



# AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: <http://www.ajptr.com/>

## Microspheres: A Novel Drug Delivery System

Patil NV, Wadd NV, Thorat SS, Upadhye Shashikant Sudarshan

*Annasaheb Dange College of B. Pharmacy Ashta*

### ABSTRACT

The microspheres are also called as micro-particles. To overcome some of the problems of conventional therapy and enhance the therapeutic efficacy of a given drug they are designed. At the target tissue the drug should deliver in an optimal amount in the right period of time with the minimum side effect & maximum therapeutic effect, to get the desired effect. The microspheres received much attention not only for the prolonged release but also for targeting of the anticancer drugs to the tumour. The microsphere are spherical microparticles & are used where predictable & consistent particle surface area is important. . The microspheres has the drug located centrally within the particle where it is encased within the unique polymeric membrane. This review focuses on types, materials used, different methods of preparation, evaluation & applications of microspheres.

**Keywords:** Microspheres, Therapeutic effect, Targeting.

\*Corresponding Author Email: [ssupadhye7@gmail.com](mailto:ssupadhye7@gmail.com)

Received 04 March 2020, Accepted 24 March 2020

Please cite this article as: Upadhye SS *et al.*, Microspheres: A Novel Drug Delivery System. American Journal of PharmTech Research 2020.

## INTRODUCTION

The DDS [Drug delivery systems] have had an enormous impact on the health care system that can precisely control the release rates or target drugs to the specific body site. A ideal DDS [drug delivery system] delivers the drug at a rate decided by the need of the body throughout the period of the treatment & it provides the active entity solely to a site of action. So for the drug delivery the carrier technology offers an intelligent approach by the coupling of drug to the carrier particle such as the nanoparticles, liposomes, microspheres etc which modulates the release & absorption characteristics of the drug.

### Microsphere

The microspheres are the solid spherical particles ranging in size from 1 to 1000µm. They consist of proteins or synthetic polymers & they are spherical free flowing particles, which are biodegradable in nature. There are 2 types of microspheres as: a) Microcapsules. b) Micromatrices. The microcapsules are those in which the entrapped substance is distinctly surrounded by the distinct capsule wall & micromatrices in which the entrapped substance is dispersing throughout the microspheres matrix. The solid biodegradable microspheres which incorporated the drug dispersed or dissolved through the particle matrix, for the controlled release of the drug they have the potential. They are made up of waxy, polymeric or other protective materials that are modified natural products & biodegradable synthetic polymers.<sup>1,2</sup>

### Advantages

1. The microspheres have the ability to bind & release the high concentration of the drug.
2. Due to the smaller size & spherical shape they could be injected into the body.
3. The microsphere morphology allows the controllable variability in the drug release & degradation.
4. The microspheres provide a constant & prolonged therapeutic effect.
5. The microspheres avoid first pass metabolism.
6. The microspheres reduce the dosing frequency & thereby improve the patient compliance.
7. The better utilization of drug will improve the bioavailability & reduce the incidence or intensity of the adverse effects.
8. They have improved protein & peptide drug delivery system.
9. Simple method of preparation. It enhances biological half-life.

### Disadvantages

1. The controlled release formulations generally contain the higher drug load & thus any loss of the integrity of the release characteristics of the dosage form may lead to the potential toxicity.
2. From the variety of factors like food & the rate of transit through the gut the release rate of the controlled release dosage form may vary.
3. The dosage forms of this kind should not be chewed & crushed.
4. From one dose to another there is differences in the release rate.<sup>3-5</sup>

## **TYPES OF MICROSPHERES**

### **The Magnetic microspheres**

This type of delivery system is very important which localizes the drug to the diseased site. In this, by smaller amount of magnetically targeted drug the larger amount of freely circulating drug can be replaced. The magnetic carriers receive the magnetic responses to the magnetic field from the incorporated materials that are used for the magnetic microspheres are dextran, chitosan etc. To deliver the chemotherapeutic agent to the liver tumour the different type of therapeutic magnetic microspheres are used. Through this system the drugs like peptides & proteins can also be targeted.<sup>6,7</sup>

### **The Floating microspheres**

The bulk density is less than the gastric fluid in floating types & without affecting gastric emptying rate it remains buoyant in the stomach. At the desired rate the drug is released slowly, if the system is floating on gastric content it increases the gastric residence & fluctuation in the plasma concentration. Also it reduces the chances of striking & dose dumping & produces the prolonged therapeutic effect. Through this form the drug [ketoprofen] is given.<sup>8</sup>

