Research Article

A BRIEF EVALUATION ON MICROSPHERS: AN UPDATE

Nishant Kumar*., Mohini Rawat., Vikram Singh and Divya juyal

Himalayan Instiute of Pharmacy and Research, Atak Farm, Rajawala, Dehradun, Uttarakhand, India

DOI: http://dx.doi.org/10.24327/ijrsr.2018.0905.2122

ARTICLE INFO

Article History:

Received 17th February, 2018
Received in revised form 21th March, 2018
Accepted 28th April, 2018
Published online 28th May, 2018

Key Words:

Microspheres, controlled drug delivery system, solvent evaporation, core material.

ABSTRACT

The targeted drug delivery system is designed to deliver the drug to the target site in reliable dose that should not affect the remaining tissue other than the target site. As a result, drug is localized on the targeted site. Hence, surrounding tissues are not affected by the drug. Thus, the carrier technology provides an approach for drug delivery, drug is coupled with a carrier molecule such as microspheres which take the drug at the target site and also modulate the release as well as absorption of drug from it. The core microspheres sustained the release for 10hrs in a pH progression medium mimicking the condition of GIT. Drug release studies microspheres were carried out in a similar dissolution media. In acidic medium the release rate of drug form the microspheres was very slow, but the drug was released fast at pH 7.4 and release was sustained up to 24 hrs.

INTRODUCTION

Microspheres are defined as solid, sphere-shaped, free flowing, and smooth surface particle range in size from 1 to 1000 µm. They are prepared of polymeric, waxy or other protective materials that are biodegradable, synthetic polymers and modified natural products (starch, gums, proteins, fats and waxes). Microspheres improve effectiveness of drug therapy over conventional therapy. A number of drugs which encapsulated into the microspheres together with NSAIDs, hormones, proteins, peptides and tissues. There are two types of microspheres; (Rastogi Bhavya *et al*. 2012).

- Microcapsules
- Micromatrices.

Advantages of microspheres

- It helps in taste and order making.
- Exchange oils and other liquids to solids for easy handling.
- Protect drugs against the environmental effects (moisture and light)
- Separation of incompatible materials
- Increase the flow of powders
- Aid dispersion of water insoluble substance in aqueous media
- Formulation of Controlled and Sustained released medications.

Prerequisites for ideal Microparticulate Carriers

- Longer duration of action
- Control of content release
- Increase of therapeutic efficacy
- Protection of drug
- Reduction of toxicity
- Biocompatibility
- Sterilizability
- Relative stability
- Water solubility or dispersibility
- Bioresorbability
- Targetability Polyvalent

Types of Microsphrers

Bioadhesive microspheres

The bioadhesion describes that the materials having the property to adhere at biosubstrate; such as mucosal membranes. Adhesions of bioadhesive drug delivery devices to mucosal tissue provide prolong contact of device with the site of administration. This prolonged contact time increase the absorption of drug from its device and controlled release of drug from device also maintained it improved patient

Corresponding author:* **Nishant Kumar
Himalayan Instiute of Pharmacy and Research, Atak Farm, Rajawala, Dehradun, Uttarakhand, India

compliance by reducing the frequency of administration. Carrier system of drug delivery gives an approach pair the drug to a carrier system such as microspheres. Which mediate the release and absorption of the drug. Microspheres play an important role in these types of drug delivery systems due to their small size and efficient carrier capacity (Subbiah Ganesh *et al*. 2010).

Magnetic microspheres

This type of delivery system is very much important which localize the drug to the disease site. In this larger amount of freely circulating drug can be replaced by smaller amount of magnetically targeted drug. The therapeutic magnetic microspheres are used to deliver chemotherapeutic agent. These microspheres also have the capacity to deliver drugs like proteins and peptides to the targeted site. This system is based on the two facts 1. Drug should be encapsulated into a magnetic microsphere 2. Drug should conjugate on the surface of the microspheres. The accumulation of the carrier at the target site allows them to deliver the drug locally (Farah Hamad Farah *et al* 2016).

