World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(REVIEW ARTICLE)

A review on natural polymer-based microsphere

Pooja Choudhary, Seema Yadav and Rajesh Asija *

Maharishi Arvind Institute of Pharmacy, Jaipur, Rajasthan India.

World Journal of Biology Pharmacy and Health Sciences, 2022, 12(03), 088–093

Publication history: Received on 22 October 2022; revised on 04 December 2022; accepted on 06 December 2022

Article DOI: https://doi.org/10.30574/wjbphs.2022.12.3.0230

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. Microspheres are the multiparticulate drug delivery systems which are consisting from natural and synthetic material. Microspheres received much attention not only for prolonged release, but also for targeting of anticancer drugs. In future by combining various other strategies, microspheres will find the central place in novel drug delivery, particularly in diseased cell sorting, diagnostics, gene & genetic materials, safe, targeted and effective in vivo delivery and supplements as miniature versions of diseased organ and tissues in the body.

Keywords: Microspheres; Novel drug delivery; Controlled release; Therapeutic efficacy

1. Introduction

Conventional drug therapy involves administering the drug or pharmaceutical agent directly into the body, through oral, pulmonary, or parenteral routes. However, several demerits to this approach are the rapid release of the drug into the body at the site of administration, loss of drug dose on the way from the site of administration to the target site (due to biological degradation), the requirement for administering higher doses of the drugs to compensate for this loss, higher chances of over- or under-medication, side effects due to the interaction of the drugs with untargeted sites, the requirement of frequent dosing, lower drug bioavailability, lower per-unit cost (but higher overall healthcare cost), and higher total dosage requirement into the body. Sustained release technology has rapidly emerged over the past three decades as a new interdisciplinary science that offers novel approaches for the delivery of the drug into systemic circulation at a predetermined rate. Such a therapeutical approach has enabled the site-specific, slow, sustained, and controlled release of drugs, thus improving their bioavailability, pharmacokinetics, and increased efficacy, as well as minimizing the side effects to the untargeted sites and overall risk to the patient, thereby reducing the overall medication cost, due to the decreased frequency of drug administration and increasing patient compliance.[1]

2. Microspheres

Microsphere, as carrier for drug is one such approach which can be used in a sustained controlled release fashion.The range of techniques for the preparation of microspheres offers a variety of opportunities to control drug administration issue. This approach allows the accurate delivery of small quantity of the potent drugs, reduced drug concentration at the site other than the target site and the protection of the labile compound before and after the administration and prior to the site of action. The behaviour of the drugs in vivo can be manipulated by combining the drug to a carrier particle. The clearance kinetics, tissue distribution, metabolism i.e. kinetics and cellular interaction of the drug are strongly influenced by the behaviour of the carrier. The exploitation of these changes in pharmaco dynamics behaviour may lead to enhanced therapeutic efficiency. However, an intelligent approach to therapeutics employing drug carriers phenomenon requires a detailed understanding of the carrier interaction with cellular and organ systems and of the

* Corresponding author: Rajesh Asija

Copyright © 2022 Author(s) retain the copyright of this article. This article is published under the terms of the Creative Commons Attribution Liscense 4.0.

limitations of the systems with respect to the formulation procedures and stability issues. A variety of substances have been used as drug carrier, including immunoglobulins serum proteins, liposomes, microspheres, microcapsules, nanoparticles and even cells such as erythrocytes.[2]

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.

3. There are two types of microspheres

- microcapsule-entrapped substance distinctly surrounded by distinct capsule wall
- micromatricess-entrapped substance is dispersed throughout the matrix

Controlled drug delivery system overcome the problems of conventional therapy and enhance therapeutic efficacy of given drug 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.[3]

3.1. Types of microspheres

- Bioadhesive microspheres
- Magnetic microspheres
- Floating microspheres
- Radioactive microspheres
- Polymeric microspheres
- Biodegradable polymeric microspheres
- Synthetic polymeric microspheres

