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# REVIEW ON: MICROSPHERE AS A NOVEL DRUG DELIVERY SYSTEM

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## ABSTRACT

The microspheres also are referred to as as micro-particles. To conquer a number of the troubles of conventional remedy and decorate the healing efficacy of a given drug they are designed. At the goal tissue the drug must deliver in an most useful quantity in the proper period of time with the minimal facet impact and most healing impact, to get the favored effect. The microspheres acquired much interest no longer only for the prolonged release however also for focused on of the anticancer drugs to the tumour. The microsphere are round microparticles and are used where predictable and consistent particle surface location is critical. . The microspheres has the drug placed centrally in the particle wherein it's miles encased inside the unique polymeric membrane. This assessment makes a speciality of types, materials used, one of a kind methods of guidance, evaluation and applications of microspheres.

**Keywords: Microspheres, Micro-particles, Therapeutic effect, Targeting, Polymeric Membrane**

## INTRODUCTION

The DDS [Drug delivery systems] have had an tremendous effect on the health care machine which can exactly manage the discharge prices or goal pills to the precise frame site. A best DDS [drug delivery system] promises the drug at a price determined by means of the need of the frame throughout the length of the treatment

and it affords the energetic entity totally to a site of action. So for the drug shipping the provider generation offers an sensible approach via the coupling of drug to the service particle together with the nanoparticles, liposomes, microspheres etc which modulates the release and absorption traits of the drug **[1-3]**.

**Microsphere**

The microspheres are the strong spherical debris ranging in size from 1 to1000µm. They consists of proteins or artificial polymers and they are spherical loose flowing particles, which are biodegradable in nature. There are 2 kinds of microspheres as: a] Microcapsules. B] Micromatrices. The microcapsules are the ones wherein the entrapped substance is extraordinarily surrounded by way of the awesome pill wall and micromatrices wherein the entrapped substance is dispersing all through the microspheres matrix. The solid biodegradable microspheres which incorporated the drug dispersed or dissolved via the particle matrix, for the controlled release of the drug they have got the capacity. They are made of waxy, polymeric or other shielding substances which might be changed natural merchandise and biodegradable artificial polymers **[4-6]**.

**Advantages**

1. The microspheres have the potential to bind and release the high awareness of the drug.
2. Due to the smaller size and spherical shape they will be injected into the body.
3. The microsphere morphology lets in the controllable variability in the drug launch and degradation.
4. The microspheres provide a steady and extended therapeutic impact.
5. The microspheres keep away from first skip metabolism.
6. The microspheres reduces the dosing frequency and thereby improves the patient compliance.
7. The better utilization of drug will improve the bioavailability and lessen the occurrence or intensity of the unfavourable outcomes.
8. They have improved protein and peptide drug transport system.
9. Simple method of education. It decorate organic half-existence.

**Disadvantages**

1. The managed release formulations typically include the higher drug load and for this reason any lack of the integrity of the release traits of the dosage form may also cause the

capacity toxicity.

2. From the range of things like meals and the price of transit through the intestine the discharge rate of the managed release dosage form may additionally range.
3. The dosage sorts of this type have to no longer be chewed and crushed.
4. From one dose to every other there may be differences inside the launch charge.

**TYPES OF MICROSPHERES**

**The Magnetic microspheres**

This kind of transport system is very vital which localizes the drug to the diseased web page. In this, via smaller amount of magnetically centered drug the larger amount of freely circulating drug may be changed. The magnetic providers get hold of the magnetic responses to the magnetic subject from the incorporated substances that are used for the magnetic microspheres are dextran, chitosan and so on. To deliver the chemotherapeutic agent to the liver tumour the extraordinary kind of therapeutic magnetic microspheres are used. Through this system the drugs like peptides and proteins also can be targeted **[6, 7]**.

**The Floating microspheres**

The bulk density is much less than the gastric fluid in floating types and with out affecting gastric emptying price it stays buoyant in the belly. At the desired rate the drug is released slowly, if the device is floating on gastric content material it increases the gastric house and fluctuation within the plasma attention. Also it reduces the chances of placing and dose dumping and produces the extended healing effect **[8]**.

