WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 12, Issue 19, 70-79. Review Article ISSN 2277– 7105

A REVIEW ON MICROBEADS – PHARMACEUTICAL CARRIER DRUG DELIVERY SYSTEM

Krishnaveni Manubolu[1]* and Yejerla Ratna Kumari[2]

[1,2]Faculty of Pharmaceutical Sciences, Narayana Pharmacy College, Nellore 524002.

Article Received on
08 Sept. 2023,
Revised on 29 Sept. 2023,
Accepted on 20 Oct. 2023
DOI: 10. 20959/wjpr202319-29883

***Corresponding Author**
Krishnaveni Manubolu
Faculty of Pharmaceutical Sciences, Narayana Pharmacy College, Nellore 524002.

ABSTRACT

This review discussed the usage of microbeads as a medication delivery mechanism and natural polymers. Any drug delivery system's purpose is to deliver a therapeutic amount of medicine to the appropriate place in the body while also achieving and maintaining the correct drug concentration. This could be accomplished using a multiparticulate dosage form, such as beads, which are divided into numerous separate pieces, known as subunits, each of which possesses some desired features. The advantages of micro particle drug delivery systems over single unit dose form are well documented. One of the solutions that does not entail the use of harsh chemicals or elevated temperatures is the production of microbeads medication delivery systems. Conventional procedures include the use of ionotropic gelation, emulsion gelation, polyelectrolyte complexation, and other methods. Because of the ease of preparation, the majority of work has been done on the preparation of microbeads using the ionotropic gelation process rather than alternative approaches. The ionotropic gelation approach relies on the capacity of polyelectrolytes to crosslink with counter ions to generate a hydrogel sustained release formulation.

KEYWORDS: Microbeads, controlled drug delivery, oral, natural polymer.

INTRODUCTION

Oral ingestion is the oldest and commonest mode of drug administration. It is increasingly being used for the delivery of therapeutic agents due to its low cost, safety, ease of administration and high levels of patient compliance. More than 50% of the drug delivery systems available in market are oral drug delivery systems.[1] Sustained release-drug delivery systems (SRDDS) provide drug release at a drug concentration which is maintained in the

therapeutic window for a prolonged period of time (sustained release), thereby ensuring sustained therapeutic action. This allows the enhancement of duration of action of all short half-life drugs, elimination of side effects, reducing frequency of dosing and wastage of drugs, optimized therapy and better patient compliances.

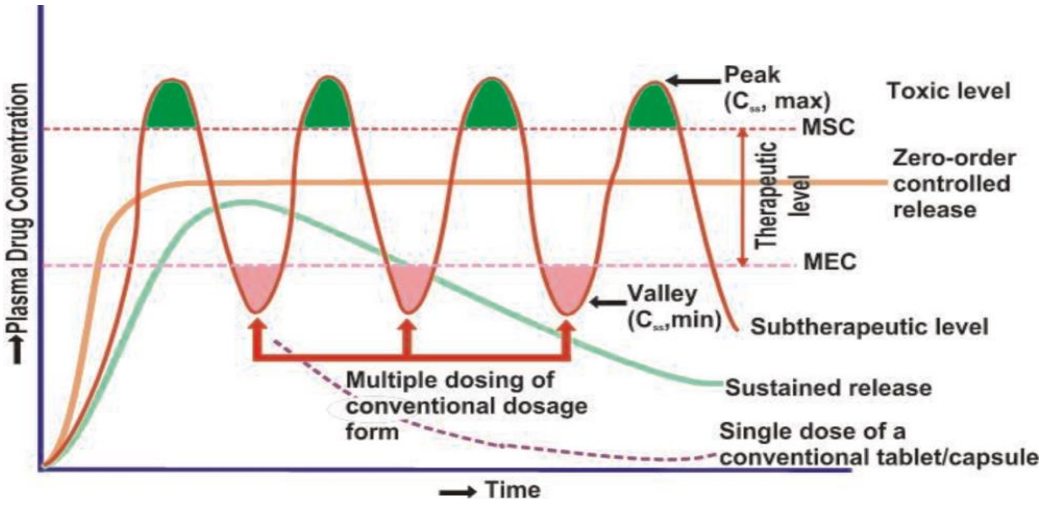

Fig-1: Sustained release Drug Profile.