4. Characteristics of microspheres

- Microsphere size may be critical to the proper function of an assay, or it may be secondary to other characteristics. Considering traditional diagnostic methods, the test or assay format commonly dictates particle size, such as the use of very small spheres (~0.1- 0.4μm) to ensure satisfactory wicking in lateral flow tests, or the use of larger, cell-sized spheres (~4-10μm) for bead-based flow cytometric assays.[5]
- Common microsphere compositions include polystyrene (PS), poly (methyl methacrylate) (PMMA), and silica. These materials possess different physical and optical properties, which may present advantages or limitations for different applications. Polymer beads are generally hydrophobic, and as such, have high protein binding abilities. However, they often require the use of some surfactant (e.g. 0.01-0.1% Tween® 20 or SDS) in the storage buffer to ensure ease of handling. During synthesis, functional monomers may be co-polymerized with styrene or methyl methacrylate to develop beads with surface reactive groups. Functional groups may be used in covalent binding reactions, and also aid in stabilizing the suspension. Silica microspheres are inherently hydrophilic and negatively charged. Consequently, aqueous silica suspensions rarely require use of surfactants or other stabilizers. Carboxyl- and amine functionalized silica spheres are available for use in common covalent coating protocols, and plain silica microspheres may be modified using a variety of silanes to generate functional groups or alter surface properties.[5]
- Microspheres may be coated with capture molecules, such as antibodies, oligonucleotides, peptides, etc. for use in diagnostic or separation applications. Microsphere coatings are typically optimized to achieve desired specific activity, while minimizing nonspecific interactions. Consideration should also be given to the required stability, development time frame and budget, and the specific biomolecule to be coated. These factors will aid in determining the most fitting coating strategy for both short- and long-term objectives. Standard microsphere products support three basic coating strategies: adsorption, covalent coupling, and affinity binding.[6]
- Many applications in the life sciences demand added properties, such as fluorescence or a visible color, or iron oxide inclusions for magnetic separations. Polymer spheres (and polymer based magnetic spheres) are often internally dyed via organic solvent swelling, and many standard products are available. Dye concentrations can be adjusted to produce beads with different intensities to meet special needs, such as QuantumPlex™ for multiplexed flow cytometric assays, or our Dragon Green or Flash Red Intensity Standards, which support imaging applications and associated instrument QC. Many surface- or internallylabeled fluorescent beads are also available as specialized flow cytometry standards.[5]

4.1. Advantages[7]

- Microspheres provide constant and prolonged therapeutic effect.
- Reduces the dosing frequency and thereby improve the patient compliance.
- They could be injected into the body due to the spherical shape and smaller size.
- Better drug utilization will improve the bioavailability and reduce the incidence or intensity of adverse effects.
- Microsphere morphology allows a controllable variability in degradation and drug release.

4.2. Limitation[8]

Some of the disadvantages were found to be as follows:

- The modified release from the formulations.
- 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.
- Differences in the release rate from one dose to another.
- 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.
- Dosage forms of this kind should not be crushed or chewed

4.3. Applications

- For Taste and odour masking
- To delay the volatilisation
- For Separation of incompatible substances
- For Improvement of flow properties of powders
- To Increase the stability of the drug against the external conditions
- For Safe handling of toxic substances
- To Improve the solubility of water insoluble substances by incorporating dispersion of such material in aqueous media.[9]

4.4. Novel Applications of Microsphere

4.4.1. Monoclonal antibodies mediated microspheres targeting

Monoclonal antibodies (Mabs) targeting microspheres are immunomicrospheres. This targeting is a method used to achieve selective targeting at specific sites. Monoclonal antibodies are extremely specific molecules. This extreme specificity of monoclonal antibodies (Mabs) can be used to target microspheres loaded bioactive molecules to selected sites by means of covalent coupling. The free amino groups, aldehyde groups, or hydroxyl groups on the external surface of the microspheres can be linked to the antibodies.[10] Attachment of microspheres to Mabs by any of the following methods

- Non-specific adsorption
- Specific adsorption
- Direct coupling
- Coupling with reagents

4.4.2. Targeting by using microparticulate carriers

The concept of targeting, i.e. site specific drug delivery is a well-established dogma, which is gaining full attention. The therapeutic efficacy of the drug depends on its access and specific interaction with its candidate receptors. Placement of the particles indiscrete anatomical compartment leads to their retention either due to the physical properties of the environment or biophysical interaction of the particles with the cellular content of the target tissue.[11]

4.4.3. Microspheres in vaccine delivery

The prerequisite of a vaccine is protection against microorganism or its toxic product. An ideal vaccine must fulfil the requirement of efficacy, convenience in application and cost. The aspect of safety and minimization of side effect is a complex issue.

Biodegradable delivery systems for vaccines that are given by i.v. route may overcome the shortcoming of the conventional vaccines. The interest in parenteral (subcutaneous, intramuscular, intradermal) carrier lies because they offer specific advantages including:

- Modulation of antigen release
- Improved antigenicity
- Stabilization of antigen.

4.4.4. Topical porous microspheres

These microsponges are having capacity to entrap wide range of active ingredients such as emollients, fragrances, volatile oils etc., are used as the topical carries system furthermore, these porous microspheres with active medicaments can be incorporated into formulations such as creams, lotions and powders.