### **The Polymeric microspheres**

The polymeric microspheres can be classified as:

#### **Synthetic polymeric microspheres**

The synthetic polymeric microspheres are widely used in the clinical application, moreover that also used as the embolic particles, bulking agent, drug delivery vehicles, fillers etc & proved to be the safe & biocompatible. But the main drawback of these kind of microspheres are that they tend to migrate away from the injection site & lead to the potential risk, embolism and further damage of organ.<sup>9</sup>

#### **Biodegradable polymeric microspheres**

With the concept that they are bioadhesive, biodegradable & biocompatible in nature the natural polymers such as starch are used. The biodegradable polymers prolongs the residence time when they come in contact with the mucous membrane due to its high degree of swelling property with

the aqueous medium thus results in gel formation. By the concentration of polymer & the release pattern in the sustained manner, the rate & extent of the drug release is controlled. The main disadvantage is that in clinical use the drug loading efficiency of the biodegradable microspheres is complex & it is difficult to control the release of drug.<sup>10</sup>

### **The Bioadhesive microspheres**

The sticking of drug to the membrane by using the sticking property of the polymers that are water soluble is defined as adhesion. The bioadhesion can be termed as the adhesion of the drug delivery device to the mucosal membrane such as rectal, buccal, nasal, ocular etc. The term bioadhesion describes the materials that bind to the biological substrates such as the mucosal members. The adhesion of the bioadhesive drug delivery devices to the mucosal tissue offers the possibility of creating an intimate & prolonged contact at the site of administration. This residence time which is prolonged can result in the enhanced absorption & in combination with the controlled release of the drug by reducing the frequency of administration it also improves the patient compliance. For the drug delivery the carrier technology offers an intelligent approach by coupling the drug to the carrier particle such as nanoparticles, microspheres, liposomes, nanospheres etc which modulates the absorption & release of the drug. The microspheres constitute an important part of these particulate drug delivery systems by virtue of their small size & efficient carrier capacity.<sup>11</sup>

### **The Radioactive microspheres**

The radio mobilisation therapy microspheres of sized 10 to 30 nm are of larger than the capillaries & it gets trapped in the first capillary bed when they come across. In to the arteries they are injected that lead to the tumour of interest. Without damaging the normal surrounding tissues, these radioactive microspheres deliver the high radiation dose to the targeted areas. from the drug delivery system It differs, as the radio activity is not released from the microspheres but acts from within the radioisotope typical distance & the different kinds of the radioactive microspheres are  $\gamma$  emitters,  $\alpha$  emitters &  $\beta$  emitters.<sup>12</sup>

### **The Diagnostic microspheres**

The magnetic drug transport technique is based on the fact that the drug can be either encapsulated into the magnetic microsphere or it can be conjugated on the surface of the microsphere. The accumulation of the carrier at the site of target allow them to deliver the drug locally.<sup>14</sup>

### **The Mucoadhesive microspheres**

The mucoadhesive microspheres which are of 1 to 1000mm in diameter & consisting either the entirely of the mucoadhesive polymer or having the outer coating of it & coupling of the mucoadhesive properties to the microspheres has the additional advantages. For e.g: The enhanced

bioavailability & the efficient absorption of the drugs due to the high surface to volume ratio, the much more intimate contact with a mucus layer, the specific targeting of the drug to the absorption site which is achieved by anchoring the plant lectins, antibodies & bacterial adhesions, etc. on the surface of microspheres. To adhere to any mucosal tissue the mucoadhesive microspheres can be tailored which includes those found in the GIT [gastrointestinal tract], nasal cavity, eye & urinary tract, thus offering the possibilities of the localized as well as the systemic controlled release of the drugs.<sup>1</sup>

## **MATERIALS USED**

**The microspheres used usually are polymers. They are classified into 2 types:**

A] Natural polymers

B] Synthetic Polymers

### **A] Natural polymers**

The natural polymers that are obtained from the different sources like carbohydrates, chemically modified carbohydrates & proteins.

- Carbohydrates: E.g: Starch, Agarose, Chitosan, Carrageenan.
- Chemically modified carbohydrates: E.g: Poly starch, Poly dextran,.
- Proteins: E.G: Collagen, Albumin & Gelatin.