Type-2 Diabetes Mellitus is a disease of progressive beta-cell dysfunction in the presence of insulin resistance, leading to loss of glycemic control. The pathological loss of beta cell may be the result of a number of factors including:

1. β-cell secretory defects.
2. Glucotoxicity due to hyperglycemia.
3. Lipotoxicity due to dyslipidemia.
4. Possible abnormalities in secretion or response to incretin hormones.

- It usually develops in adults over the age of 45 years but is increasingly occurring in younger age groups including children, adolescents and young adults.
- Is more likely in people with a family history of type 2 diabetes or from particular ethnic backgrounds.
- For some, the first sign may be a complication of diabetes such as a heart attack, vision problems or a foot ulcer
- Is managed with a combination of regular physical activity, healthy eating and weight reduction.
- As type 2 diabetes is often progressive, most people will need oral medications and/or insulin injections in addition to lifestyle changes over time**.**

SUSTAINED RELEASE DRUG DELIVERY SYSTEM

Oral controlled drug delivery systems represent the most popular form of sustained drug delivery systems for the obvious advantages of oral route of drug administration. Such systems release the drug with constant or variable release rates. The oral controlled release systems shows a typical pattern of drug release in which the drug concentration is maintained in the therapeutic window for a prolonged period of time (sustained release), thereby ensuring sustained therapeutic action. In recent years, scientific and technological advancements have been made in the research and development of rate controlled oral drug delivery systems. These formulations are designed to deliver the drugs at a pre determined rate, thus maintaining their therapeutically effective concentration in systemic circulation for prolonged periods of time.[3]

Microparticles are characteristically free flowing powders consisting of particles of size rangigng from several tenths of a micron to 5 thousands microns. They consists proteins or synthetic polymers which are biodegradable in nature. A well designed controlled drug delivery system can overcome some of the problems of conventional therapy and enhance the therapeutic efficacy of a given drug. Each particle is basically a mixture of drug, dispersed in a polymer form with release occurs by first order process. Drug release is controlled by dissolution/degradation of matrix. Microparticles are the drug loaded particles in micron size where as microspheres are the drug loaded microparticles with a spherical shape which offer a ball bearing effect.

Recent advances in polymer science and drug carrier technologies have promulgated the development of novel drug carriers such as bioadhesive microspheres that have boosted the use of "bioadhesion" in drug delivery.[4]

MECHANISM OF SUSTAINED RELEASE MICROBEADS

There are three main mechanisms involved in the release of drug from microspheres. It is based upon the type of microspheres formulated whether matrix type or reservoir type. The drug gets either diffused from the membrane or gets enzymatic lysis or hydrolysis when exposed to thesurrounding gastric fluids.

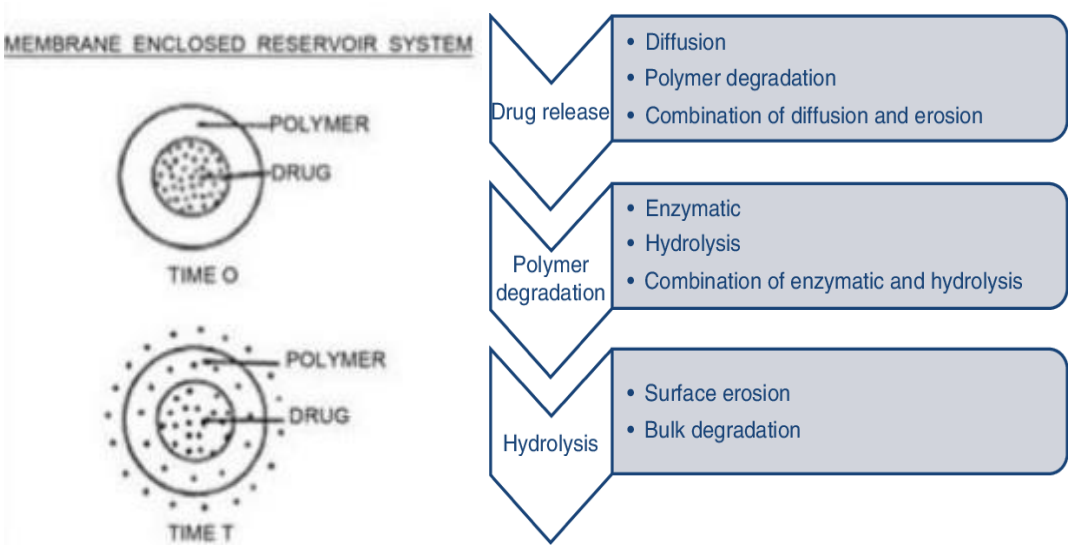

Fig.No:2- Mechanism of release of Microbeads.