**The Polymeric microspheres**

**The polymeric microspheres can be classified as:**

**Synthetic polymeric microspheres**

The artificial polymeric microspheres are widely used inside the medical application, furthermore that also used because the embolic debris, bulking agent, drug shipping cars, fillers and many others and proved to be the safe and biocompatible. But the principle drawback of these sort of microspheres are that they tend to migrate far from the injection website and result in the potential chance, embolism and similarly harm of organ **[9]**.

**Biodegradable polymeric microspheres**

With the concept that they're bioadhesive, biodegradable and biocompatible in nature the natural polymers which includes starch are used. The biodegradable polymers prolongs the house time when they arrive in touch with the mucous membrane due to its excessive degree of swelling belongings with

the aqueous medium accordingly effects in gel formation. By the concentration of polymer and the release sample within the sustained way, the price and volume of the drug release is managed. The major drawback is that in medical use the drug loading efficiency of the biodegradable microspheres is complex and it is hard to control the release of drug **[10]**.

**The Bioadhesive microspheres**

The sticking of drug to the membrane by using the usage of the sticking belongings of the polymers that are water soluble is described as adhesion. The bioadhesion may be termed because the adhesion of the drug transport device to the mucosal membrane consisting of rectal, buccal, nasal, ocular and so on. The time period bioadhesion describes the substances that bind to the biological substrates which includes the mucosal members. The adhesion of the bioadhesive drug delivery gadgets to the mucosal tissue offers the possibility of creating an intimate and prolonged contact at the web page of administration. This house time which is prolonged can result in the enhanced absorption and in aggregate with the managed launch of the drug by means of decreasing the frequency of management it also improves the affected person compliance. For the drug shipping the carrier technology offers an sensible approach with the aid of coupling the drug to the carrier particle including nanoparticles, microspheres, liposomes, nanospheres and many others which modulates the absorption and launch of the drug. The microspheres constitute an vital part of these particulate drug delivery structures through distinctive feature of their small length and green provider ability **[11]**.

**The Radioactive microspheres**

The radio emobilisation remedy microspheres of sized 10 to 30 nm are of large than the capillaries and it receives tapped within the first capillary bed after they encounter. In to the arteries they are injected that lead to the tumour of hobby. Without detrimental the regular surrounding tissues, these radioactive microspheres supply the high radiation dose to the focused areas. From the drug delivery machine It differs, as the radio hobby is not launched from the microspheres however acts from within the radioisotope typical distance and the specific styles of the radioactive microspheres are γ emitters, α emitters and β emitters **[12]**.

**The Diagnostic microspheres**

The magnetic drug transport method is primarily based on the reality that the drug can be either encapsulated into the magnetic microsphere or it could be conjugated at the surface of the microsphere. The

accumulation of the carrier on the web site of goal permit them to supply the drug regionally **[13, 14]**.

**The Mucoadhesive microspheres**

The mucoadhesive microspheres which can be of one to 1000mm in diameter and consisting both the totally of the mucoadhesive polymer or having the outer coating of it and coupling of the mucoadhesive homes to the microspheres has the extra blessings. For ex: The stronger bioavailability and the efficient absorption of the medication due to the high surface to quantity ratio, the a lot more intimate contact with a mucus layer, the precise focused on of the drug to the absorption website online that's achieved by means of anchoring the plant lectins, antibodies and bacterial adhesions, and many others. On the floor of microspheres. To adhere to any mucosal tissue the mucoadhesive microspheres can be tailored which incorporates those determined within the GIT [gastrointestinal tract], nasal hollow space, eye and urinary tract, for that reason imparting the possibilities of the localized in addition to the systemic managed launch of the medication **[13, 14]**.

**MATERIALS USED**

The microspheres used normally are polymers. They are labeled into 2 types:

**A] Natural polymers B] Synthetic Polymers**

**A] Natural polymers**

The natural polymers which are obtained from the exceptional resources like carbohydrates, chemically changed carbohydrates and proteins.

- **Carbohydrates:** E.G: Starch, Agarose, Chitosan, Carrageenan.
- **Chemically changed carbohydrates: E.G:** Poly search, Poly dextran,.
- **Proteins: E.G:** Collagen, Albumin and Gelatin.