### **B] Synthetic polymers**

Into 2 types the synthetic polymers are divided as

- Biodegradable polymers  
For e.g. Poly anhydrides, Lactides, Poly alkyl cyanoacrylates, Glycolides & their copolymers,
- Non-biodegradable polymers  
For e.g. PMMA [Polymethylmethacrylate], Epoxy polymers, Acrolein, Glycidyl methacrylate.<sup>15-17</sup>

## **CRITERIA FOR MICROSPHERE PREPARATION**

By micro encapsulation technique the Incorporation of liquid, solid or gases into one or more polymeric coatings can be done. The various methods that are used for the preparation of various microspheres depends on the route of administration, particle size, drug release duration & these above characters related to the rpm, the cross linking method, drug of cross linking, co precipitation, the evaporation time, etc. The preparation of microspheres should satisfy certain criteria:

- The release of active reagent with the good control over the wide time scale.
- It should have the ability to incorporate reasonably high concentrations of the drug.

- It should have the susceptibility to chemical modification.
- The stability of the preparation after synthesis with the clinically acceptable shelf life.
- The biocompatibility with the controllable biodegradability.
- The controlled particle size & dispersability in the aqueous vehicles for injection.<sup>5,6,18</sup>

## **METHOD OF PREPARATION**

### **The solvent evaporation method**

In vehicle phase of liquid manufacturing this process is carried out. In the volatile solvent the microcapsule coating is dispersed which is immiscible with the vehicle phase of the liquid manufacturing. In the coating polymer solution the core material which is microencapsulated is dissolved. To obtain the appropriate size microcapsule the agitation with the core material mixture is dissolved in the liquid manufacturing vehicle phase. If necessary, the mixture is heated to evaporate & the solvent for the polymer of a core material is dissolved in the polymer solution around a core polymer shrinks. The matrix type microcapsules are formed if the core material is dissolved in the coating polymer solution. The core materials are either soluble materials or water soluble.<sup>19-22</sup>

### **The spray drying method**

In this technique, in the volatile organic solvent such as acetone, dichloromethane etc, the polymer is dissolved first. A drug in the solid form is then dispersed in to the polymeric solution with a high-speed homogenization. In the hot air stream this dispersion is then atomized. The atomization leads to the form the small droplets from which the solvent evaporates instantly which leads the formation of microspheres in the size range 1 to 100µm. From hot air by the cyclone separator the micro particles are separated while by vacuum drying the trace of solvent is removed. The major advantages of this process is under aseptic conditions there is feasibility of operation.<sup>23</sup>

### **The double emulsion technique**

This method involves the formation of multiple emulsions or double emulsion of the type w/o/w & is best suited to the water soluble drugs, proteins, vaccines, peptides. This method can be used with the both synthetic & natural polymers. In the lipophilic organic continuous phase the aqueous protein solution is dispersed. This protein solution may contain the active constituents.<sup>24</sup>

### **The single emulsion technique**

By the single emulsion technique the micro particulate carriers of the natural polymers i.e. carbohydrates & proteins are prepared. The natural polymers are dissolved in the aqueous medium which is followed by a dispersion in the non aqueous medium like oil. The cross linking of the dispersed globule is carried out in the next step. By the heat or by using the chemical cross linkers the cross linking can be achieved. Formaldehyde, glutaraldehyde, acid chloride are the chemical

cross linking agents that are used. For the thermo labile substance the heat denaturation is not suitable. The chemical cross linking having the drawback of excessive exposure of the active ingredient to the chemicals if added at the time of preparation & then subjected to the centrifugation, separation, washing, nature of the surfactants used to stabilize the emulsion phases can be influenced greatly by the size distribution, size, loading drug release, surface morphology & bio performance of the final multiparticulate product.<sup>23</sup>

### **The Spray drying & spray congealing**

On the drying of the mist of polymer and drug in the air, these methods are based. These two processes are named spray drying and spray congealing depending upon the removal of the solvent or cooling of the solution.<sup>25</sup>

### **The phase separation coacervation technique**

This technique is based on the principle of the decreasing the solubility of the polymer in the organic phase which affect the formation of the polymer rich phase called as the coacervates. In this technique the drug particles are dispersed in the solution of the polymer & an incompatible polymer is added to the system which makes the first polymer for the separation of phase.<sup>23</sup>

### **The quasi emulsion solvent diffusion**

The novel quasi-emulsion solvent diffusion method is used for the manufacturing of a controlled release microspheres of the drugs with acrylic polymers, in the literature has been reported. By using external phase which contains distilled water and polyvinyl alcohol the microsponges can be manufactured by the quasi emulsion solvent diffusion method. The internal phase consists of the polymers, drug & ethanol. The internal phase is manufactured first at 60°C & after then it is added to the external phase at the room temperature. Then emulsification the mixture is stirred continuously for two hours. Then for the separation of the microsponges the mixture can be filtered.<sup>25-26</sup>