ADVANTAGES OF SUSTAINED RELEASE MICROBEADS

- Control of drug therapy is achieved.
- Rate and extent of drug absorption can be modified.
- Frequency of drug administration is reduced.
- Patient compliance can be improved.
- Drug administration can be made convenient.
- Maximizing the availability of drug with minimum dose.
- The safety margin of high potency drugs can be increased.

DISADVANTAGES OF SUSTAINED RLEASE MICROBEADS

- Highly molecular weight compounds have a limited and restricted loading and their release may be difficult.
- Formation of complexes with the blood components.
- There is high cost of production.
- There is reduced ability to adjust the dose.
- It is a highly sophisticated technology and requires skills to manufacture.
- It is difficult to maintain the stability of dosage form.

DRUG CANDIDATES FOR SUSTAINED RELEASE DOSAGE FORM

1. Drugs which are uniformly absorbed in GIT like ***Metformin, Vilgagliptin***
2. Drugs which can be formulated even in smaller doses.

3. The drugs having good margin of safety i.e. their therapeutic index should be in relative range.
4. The drugs which do not show any cumulative action, any undesired side effect as in case of dose dumping it might produce toxicity.

1.1.5 DRUG NON-CANDIDATES FOR SUSTAINED RELEASE DOSAGE FORM

1. The drugs which are absorbed and excreted rapidly like ***Pencillin-G and Furosemide.***
2. The drugs with long biological half life (>12hrs) like ***Diazpam and Phenytoin.***
3. The drugs which require to be administered in large doses (>1gm) like ***Sulfonamides.***
4. The drugs having extensive binding of plasma proteins will have long elimination half life and such drugs generally do not require to be formulated to SRDF.[5]

TECHNIQUES OF MANUFACTURE OF SUSTAINED RELEASE MICROBEADS

There are Several Techniques for the preparation of Microparticles These are as follows.[7]

- Single emulsion technique
- Double emulsion technique
- Polymerization technique
- Normal polymerization technique
- Interfacial polymerization technique
- Phase separation coacervation technique
- Spray drying & spray congealing technique
- Solvent extraction technique
- Solvent evaporation technique
- Solvent diffusion technique
- Ionotropic gelation technique.[7]

TYPES OF MICROPARTICLES

1. Bio-adhesive microparticles

Adhesion can be defined as sticking of drug to the membrane by using the sticking property of the water soluble polymers. Adhesion of drug delivery device to the mucosal membrane such as buccal, ocular, rectal, nasal etc can be termed as bio adhesion. These kinds of microspheres exhibit a prolonged residence time at the site of application and causes intimate contact with the absorption site and produces better therapeutic action.

2. Magnetic microparticles

This kind of delivery system is very much important which localises the drug to the disease site. In this larger amount of freely circulating drug can be replaced by smaller amount of magnetically targeted drug. Magnetic carriers receive magnetic responses to a magnetic field from incorporated materials that are used for magnetic microspheres are chitosan, dextran etc.

3. Therapeutic magnetic microparticles

Are used to deliver chemotherapeutic agent to liver tumour. Drugs like proteins and peptides can also be targeted through this system.

4. Diagnostic microparticles

It can be used for imaging liver metastases and also can be used to distinguish bowel loops from other abdominal structures by forming nano size particles supra magnetic iron oxides.

5. Floating microparticles

In floating types the bulk density is less than the gastric fluid and so remains buoyant in stomach without affecting gastric emptying rate. The drug is released slowly at the desired rate, if the system is floating on gasteric contentand increases gastric residence and increases fluctuation in plasma concentration. Moreover it also reduces chances ofstriking and dose dumping. One another way it produces prolonged therapeutic effect and therefore reduces dosing frequencies. Drug (ketoprofen) given through this form.

6. Radioactive microparticles

Radio emobilisation therapy microspheres sized 10-30 nm are of larger than capillaries and gets tapped in first capillary bed when they come across. They are injected to the arteries that lead to tumour of interest. So all these conditions radioactive microspheres deliver high radiation dose to the targeted areas without damaging thenormal surrounding tissues. It differs from drug delivery system, as radio activity is not released from microspheres but acts from within a radioisotope typical distance and the different kinds of radioactive microsphers are α emitters, β emitters, γ emitters.

7. Polymeric microparticles

The diffenttypes of polymeric microspheres can be classified as followsand they are biodegradable polymeric microspheres and Synthetic polymeric microspheres.