Floating microspheres

Floating type microspheres are the preparation with less bulk density than the gastric fluid and so remains floating in stomach without disturbing gastric emptying time. From the floating microspheres drug is released slowly at the preferred rate, if the system is buoyant on gastric content, it increases gastric residence time and difference in plasma concentration. It also decreases the chance of striking and dose dumping and produces extended therapeutic effect (Kumar Sarvan K. *et al. 2017).*

Radioactive microspheres

They are series from 10-30 nm in dimension. The bigger than capillary Gets tap in primary capillary bed when they come across. They inject into the arteries that lead to the tumor of importance. These radioactive microspheres provide the delivery of high radiation dose at the site of action without harming the normal tissues. This is another type of drug delivery system, the radioactivity property of the radioactive substance is avoided to release from microspheres, but acts from with a radioisotope typical distance and the different type of radioactive microspheres are α emitters, β emitters, γ emitters (Ghahramani MR *et al*. 2014).

Mucoadhesive microspheres

These are of size from 1-1000mm in diameter and constituting either totally of mucoadhesive polymer or have an external layer of it and combination of mucoadhesive properties to microspheres has added advantages, e.g. efficient absorption and improved bioavailability of drug due to a high surface to volume ration, a much more intimate contact with mucus layer, specific targeting of drug to the absorption on the surface of the microspheres. These are able to be customized to attach to any mucosal tissue therefore offering the potential of localized as well as a systemic controlled release of drugs (Rao Shrinivas D *et al*. 2014).

Polymeric microspheres

They can be classified as;

Biodegradable polymeric microspheres

Natural polymer prolong the residence time while making contact with mucous membrane because of its high extent of swelling quality with the aqueous medium, this results in producing the gels. The rate and extent of drug release are controlled by the concentration of polymers and the release pattern in a sustained manner. The most important disadvantage is drug load competence of biodegradable microspheres is complex and is difficult to control the drug release.

Synthetic polymeric microspheres

The synthetic polymeric microspheres are broadly used in clinical use, besides they are also applied as bulking agent, fillers, embolic particles, drug delivery medium and shows that they are safe and biocompatible. One of the most important disadvantages of this type of microsphere is the migration from injection site and lead to possible risk, obstruction of blood vessel and further organ damage (Ravi *el al*. 2008).

Polymer Used In Microspheres Prepration (Patel Nirav R. *et al.*2011).

Synthetic Polymers

Non-biodegradable

PMMA
Acrolein
Epoxy polymer

Biodegradable

Lactides and Glycolides
Copolymers
Polyalkyl cyanoacrylates
Polyanhydrides

Natural polymers

Proteins
Albumin
Gelatin
Collagen

Carbohydrates

Starch agarose
Carrageenan
Chitosan

Chemically modified carbohydrates

Poly (acryl) dextran
Poly (acryl) starch
DEAE cellulose

General methods of preparation

- Emulsion solvent evaporation technique
- Emulsion cross linking method
- Coacervation method
- Spray drying technique
- Emulsion-solvent diffusion technique
- Multiple emulsion method
- Ionic gelation
- Hydroxyl appetite (HAP) microspheres in sphere morphology

Emulsion solvent evaporation technique

In this method the drug was dissolved in polymer solution which was previously prepared in chloroform and this prepared drug-polymer solution was added to an aqueous phase containing 0.2% sodium of PVP as emulsifying agent. The above mixture was agitated at 500 rpm then the drug and polymer was transformed into droplet which solidified into rigid microspheres by solvent evaporation and then collected by filtration and washed with demineralised water and desiccated at room temperature for 24hrs (A. Aejaz *et al.* 2013).

Emulsion cross linking method

In this method accurate amount of drug was dissolved in prepared aqueous solution of gelatin which was heated for 1 hr at 40^0C. The solution was poured drop wise to oil phase with stirring the mixture maintaining 1500rpm for 15 min at room temperature it gives oil in water emulsion stirring is continued for 10 min at 15^0C. Prepared microspheres were washed three times with acetone and isopropyl alcohol and air dried. When properly dried they are dispersed in 5 ml of aqueous glutaraldehyde saturated solution of toluene at room temperature for 3 hrs for chemical cross linking and then was treated with 100mL of 10mm glyciene solution containing 0.1% w/v of tween 80 at 37^0C for 10 min to remove unreacted glutaraldehyde (Sharma Neha *et al.* 2014).

Coacervation method

Coacervation thermal change, in this accurately weigh required amount of ethyl cellulose dissolve in cyclohexane with continous stirring maintain the temperature 80^0C, after that drug is powdered in fine particle and added in previous prepared solution with continuous stirring and phase separation is carried out by reducing temperature instantly using ice bath. Then the prepared product was washed two time with cyclohexane and air dried then passed through sieve to obtain microcapsule.