### **The solvent extraction**

For the manufacturing of microparticles the solvent evaporation method is used & it involves the removal of the organic phase by extraction of the non-aqueous solvent. This method involves the water miscible organic solvent which is the isopropanol.<sup>23</sup>

## **EVALUATION OF MICROSPHERES**

### **Particle size and shape**

To visualize the microspheres the most widely used procedures are the conventional SEM [scanning electron microscopy] & LM [light microscopy] . To determine the shape and outer structure of microspheres both procedures can be used. The light microscopy provides the control over the coating parameters in case of the double walled microspheres. Before & after coating the

microspheres structures can be visualized & the changes can be microscopically measured. The scanning electron microscopy provides the higher resolution in contrast to the light microscopy. The scanning electron microscopy allows the investigations of the microspheres surfaces & after the particles are cross-sectioned, for the investigation of double walled systems it can be used. For the structure characterization of multiple walled microspheres the confocal fluorescence microscopy is used. The laser light scattering & multi size coulter counter other than the instrumental methods which can be used for the characterization of the shape, morphology & size of the microspheres.<sup>3,27</sup>

### **Angle of contact**

To determine the wetting property of the micro particulate carrier the angle of contact is measured. In terms of hydrophobicity or hydrophilicity it determines the nature of the microspheres. This thermodynamic property is specific to the solid & is affected by the presence of the adsorbed component. At the solid/air/water interface the angle of contact is measured. By placing the droplet in the circular cell mounted above objective of inverted microscope the advancing & receding angle of contact are measured. Within a minute of the deposition of the microspheres the contact angle is measured at 200C

### **Isoelectric point**

To measure the electrophoretic mobility of the microspheres the apparatus used is micro electrophoresis from which the isoelectric point can be determined. By measuring the time of movement of particle over the distance of 1 mm the mean velocity at different Ph values ranging from 3 to 10 is calculated. The electrical mobility of the particle can be determined by using this data. To the surface contained charge, the ionisable behaviour or the ion absorption nature of the microspheres, the electrophoretic mobility can be related.<sup>28</sup>

### **Density determination**

By using the multi volume pycnometer the density of the microspheres can be measured. Into the multi volume pycnometer the accurately weighed sample in a cup is placed. In the chamber the helium is introduced at the constant pressure & allowed to expand. This expansion results in the decrease in pressure within the chamber. The 2 consecutive readings of the reduction in pressure at different initial pressure are noted. From 2 pressure readings the density & volume of the microspheres carrier is determined.<sup>29</sup>

### **Fourier Transform-Infrared Spectroscopy**

To determine the degradation of the polymeric matrix of the carrier system the Fourier Transform-Infrared Spectroscopy is used. The surface of the microspheres is investigated measuring ATR [alternated total reflectance]. The IR beam passing through the alternated total reflectance cell

reflected many times through the sample to provide the IR spectra mainly of the surface material. Depending upon the manufacturing procedures & conditions the alternated total reflectance-Fourier Transform-Infrared Spectroscopy provides the information about the surface composition of the microspheres.

### **Electron spectroscopy for chemical analysis**

By using the ESCA [Electron spectroscopy for chemical analysis] the surface chemistry of the microspheres can be determined. For the determination of the atomic composition of the surface the electron spectroscopy for chemical analysis provides a means. To determine the surficial degradation of the biodegradable microspheres, the spectra obtained using electron spectroscopy for chemical analysis can be used.<sup>30</sup>

### **Entrapment efficiency**

By allowing the washed microspheres to lysate the capture efficiency of the microspheres or the percent entrapment can be determined. To the determination of active constituents as per monograph requirement the lysate is then subjected. By using the following equation the percent encapsulation efficiency is calculated:

$$\% \text{ Entrapment} = \text{Actual content} / \text{Theoretical content} \times 100^3$$

### **Characterization**

The characterization of the micro particulate carrier helps to design the suitable carrier for the drug, proteins or antigen delivery. These microspheres have different microstructures. The release & the stability of the carrier is determined by these microstructures.<sup>31</sup>

### **In Vivo Methods**

The methods used for studying the permeability of the intact mucosa comprise of the techniques that exploit the biological response of the organism systemically or locally & those that involve direct local measurement of the uptake or the accumulation of the penetrants at the surface. The some of the simple & earliest studies of the mucosal permeability utilized the systemic pharmacological effects produced by the drugs after the application to the oral mucosa. The in vivo studies using animal models, buccal absorption tests, and perfusion chambers are however the most widely used methods for studying the drug permeability.