8. Biodegradable polymeric micropaticles

The natural polymers such as starch are used with the concept that they are biodegradable, biocompatible, and also bio adhesive in nature. Biodegradable polymers prolongs the residence time when contact with mucous membrane due toit's high degree of swelling property with aqueous medium, results gel formation. 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.

9. Synthetic polymeric microparticles

The interest of 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 kind of microspheres, are tend to migrate away from injection site and lead to potential risk, embolismand further organ damage. Differentkinds of polymers used for microsphere.[8]

POLYMERS USED IN FORMULATION OF MICROBEADS

In the formulation of FDDS, several polymers are used. They are classified into two types:

1. Synthetic Polymers
2. Natural Polymers

1. Synthetic Polymers

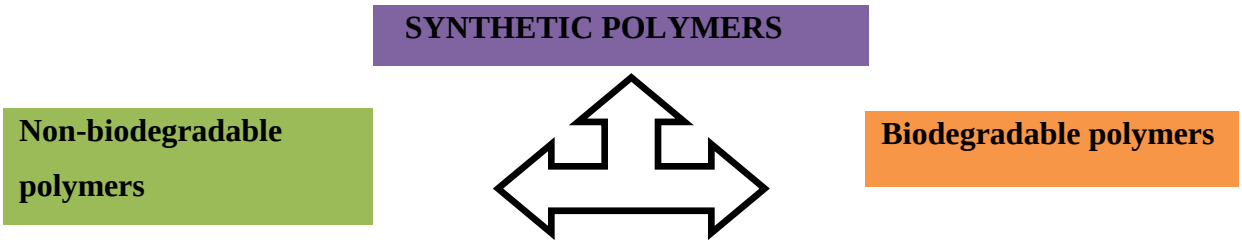

Fig. No. 3: Types of synthetic Polymers.

Non-biodegradable polymers:– Polymethyl Methacrylate, Glycidyl Methacrylate, Acrylates.

Biodegradable polymers:– Lactides and Glycolides, Copolymers, Polyalkyl Cyano Poly Anhydrides.

2. Natural polymers

In recent years, polymers those are derived from plant origin have evoked tremendous interest because of their diverse pharmaceutical applications. These natural gums and Mucilages are preferred over the synthetic ones because they are biocompatible, cheap, and easily available than the synthetic ones.

Table 1: Some Natural Gums Used in Formulation of controlled drug delivery dosageforms.

Common Name	Botanical Name	Family	Reference
Okra Gum	*Hibiscus esculentus*	Malvaceae	[9]
Hibiscus Mucilage	*Hibiscus rosasinensis. Linn*	Malvaceae	[10,11,12]
Tamarind Seed Polysaccharide	*Tamarindus indica*	Leguminoseae	[13]
Fenugreek mucilage	*Trigonella foenum graecum*	Leguminoseae	[14,15]

A. Okra Mucilage

The okra gum is obtained from the fresh fruits of the *plant* ***Abelmoschus esculentus*** *(family* ***:malvaceae).*** The okra polysaccharide contains the major polysaccharide component differing widely in the molar ratios of galactose, galacturonic acid, and rhamnose and with some fractions of glucose, mannose, arabinose, and xylose. Mucilage from the pods of Abelmoschus esculentus is evaluated for its safety and suitability as suspending agent.[9]

B. Hibiscus rosasinensis

Mucilage is obtained from fresh leaves of ***Hibiscus rosa-sinensis*** (family: ***malvaceae***). Mucilage of Hibiscus rosa-sinensis contains L-rhamnose, D-galactose, D-galacturonic acid, and D-glucuronic acid. The use of its mucilage for the development of sustained release tablet has been reported.[10]

C. Tamarind Seed Polysaccharide

Tamarind xyloglucan is obtained from the endosperm of the seed of the tamarind tree, ***Tamarindus indica*** (family: ***fabaceae***). Tamarind gum is a polysaccharide composed of glucosyl: xylosyl: galactosyl in the ratio of 3: 2: 1. It was seen that the matrix tablets prepared by using tamarind gum were able to carry most of the drug to the colon and restrict the release in upper GIT.[13]

D. Fenugreek Mucilage

This mucilage is obtained from seeds of ***Trigonella foenumgraceum*** (family: ***Leguminosae***). Its seeds contain a high percentage of mucilage and do not dissolve in water but form viscous tacky mass and swell up when exposed to fluids.[14]

FORMULATION LIST

Table 2: List of Drugs Formulated with controlled drug delivery.