**B] Synthetic polymers**

**Into 2 kinds the synthetic polymers are divided as**

- **Biodegradable polymers**

For e.G. Poly anhydrides, Lactides, Poly alkyl cyanoacrylates, Glycolides and their copolymers,

- **Non-biodegradable polymers**

For e.G. PMMA [Polymethylmethacrylate], Epoxy polymers, Acrolein, Glycidyl methacrylate. **[15-17]**

**CRITERIA FOR MICROSPHERE PREPARATION**

By micro encapsulation approach the Incorporation of liquid, stable or gases into one or more polymeric coatings can be carried out. The various techniques which

might be used for the coaching of diverse microspheres relies upon at the route of management, particle length, drug launch period and these above characters associated with the rpm, the pass linking approach , drug of pass linking, co precipitation, the evaporation time, and so forth. The education of microspheres should satisfy certain criteria:

- The launch of energetic reagent with the coolest manage over the huge time scale.
- It must have the potential 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 ideal shelf existence.
- The biocompatibility with the controllable biodegradability.
- The controlled particle size and dispersability in the aqueous motors for injection **[18]**.

**METHOD OF PREPRATION**

**The solvent evaporation approach**

In car phase of liquid manufacturing this procedure is finished. In the unstable solvent the microcapsule coating is dispersed which is immiscible with the vehicle segment of the liquid manufacturing. In the coating polymer solution the middle fabric which is microencapsulated is dissolved. To obtain the right length microcapsule the agitation with the center material aggregate is dissolved inside the liquid manufacturing automobile section. If important, the combination is heated to evaporate and the solvent for the polymer of a core cloth is dissolved within the polymer solution around a core polymer shrinks. The matrix kind microcapsules are shaped if the center material is dissolve inside the coating polymer solution. The center substances are both soluble substances or water soluble **[19-22]**.

**The spray drying technique**

In this technique, inside the risky organic solvent along with acetone, dichloromethane and many others, the polymer is dissolved first. A drug inside the solid shape is then dispersed in to the polymeric solution with a high- velocity homogenization. In the recent air move this dispersion is then atomized. The atomization ends in the shape the small droplets from which the solvent evaporates immediately which leads the formation of microspheres inside the length range 1 to 100μm. From hot air through the cyclone separator the micro debris are separated whilst by way of vacuum drying the trace of solvent is removed. The essential advantages of this procedure is below aseptic situations

there may be feasibility of operation **[23]**.

**The double emulsion technique**

This method involves the formation of a couple of emulsions or double emulsion of the kind w/o/w and is great acceptable to the water soluble tablets, proteins, vaccines, peptides. This approach may be used with the both synthetic and herbal polymers. In the lipophilic natural continuous segment the aqueous protein answer is dispersed. This protein answer may include the lively parts **[24]**.

**The single emulsion technique**

By the single emulsion technique the micro particulate providers of the natural polymers i.E. Carbohydrates and proteins are prepared. The natural polymers are dissolved inside the aqueous medium that's observed by a dispersion in the non aqueous medium like oil. The go linking of the dispersed globule is executed inside the next step. By the warmth or by using the use of the chemical move linkers the move linking may be accomplished. Formaldehyde, glutaraldehyde, acid chloride are the chemical go linking agents which can be used. For the thermo labile substance the heat denaturation isn't suitable. The chemical pass linking having the downside of excessive publicity of the energetic ingredient to the chemical compounds if introduced on the time of guidance and then subjected to the centrifugation, separation, washing, nature of the surfactants used to stabilize the emulsion phases may be stimulated greatly via the dimensions distribution, length, loading drug launch, surface morphology and bio overall performance of the final multiparticulate product **[23, 24]**.

**The Spray drying and spray congealing**

On the drying of the mist of polymer and drug within the air, those methods are primarily based. These two methods are named spray drying and spray congealing depending upon the elimination of the solvent or cooling of the solution **[25]**.

**The phase separation coacervation approach**

This technique is based on the principle of the reducing the solubility of the polymer within the natural segment which affect the formation of the polymer rich segment known as because the coacervates. In this approach the drug debris are dispersed in the answer of the polymer and an incompatible polymer is delivered to the device which makes the first polymer for the separation of segment **[23-25]**.