#### **i] Buccal absorption test**

In 1967, Beckett & Triggs developed the buccal absorption test. It is the reliable & simple method for measuring the extent of the drug loss of the human oral cavity for the single & multicomponent mixtures of the drugs. The test has been successfully used while the drug is held in the oral cavity to

investigate the relative importance of the drug structure, initial drug concentration, contact time & pH of the solution.<sup>32</sup>

### **ii] Animal models**

For the screening of the series of compounds, investigating the mechanisms and usefulness of permeation enhancers or evaluating a set of formulations the animal models are mainly used. In the literature the number of animal models have been reported, however very few in vivo (animal) animal models such as the sheep, hamster, dog<sup>33-35</sup>, rabbits, rats, cat & pigs have been reported. The procedure in general involves the anesthetizing the animal followed by the administration of the dosage form. To prevent absorption pathways other than oral mucosa the oesophagus is ligated, in case of rats. The blood is withdrawn & analyzed at different time intervals.<sup>36-39</sup>

### **In Vitro Methods**

There is the need for the experimental methods which allow the permeability & release characteristics of the drug through the membrane to be determined. A number of in vitro and in vivo techniques have been reported for this purpose,. The in vitro drug release studies have been employed as the quality control procedure in the pharmaceutical production in the product development etc. The sensitive & reproducible release data derived from the physic chemically & hydro dynamically defined conditions are necessary. The influence of the technologically defined conditions & difficulty in simulating the in vivo conditions has led to the development of the number of in vitro release methods for the buccal formulations, however no standard in vitro method yet has been developed. Depending on the shape & application of the dosage form developed the different workers have used apparatus of the varying designs & under varying conditions.<sup>3</sup>

### **i] Interface diffusion system**

Dearden & Tomlinson developed this method. It consists of 4 compartments. The compartment A represents the oral cavity & initially contained an appropriate concentration of the drug in the buffer. The compartment B represents the buccal membrane contained 1-octanol. The compartment C represents the body fluids contained 0.2 M HCl. The compartment D represents the protein binding also contained 1-octanol. The aqueous phase and 1-octanol were saturated with each other before use. The samples were withdrawn with the syringe & returned to compartment A.

### **ii] Beaker method**

In this method the dosage form is made to adhere at the bottom of the beaker containing the medium & stirred uniformly by using the overhead stirrer. The stirrer speed varies from 60 to 300 rpm in the literature for the studies & the volume of the medium used varies from 50 to 500 ml.<sup>40-42</sup>

### **iii] Dissolution apparatus**

The standard USP or BP dissolution apparatus have been used to study the in vitro release profiles by using rotating elements, paddle and basket . The dissolution medium that is used for the study varied from 100 to 500 ml & speed of the rotation from 50 to 100 rpm.<sup>43-44</sup>

#### iv] Modified Keshary Chien Cell

The specialized apparatus was designed in the laboratory. It comprised of the Keshary Chien cell containing the distilled water [50ml] at 37°C as the dissolution medium. The Trans Membrane Drug Delivery System [TMDDS] was placed in the glass tube fitted with the 10# sieve at the bottom which reciprocated in the medium at 30 strokes/min.<sup>45</sup>

#### In Vitro-In Vivo Correlations

The correlations between the in vitro dissolution rates & the rate & extent of the availability as determined by the blood concentration & or urinary excretion of the drug or metabolites are referred to as the in vitro-in vivo correlations. Such correlations allow one to develop the product specifications with bioavailability.<sup>3</sup>

**Table 1: List of Marketed Microspheres Drug Products<sup>46</sup>**

| Sr. No | Drug          | Technology              | Commercial name                              |
|--------|---------------|-------------------------|--|
| 01     | Bromocriptine | Spray drying            | Parlodel LAR <sup>TM</sup>                   |
| 02     | Triptorelin   | Phase separation        | Trelstar Depot, Decapeptyl <sup>R</sup> SR   |
| 03     | Octreotide    | Phase separation        | Sandostatin <sup>R</sup> LAR                 |
| 04     | Naltrexon     | Double emulsion (o/w)   | Vivitrol <sup>R</sup>                        |
| 05     | Minocycline   | N/A                     | Arestin <sup>R</sup>                         |
| 06     | Lanreotide    | Phase separation        | Somatuline <sup>R</sup> LA                   |
| 07     | Somatropin    | Spray drying            | Nutropin <sup>R</sup>                        |
| 08     | Leuprolide    | Double emulsion (o/w/o) | Leupron Depot <sup>R</sup>                   |
| 09     | Risperidone   | Double emulsion (o/w)   | Risperdal <sup>R</sup> , Consta <sup>R</sup> |

## APPLICATIONS OF MICROSPHERES

### The fluorescent microspheres

The fluorescent microspheres are made up of polystyrene or poly vinyl toluene mono disperse system ranging in the size from 20nm- 4µm. The preparation of the fluorescent microspheres comprising swelling the polymeric microsphere so that the fluorescent dyes may enter the microsphere pores. Unswelling the polymeric microspheres so that a fluorescent dyes become physically entrapped in to the pores.