Coacervatio non solvent addition, take accurate weight amount of ethyl cellulose and dissolved in toluene which previously contains propylisobutylene in close beaker and stare with magnetic stirrer atleast 6 hrs at 500 rpm the drug is dispersed in it and stirring is continued for 15 mins. Then phase separation is done by petroleum benzoin with continuous stirring. After that the microcapsules were washed with n-hexane and air dried for 2 hr and then in oven at 50^0C for 4 hrs (Jhansi reddy K *et al.* 2011)

Spray drying technique

This was used to prepare polymeric blended microsphere loaded with drug. It involves dispersing the core material into liquefied coating material and then spraying the mixture in the environment for solidification of coating followed by rapid evaporation of solvent. Solution of poly (epsilon caprolactone) (PCL) and cellulose acetate butyrate (CAB), wastaken and drug was dissolved in different ratio after that it was sprayed in different–different conditions of experiment for achieving drug loaded microspheres. This method is fast but main disadvantage is, it can loose crystalinity because of fast drying process (Savale Kishore Sagar *et al.* 2016).

Emulsion-solvent diffusion technique

To get better residence time in colon floating microparticles were prepared by the emulsion solvent diffusion method. Accurately weighed amount of drug was mixed properly with polymer further this mixture was dissolved in ethanol and dichloromethane ratio (1:1). Then this prepared mixture was added drop wise into the solution of sodium lauryl sulphate (SLS) with stirring at room temperature maintaining 150rpm for 1 hr. The formed floating microspheres were filtered and washed and dried in a desecrator at room temperature. The prepared microparticles were screened through sieve for individual collecion (Deore B.V *et al.* 2009).

Ionic gelation

An accurately weighed amount of drug (w/v) was dissolved into the 1.2% (w/v) aqueous solution of sodium alginate. Now it was stirred continuously to get the complete solution after that prepared solution was added drop wise to previously prepared solution of chitosan in acetic acid containing calcium ion and aluminums ion. This prepared system was kept in original solution for 24 hrs for internal gellification after that it was filtered and microsphere obtsined. Drug release was obtained at pH 6.4-7.2 (Konar Sanjoy *et al.* 2013).

Hydroxyl appetite (HAP) microspheres in sphere morphology

In this technique, microspheres were prepared o/w emulsion followed by solvent evaporation. At first o/w emulsion was prepared by mixing organic phase in the aqueous phase containing the surfactant. The organic phase was dispersed in an aqueous phase in the form of small droplets, those droplets were surrounded by molecules of surfactant, which avoids droplets from co-solvencing and take them to stay individual droplets. While stirring DCM was slowly evaporated and the droplets solidify individual to become microspheres (Saxena C *et al*. 2014).

Evluation of Microspheres

Morphological examination

The morphology of microspheres was done by scanning electron microscopy. Sample of microspheres were dusted onto double sided tape on an aluminum stub and coated with gold using a cold sputter coater to a thickness of 400Å and then imaged using a 25kv electron beam.

Practical Yield

The percent practical yield was calculated from the weight of dried microspheres (w_1) recover from each of 3 bathes and the sum of the initial dry weight of starting materials (w_2) as the following equation:-

$$\%yield = \frac{w1}{w2} \times 100$$

Drug Entrapment efficacy

Weighed amount of microspheres were dissolved in methanol and sonicated for 15 min the solution was filtered and diluted suitably and the filtrate was analyzed for drug concentration by spectrophotometerically by the following equation:

$$\%Entrapment = (Actual\ content/Theoretical\ content) \times 100$$

Particle size measurement

The most widely used technique for determination the particle size and shape is scanning Electron microscopy, Thermal Electron microscopy. The particle size can be determined by using light microscopy while confocal florescence microscopy is used for the structural characterization. In this technique, the field viewed through the microscope can be projected on a screen or photograph for latter measurement. Particle may also be counted with electronic scanners to avoid the strain of visual observation. For measuring very small particle size, an electron microscope or a scanning electron microscope may be used. The letter is also capable of proving an estimate of the particle depth.