4.4.5. Surface modified microspheres

Different approaches have been used to change the surface properties of carriers to protect them against phagocytic clearance and to modify their body distribution patterns. The adsorption of poloxamer on surface of the polystyrene, polyester or poly methyl methacrylate microspheres deviate them more hydrophilic and hence they decrease their MPS uptake. Protein microspheres can be covalently modified by PEG derivatives show decreased immunogenicity and clearance.[12]

4.5. Recent advancement in microsphere

4.5.1. Important utilizations of chitosan polymer Cholesterol-lowering effects

Chitosan and cellulose were used as examples of fibers with high, intermediate and low bile acid-binding capacities, respectively. The serum cholesterol levels in a control group of mice fed a high fat/high cholesterol diet for 3 weeks increased about 2-fold to 4·3mM and inclusion of any of these fibers at 7·5% of the diet prevented this increase from occurring. In addition, the amount of cholesterol accumulated in hepatic stores due to the HFHC diet was reduced by treatment with these fibers. The three kinds of fibers showed similar hypocholesterolaemic activity; however, cholesterol depletion of liver tissue was greatest with cholestyramine. The mechanisms underlying the cholesterollowering effect of cholestyramine were, 1) Decreased cholesterol (food) intake, 2) Decreased cholesterol absorption efficiency, and 3) Increased faecal bile acid and cholesterol excretion. The latter effects can be attributed to the high bile acid-binding capacity of cholestyramine. In contrast, incorporation of chitosan or cellulose in the diet reduced cholesterol (food) intake, but did not affect either intestinal cholesterol absorption or faecal sterol output. The present study provides strong evidence that above all satiation and satiety effects underlie the cholesterol lowering.[14]

4.5.2. Increase stability of drug

Chitosan polymer is used to increase the stability of the drug in which the drug is complexed with chitosan and make slurry and kneading for 45 minutes until dough mass. This dough mass is pass through sieve no.16 and make a granules is completely stable at different condition.[14]

4.5.3. Orthopaedic patients

Chitosan is a biopolymer that exhibits osteo conductive, enhanced wound healing and antimicrobial properties which make it attractive for use as a bioactive coating to improve Osseo integration of orthopedic and craniofacial implant devices. It has been proven to be useful in promoting tissue growth in tissue repair and accelerating wound-healing and bone regeneration.[15]

4.5.4. Cosmetics industry

Cosmetic compositions are disclosed for the treatment of hair or skin, characterized by a content of new quaternary chitosan derivatives of the formula. The chitosan derivatives have a good substantial, particularly to hair keratin, and prove to have hair strengthening and hair conditioning characteristics. e.g.; Hair setting lotion, Oxidation Hair-coloring Composition, Hair toning Composition, Skin Cream, Hair treatment Composition, Gel-form.[15]

4.5.5. Dental Medicine

Chitosan have been recognized to accelerate wound healing to attain an aesthetically valid skin surface, and to prevent excess scar formation. In dental medicine, chitosan is also applied as a dressing for oral mucous wound and a tampon

following radical treatment of maxillary sinusitis. Furthermore, it is being investigated as an absorbing membrane for periodontal surgery. Chitosan has a variety of biological activities and advertised as a healthy food that is effective for improvement and/or care of various disorders, arthritis, cancer, diabetes, hepatitis, etc.[15]

4.5.6. Chitosan as Permeation Enhancer

It has been reported that chitosan, due to its cationic nature is capable of opening tight junctions in a cell membrane. This property has led to a number of studies to investigate the use of chitosan as a permeation enhancer for hydrophilic drugs that may otherwise have poor oral bioavailability, such as peptides. Because the absorption enhancement is caused by interactions between the cell membrane and positive charges on the polymer, the phenomenon is pH and concentration dependant. Furthermore increasing the charge density on the polymer would lead to higher permeability. Chitosan as Mucoadhesive Excipient Bioadhesivity is often used as an approach to enhance the residence time of a drug in the GI tract, hereby increasing the oral bioavailability. A comparison between chitosan and other commonly used polymeric excipients indicates that the cationic polymer has higher bioadhesivity compared to other natural polymers, such as cellulose, Xantham gum, and starch.[16]