### The microspheres for Lymph targeting

To provide an effective anticancer chemotherapy to prevent the metastasis of tumor cells by accumulating the drug in the regional lymph node is the major purpose of the lymph targeting. For example, i] For the lymphatic of diagnostic agents the poly [lactide-co-glycolide] microspheres. ii]

For the tumor of peritoneal cavity the poly alkyl cyanoacrylate microspheres bearing the anticancer drugs.

### **The microspheres for Ocular delivery**

Most of the applications of the drug loaded ophthalmic delivery systems are for the glaucoma therapy especially the cholinergic agonists like the pilocarpine. From the very short time [1 to 3 minutes] the short elimination half-life of the aqueous eye drops can be extended to prolonged time [15-20 minutes] using the microspheres which have the biodegradable properties. For eg- Poly alkyl cyano acrylate

### **The microspheres for DNA Delivery**

For the transfer of plasmid DNA the microspheres have been recently used as the delivery vehicle which leads to improve the transfer of the plasmid DNA & their stability in the bio- environment<sup>38</sup>. In 1998, Truong-Le and co-workers developed the novel system for the gene delivery based on the use of DNA-gelatin nanoparticles/microspheres formed by the salt induced complex coacervation of the gelatin and plasmid DNA .

### **The adjuvant effect for vaccines**

In several studies on the substances or the oral administration an adjuvant effect of the nanoparticles/microspheres with either matrix entrapped or the surface adsorbed vaccines have been demonstrated. The Kreuter and co-workers observed that the poly methyl methacrylate microspheres containing the influenza antigen induced significant antibody response. The oral delivery of the antigens with the microspheres may be an elegant means of producing an increase response of Ig A [Immunoglobulin A] antibody.<sup>13,47</sup>

### **The microspheres in chemotherapy**

One of the most promising application of the microspheres are possible to use as the carriers for the anti- tumor agents. The enhanced endocytic activity & the leaky vasculature administrated microspheres. By coating with the soluble polyoxy ethylene the stealth microspheres are prepared. For the cancer chemotherapy the accumulation of the non-stealth microspheres in RES [Reticulo Endothelial System] may also be exploited.<sup>48-50</sup>

## **CONCLUSION**

Because of their advantages of sustained & controlled release action, improved the stability, reduced the dose frequency, dissolution rate & bioavailability the microspheres drug delivery system is the most popular drug delivery system. The microparticles are spherical microspheres & are used to deliver the drug at the target site with specificity if modified & to maintain the desired concentration at the site of interest without the untoward effects . The microspheres has the drug located centrally within the particle where it is encased within the unique polymeric membrane. The microspheres

are the better choice of DDS [drug delivery system] than many other types of the drug delivery system. By combining various other strategies, in future the microspheres will find the significant & central place in the novel drug delivery particularly in the diagnostics, diseased cell sorting, gene & genetic materials, targeted, safe, effective & specific in vitro delivery & supplements as the miniature versions of the diseased tissues & organ in the body.