Determination of bulk density

The density of microspheres was determined by using multivolume pychometer, by using helium. Accurate weight of microspheres (W_m) was transferred into a 100mL graduated cylinder to obtain the apparent volume (V) of between 50 and 100mL. The bulk density was calculated in gram per milliliter by the following formula:

$$Bulk\ density = \frac{\mathrm{Wm}}{\mathrm{V}}$$

Angle of repose

The angle of repose was measured from a heap carefully built up by dropping the microspheres samples through a glass funnel to the horizontal plate of a powder characteristic tester. The results were averaged from 3 determinations.

Zeta Potential

Zeta potential of microspheres dispersed in 0.0005M phosphate buffer of pH 6.8 was determined by a zeta meter. The directional movement of 200 microspheres from each formulation was observed from 3 determinations.

CONCLUSION

It was concluded that microspheres are the best novel drug delivery systems, as having the advantage of targeted delivery and better patient compliance. Its applications are broad as they are not only used for the targeted delivery of drug but also for detecting bio-molecular interaction, and imaging of tumors.

References

1. Rastogi Bhavya, Chaudhari Amit (2012), formulation development and evaluation of Aceclofenac chitosan microspheres, *journal of Advanced pharmacy education and Research,* 2(4): 215-220.
2. Subbiah Ganesh, Kumar Sudheer D, Kumar Sandeep B, Abhilash R (2010), Controlled Release formulation and Evaluation Of Idarubicin Microsphere Using Biodegradable Hydrophilic and Hydrophobic Polymer Mixtur. *Asian Journal of Pharmaceutical and clinical Research* 3(3):179-182.
3. Farah Hamad Farah (2016), Magnetic microsphere: A novel drug delivery system. *Journal of Analytical and Pharmaceutical Research* 3 (5):1-10.
4. Kumar Sarvan K, Ramu S, Ishwarya M. (2017), Floating Microspheres: A Promising Drug Delivery, *International Journal of Pharmacy and Pharmaceutical Research,* 11(1): 375-388.
5. Ghahramani MR, Garibov Aa (2014) Determination of Radiochemical Purity of Radioactive Microspheres by Paper Chromatography, *Chromatography Separation Technique* 6(1):1-4.
6. Rao Srinivas D, Reddy Haranadh S, Ramu S, Rambabu E. (2014), Preparation and Evaluation of Mucoadhesive Microspheres of Simvastatin by Inonic Gelation Technique, *American Journal of Advanced Drug Delivery;* 2(5): 594-608.
7. S. Ravi, Peh K.K, Darwis Yusrida. (2008), Development and characterization of polymeric microspheres for Controlled Release Protein Loaded Drug Delivery, *Indian journal of Pharmaceutical Sciences;* 70(3): 303-309.
8. Patel Nirav R. Patel Dhagash A. Modi Darshan. Pandya Vikram (2011), Microspheres as a novel drug delivery, *International Journal of Pharmacy and Life Sciences;*2(8): 992-997.
9. Aejaz A. Sadath A. (2013) Development and Characterization of Floating Microspheres of Clarithromycin as Gastroententive Dosage Form, *International Research Journal of Pharmacy;* 4(1): 165-168.
10. Sharma Neha, Harikumar S.L (2014), Formulation and Evaluation of Enteric Coated Microspheres of Ketoprofen using Natural Polymers for Colon Delivery, *International Journal of Pharmacy and Pharmaceutical Sciences;* 6(2): 886-892.
11. Salve Kishore Sagar (2016), Formulation and Evaluation of Microspheres with Aceclofenac, *World Journal of Pharmaceutical and Medical Research;* 2(4): 181-187.
12. Sanjoya Konar, Dutta Roy Swagata, Sahoo Himanshu Bhusan, Nandy Subhangkar (2013), Development and Optimization of Pectin microspheres of Metformin HCl, *International Journal of Drug Development and Research;* 5(1): 339-356.
13. Saxena C, Vats S, Easwari TS, Shaukla VK (2014), Floating Microsphere: A Novel Approach Used to Develop Gastroretentive Drug Delivery System, *International Journal for Pharmaceutical Research Scholars;* 2(3): 699-716.
14. Deore B.V, Mahajan H.S Deore U.V (2009), Development and characterization of sustained release microspheres by quasi emulsion solvent diffusion method, *International Journal of ChemTech Research;* 1(3): 634-642.
15. Jhansi reddy K, Reddy Jaya Shankar, Reddy Viswanathan M, Kumar Jeenvan K. (2011), Preparation and evaluation of Trospium chloride microspheres using chitosan polymer, *Journal of Pharmacy Research;* 4(8): 2550-2552.

****