4.5.7. Effect of chitosan: citric acid ratio on drug release

It has been demonstrated that polymer with appropriate viscosity and expanding property can be used as osmotic agents for the release of water-insoluble drug. Due to its high molecular weight and a linear unbranched structure, chitosan is completely biodegradable, toxicologically harmless and low cost, and exhibits an excellent gelation characteristic. Hence the potential for chitosan to be used as a polymeric osmotic agent in osmotic pump is obvious. The hydration and gel formation of chitosan are very much dependent on the pH of surroundings. It is insoluble at an alkaline and neutral pH but soluble at acid condition. Upon dissolution, amine groups of the polymer become protonated, forming a resultant viscous and soluble polysaccharide. Inclusion of citric acid as pH-regulating excipient in the developed formulations was expected to decrease the microenvironmental pH of the core to a suitable level at which chitosan could form appropriate viscous gelling solution and hence, to enhance the osmotic pressure of core tablets.[17]

5. Conclusion

Due to its advantages of regulated and prolonged release action, lower dose frequency, enhanced stability, bioavailability, and dissolving rate, microspheres are the most widely used drug delivery technology among researchers and scientists. In the future, microspheres will play a key role in innovative medication delivery thanks to the discovery of new polymers and improved formulation methods.

Compliance with ethical standards

Acknowledgments

I would like to thanks Ms Seema Yadav (Associate Professor) and Dr. Rajesh Asija (Principal) for guiding during this work and drafting the manuscript.

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Chaturvedi G and Saha RN. A Review on Microsphere Technology And Its Application. Birla institute of technology and sciences. 2009:56-58.

[2] Gholap SB, Banarjee SK, Gaikwad DD, Jadhav SL and Thorat RM. hollow microsphere: a review, International Journal of Pharmaceutical Sciences Review and Research. ,2010;1:10-15.

[3] Agusundaram M, Madhu Sudana Chetty et al. Microsphere As A Novel Drug Delivery System A Review. International Journal of ChemTech Research. 2009;1(3):526-534.

[4] Sudha Mani T and Naveen Kumar K. At preparation and evaluation of ethyl cellulose microspheres of ibuprofen for sustained drug delivery International Journal Of Pharma Research And Development. 2010;2(8):120-121.

[5] Thanoo BC, Sunny MC and Jayakrishnan A. Cross-linked chitosan microspheres: Preparation and evaluation as a matrix for the controlled release of pharmaceuticals. J Pharm Pharmacol. 1992;44:283-286.

[6] Parmar Harshad, Bakliwal, Sunil at al. Different Method Of Evaluation Of Mucoadhesive Microsphere, International Journal of Applied Biology and Pharmaceutical Technology. 2010;1(3):1164-1165.

[7] Kavita Kunchu, Raje Veera Ashwani et al. Albumin Microspheres: A Unique system as drug delivery carriers for non steroidal antiinflammatory drugs. 2010;5(2):12.

[8] Kalyan Shweta, Sharma Parmod Kumar et al. Recent Advancement In Chitosan Best Formulation And Its Pharmaceutical Application. Pelagia Research Library. 2010;1(3):195-210.

[9] Dr. Fishers Microsphere Selection Bangs laboratories inc, Tech Notes 201 A, 1-4

[10] Corrigan l. Owen and Healy Marie Anne. Surfactants in Pharmaceutical Products and Systems "Encyclopedia of Pharmaceutical Technology" 3rd edition, 2003 volume 1, edited by James Swarbrick Informa healthcare Inc. P.NO – 3590

[11] Nalini M. Anandea, Sunil K. Jain A,, Narendra K. Jain, Con-A conjugated mucoadhesive microspheres for the colonic delivery of diloxanide furoate. InternationalJournal of Pharmaceutics, 2008; 359:182-189.

[12] Guojun Liu, Husheng Yang, Jiayun Zhou, Preparation of magnetic microsphere from water-in-oil emulsion stabilized by block copolymer dispersant,. Biomacromolecules, 2005; 6:1280-1288

[13] DuttaP, StrutiJ, Ch. Niranajan patra, M.E. Bhaoji rao, 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

[14] Nair Rahul, Reddy B, Haritha et al. Application of chitosan microspheres as drug Carriers: a review. Journal of Pharmaceutical Sciences and Research. 2009;1(2):1-12.

[15] Yadav R, Bhowmick M, Rathi V, Rathi J,Design and characterization of floating microspheres for rheumatoid arthritis, Journal of Drug Delivery and Therapeutics 2019; 9(2-s):76-81

[16] ShuklaP,Vijaya Vani CH.S, review article on microsphere volume, IJPAR, 2015; 4(3):291-301

[17] PrasanthV.V., Moy A. C., Mathew S. T., Mathapan R., Microspheres An overview, Int.J.Res.Pharm.Biomed.Sci., 2011;2:332 8