## REFERENCES

1. Chowdary KP, Yarraguntla SR: Mucoadhesive microsphere for controlled drug delivery. *Biol. Pharm. Bull.*:2004:1717-24.
2. Chaudhari A, Jadhav KR, Kadam VJ: An Overview: Microspheres as a Nasal Drug Delivery System. *Int. J. of Pharmaceutical Sciences Review and Res.* 2010: 5.
3. Jain N.K., Controlled and Novel drug delivery: 04 Edition: 236-237,21.
4. Chein Y.M: Novel Drug Delivery System, second edition, revised & expanded, Marcel Dekker, Inc, New York 1992
5. Alagusundaram. M, Madhu S.C, Umashankari.K, Attuluri VB, Lavanya.C, Ramkanth.S. Microspheres as a Novel Drug Delivery System-A Review. *International Journal of ChemTech Research*: 2009:1(3): 526-534.
6. Li SP, Kowalski CR, Feld KM, Grim WM. Recent Advances in Microencapsulation Technology and Equipment. *Drug Delivery Ind. Pharm*: 1988:14:353-76.
7. Patel JK: [www.Pharmainfo.Net/Reviews/Bioadhesive microspheres-](http://www.Pharmainfo.Net/Reviews/Bioadhesive%20microspheres-) review, 24th Nov 2010.
8. Najmuddin M., Ahmed A., Shelar S, Patel V, Khan T. Floating Microspheres Of Ketoprofen: Formulation and Evaluation, *International Journal Of Pharmacy and Pharmaceutical sciences*:2010: 2(2):83-87.
9. Trivedi P, Verma AML, Garud N. Preparation and Characterization of Acclofenac Microspheres, *Asian Journal of pharmaceutics*:2008:2(2):110-15.
10. Saralidze K, Leo H., Koole, Menno L, Knetsch W:Polymeric Microspheres for Medical Applications, *Materials*:2010:3:3357- 64.
11. Patel J: Bioadhesion is a topic of current interest in the design of controlled or targeted drug delivery system.
12. Yadav AV, Mote HH: Development of Biodegradable Starch Microspheres for Intranasal Delivery, *Indian Journal of pharmaceutical Sciences*: 2008:70 (2):170-74.
13. Shanthi NC, Gupta R, Mahato KA: Traditional and Emerging Applications of Microspheres: A Review, *International Journal of Pharm. Tech Research*:2010: 2(1):675-81.

14. Chandrawanshi P, Patidar H. Magnetic microsphere: As targeted drug delivery. *J. of Pharmacy Res.* 2009.
15. Vyas S.P. and Khar R.K, Targeted and Controlled drug delivery: 07 Edition, 418.
16. Ramteke K.H, Jadhav V.B, Dhole S.N: Microspheres: as carriers used for novel drug delivery system *IOSR Journal of Pharmacy*: 2012;2(4):44-48.
17. Giri Prasad B. S, Gupta V. R., Devanna N, Jayasurya K: Microspheres As Drug Delivery System – A Review *Journal of Global Trends in Pharmaceutical Sciences*
18. Ghulam M., Mahmood A., Naveed A., Fatima R.A: Comparative study of various microencapsulation techniques. Effect of polymer viscosity on microcapsule characteristics, *Pak.J.Sci*: 2009: 22 (3):291-300.
19. Anandea N M, Jain S K, Jain N K: Con-A conjugated mucoadhesive microspheres for the colonic delivery of diloxanide furoate. *International Journal of Pharmaceutics*: 2008: 359:182-189.
20. Guojun L, Husheng Y, Jiayun Z: Preparation of magnetic microsphere from water- in-oil emulsion stabilized by block copolymer dispersant, *Biomacromolecules*:2005:6:1280- 1288.
21. Dutta P, Struti J, Niranjana P C., Bhaoji rao M.E, 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.
22. Ahmad N, Hasan N, Ahmad Z, Zishan M, Zohrameena S, *Momordica Charantia*: For Traditional Uses And Pharmacological Actions. *Journal of Drug Delivery and Therapeutics*, 2016:6(2):40-44.
23. Suvarna V, microspheres: a brief review, *Asian Journal of Biomedical and Pharmaceutical Sciences*:2015:5(47):13-19.
24. Prasanth V.V., Moy A. C., Mathew S. T., Mathapan R., *Microspheres An overview*, *Int. J. Res. Pharm. Biomed. Sci*:2011:2:3328.
25. Kawashima Y, Niwa T, Takeuchi H, T. Hino, Y. Ito: 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.
26. 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