S. No	Dosage Form	Drugs
1.	Reservoir System tablet	Morphine sulfate
2.	Matrix system tablet	Isosorbite mononitrate, Metformin HCl, Clarithromycin
3.	Diffusion controlled release	Bupropion
4.	Push pull osmotic system	Doxazosin, Verapamil, Glipizide
5.	Ion-Exchange System	Hydrocodon, Dextromethorphan
6.	P^H dependent system	Aceclofenac, Diclofenac sodium
7.	Altered density formulation	Levodopa and benserazide.[5]

MARKETD PRODUCTS LIST

Table 3: List of Marketed Products of SRDDS.

S. No	Drug	Brand Name
1.	Metformin HCL	Glucomet®SR
2.	Isosorbite mononitrate	Imdura®
3.	Verapamil	Covera HS
4.	Glipizide	Glucotrol XL
5.	Aceclofenac	Hifenac SR
6.	Propranolol HCL	Inderal® LA[5].

REFERENCES

1. Pooja R. Alli, Pratima B. Bargaje, Nilesh S. Mhaske, Sustained Release Drug Delivery System: A Modern Formulation Approach, Asian Journal of Pharmaceutical Technology and Innovation, 2016; 04(17): 108-118.
2. Chantal Mathieu, Evy Degrande, Vildagliptin: a new oral treatment for type 2 diabetes mellitus, Dec, 2008; 4(6): 1349–1360.
3. Anroop B Nair, Rachna Kumria, Bandar E Al-Dhubiab1, Mahesh Attimarad1 And Sree Harsha, Development Of Transdermal Delivery System Of Vildagliptin And It Comparison With Oral Therapy, Indian Journal Of Pharmaceutical Education And Research, 50 Jan-Mar, 2016; 130-137.

4. Anuranjita Kundu**.** Preparation And Evaluation Of Sustained Release Microbeads Of Norfloxacin Using Sodium Alginate. International Journal Of Research In Pharmacy And Chemistry, 2012; 2(3): 647-651.
5. Sudhir Karna, Shashank Chaturvedi, Vipin Agarwal, Mohammad Alim, Formulation Approaches For Sustained Release Dosage Forms: A Review. Asian Journal of Pharmaceutical and Clinical Resarch, Jul; 14: 0974-2441.
6. Herbert A. Lieberman, Leon Lachman, and Joseph B. Schwartz Pharmaceutical dosage forms IInd Eidition -I, 7.
7. Vm. Sherina, K. Santhi And C.I. Sajeeth. Formulation And Evaluation Of Sodium Alginate Microbeads As A Carrier For The Controlled Release Of Nifedipine. International Journal Of Pharmaceutical And Chemical Sciences, Apr–Jun, 2012; 1(2): 699-710.
8. Girish K Jania, Dhiren P Shahb, *, Vipul D Prajapatia, Vineet C Jain. Gums and mucilages: versatile excipients for pharmaceutical formulations. Asian Journal of Pharmaceutical Sciences, 2009; 4(5): 308-322.
9. V. D. Kalu, M. A. Odeniyi, K. T. Jaiyeoba. Matrix properties of a new plant gum in controlled drug delivery. Arch. Pharm. Res., 2007; 30: 884-889.
10. J. Edwin, S. Edwin, S. Dosi, *et al*. Application of Hibiscus leaves mucilage as a suspending agent. Indian J. Pharm. Education Res., 2007; 41: 373-375.
11. G. K. Jani, D. P. Shah. Assessing Hibiscus rosa-sinensis Linn as an excipient in sustained release tablets. Pharm. Tech., 2008; 62-75.
12. G. K. Jani, D. P. Shah. Evaluation of mucilage of Hibiscus rosasinensis Linn as rate controlling matrix for sustained release of diclofenac. Drug Dev. Ind. Pharm., 2008; 34: 807-816.
13. D. Kulkarni, A. K. Dwivedi, J. P. S. Sarin, *et al*. Tamarind seed polyose: A potential polysaccharides for sustained release of verapamil hydrochloride as a model drug. Indian J. Pharm. Sci., 1997; 59: 1-7.
14. K. Gowthamrajan, G. T. Kulkarni, A. Muthukumar, *et al*. Evaluation of Fenugreek mucilage as gelling agent. Int. J.Pharm. Expt., 2002; 3: 16-19.