27. Barkai A, Pathak V, Benita S: Polyacrylate (Eudrugit retard) microspheres for oral controlled release of nifedipine. I. Formulation design and process optimization. *Drug Dev Ind Pharm*:1990;16:2057-2075.
28. Sinha, v. R.; Agrawal, M. K.; Kumria, R: Influence of formulation and excipient variables on the pellet properties prepared by extrusion spherization. *Curr. Drug Delivery*:2005;2:1-8.
29. Bodmeier R, Chen H. Preparation and characterization of microspheres containing the anti-inflammatory agents, Indomethacin, ibuprofen and ketoprofen. *J. Controlled Release*; 1989;10: 167175.
30. Kawashia Y, Niwa T, Takeuchi H, Hino T, Itoh Y, Furuyamas: Characterization of polymorphs of tranilast anhydrate and tranilast monohydrate when crystallized by two solvent change spherical crystallization techniques. *J Pharma Sci*:1991;81:472–478.
31. Schugens C., Larvelle. N., Nihantn., Grandfils C., Jerome R. and Teyssie. P. *J.Control.Rel*:1994;32:161.
32. Rathbone, M.J: “Human buccal absorption I.A method for Estimating the transfer kinetics of drugs W cross the human buccal membrane”. *Int.J.pharm*:1991a:69:103.
33. Burnside, B.A; Keith, A.P. and snipes, W: “micro porous hollow fibers as a peptide delivery system via the buccal activity”.*proceed.inter.symp.control. Rel. Bioact. mater*:1989:16:94.
34. Ishida, M.; Nambu, N. and Nagai, T: “Ointment type oral mucosal dosage form of carbopol containing prednisolone for the treatment of aphtha”. *Chem.pharm.Bull*: 1983b :31 : 1010.
35. Rathbone, M.J: Purve, R.: Ghazati, F.A, HO, P.C: “In vivo techniques for studying the oral mucosa absorption characteristics of drugs in animals and humans.” In Rathbone, M.J. (ed.), *oral mucosal delivery systems*, Marcel Dekker Inc.Newyork:1996:121-156.
36. Oh, C.K., Ritschel. W.A: “Biopharmaceutical aspects of buccal absorption of insulin rabbits Effects of dose, size, Ph & sorption enhancers: in vivo in vitro correlation”. *Pharm.Res*:1999a:5(5):100.
37. Hussain, M.A; Aungst, B.J.; Kearney A. and Shefter, E:“Buccal and oral bioavailability of naloxone and naltrexone in rats”. *INT, J.pharm*:1987:36:127.
38. . Kellaway, I.W. and warren, S.I. “Mucoadhesive hydrogels”. *Proc. Intern. symp. Control. Rel. Bioact. Mater*:1991:18:73.
39. Hoogstrate, A.J., Verhoef, J.C.; Tuk., B.; Pijpers, A.; Vercheijden, J.H.M.; Jungiger, H.E, Bodde, H.C. “Invivo buccal delivery of fluorescein iso thiocyanate – dextran 4400 with glycodeoxy cholate as an absorption enhacer in pigs”. *J.pharm.sci*:1996b:85(5):457-460.

40. Tanaka, W; Akito, E; Yoshida, K.; Terada, T, Ninomiya, H. "Pharmaceutical preparations for oral cavity administration" US patent No.4059686. 1977.
41. Ishida M, Nambu N, Nagai T: "Highly viscous gel ointment containing carbapol for application to the oral mucosa". Chem..pharm Bull.:1983a:31:4561.
42. Collins, A.E and Deasy, P.B "Bioadhesive lozenge for the improved delivery of cetylpyridinium chloride".J.pharm.sci:1990:79 (2):116-120.
43. Parodi, B.; Russo, E.; Caviglioli, G.; Cafaggi, S, Binardi, G: "Development & characterization of a buccoadhesive dosage form of Oxydodone hydrochloride". Drug Dev.Ind.pharm:1996:22(5):445450.
44. Cassidy, J.P, Landcert, N.M, Quardos E: "Controlled buccal delivery of buprenorphine". J.control .Rel:1993:25:21-29.
45. Save T, Venkatachalam P: "Bioadhesive tablets of Nifedipine: Standardization of a novel buccoadhesive erodible carrier". Drug Dev.Ind. pharm: 1994:20(19):3005-3014.
46. Nagpal M, Midha K, Arora S: Microspheres: A recent update. International Journal of Recent Scientific Research: 2015:5(3):543-66.
47. Keys, H.M., Bundy, B.N., Stehman, F.B., Muderspach, L.I., Chafe, W.E., Suggs, C.L., Walker, J.L, Gersell D. Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. The New England J of Medicine:1999:340:1154- 1161.
48. Vyas SP, Khar RK. Targeted and Controlled drug delivery. Vallabh Prakashan, New Delhi India, 7th Edition; 102-107.
49. Kreuter J, Nefzger M, Liehl E, Czok R, Voges R: Microspheres – A Novel Approach in Drug Delivery System. J Pharm sci:1983:72:1146.
50. Costa P, Sousa Lobo J M: Modelling and comparison of dissolution profiles, European Journal of Pharmaceutical Sciences:2001:13:123- 133.

***AJPTR is***

- Peer-reviewed
- bimonthly
- Rapid publication

Submit your manuscript at: [editor@ajptr.com](mailto:editor@ajptr.com)