**The quassi emulsion solvent diffusion**

The novel quasi-emulsion solvent diffusion approach is used for the manufacturing of a controlled release microspheres of the

medicine with acrylic polymers, inside the literature has been mentioned. By the usage of external section which contains distilled water and polyvinyl alcohol the microsponges can be manufactured by using the quassi emulsion solvent diffusion approach. The inner segment includes the polymers, drug and ethanol. The internal section is synthetic first at 60$^{o}$C and after then it's miles introduced to the outside segment at the room temperature. Then emulsification the mixture is stirred continuously for 2 hours. Then for the separation of the microsponges the aggregate can be filtered **[25-26]**.

**The solvent extraction**

For the producing of microparticles the solvent evaporation approach is used and it involves the removal of the natural section by using extraction of the non-aqueous solvent. This method includes the water miscible organic solvent that is the isopropanol **[23-27]**.

**EVALUATION OF MICROSPHERES**

**Particle size and form**

To visualize the microspheres the most broadly used strategies are the conventional SEM [scanning electron microscopy] and LM [light microscopy]. To decide the form and outer structure of microspheres both tactics may be used. The mild microscopy gives the manage over the coating parameters in case of the double walled microspheres. Before and after coating the microspheres systems can be visualized and the changes can be microscopically measured. The scanning electron microscopy offers the better decision in assessment to the mild microscopy. The scanning electron microscopy lets in the investigations of the microspheres surfaces and after the debris are move-sectioned, for the research of double walled systems it is able to be used. For the shape characterization of multiple walled microspheres the conflocal fluorescence microscopy is used. The laser mild scattering and multi size coulter counter other than the instrumental strategies which can be used for the characterization of the shape, morphology and size of the microspheres **[23-27]**.

**Angle of contact**

To decide the wetting property of the micro particulate carrier the angle of touch is measured. In terms of hydrophobicity or hydrophilicity it determines the character of the microspheres. This thermodynamic property is particular to the solid and is stricken by the presence of the adsorbed issue. At the stable/air/water interface the attitude of touch is measured. By setting the droplet within the circular mobile established

above objective of inverted microscope the advancing and receding angle of touch are measured. Within a minute of the deposition of the microspheres the touch perspective is measured at 20°C.

**Isoelectric point**

To degree the electrophoretic mobility of the microspheres the equipment used is micro electrophoresis from which the isoelectric point may be determined. By measuring the time of movement of particle over the distance of one mm the imply velocity at exceptional pH values ranging from three to ten is calculated. The electrical mobility of the particle may be determined by means of the usage of this information. To the floor contained charge, the ionisable behaviour or the ion absorption nature of the microspheres, the electrophoretic mobility may be associated **[28]**.

**Density determination**

By the usage of the multi quantity pychnometer the density of the microspheres may be measured. Into the multi quantity pychnometer the correctly weighed sample in a cup is located. In the chamber the helium is brought on the regular pressure and allowed to amplify. This enlargement outcomes inside the lower in stress in the chamber. The two consecutive readings of the discount in stress at special initial stress are referred to. From two pressure readings the density and extent of the microspheres service is determined **[29]**.

**Fourier Transfom-Infrared Spectroscopy**

To decide the degradation of the polymeric matrix of the provider device the Fourier Transfom- Infrared Spectroscopy is used. The floor of the microspheres is investigated measuring ATR [alternated total reflectance]. The IR beam passing thru the alternated total reflectance cellular reflected often thru the sample to provide the IR spectra specially of the surface fabric. Depending upon the producing techniques and situations the alternated overall reflectance-Fourier Transform-Infrared Spectroscopy gives the statistics approximately the floor composition of the microspheres **[29]**.

**Electron spectroscopy for chemical evaluation**

By the usage of the ESCA [Electron spectroscopy for chemical analysis] the surface chemistry of the microspheres can be determined. For the willpower of the atomic composition of the floor the electron spectroscopy for chemical evaluation affords a way. To decide the surfacial degradation of the biodegradable microspheres, the spectra obtained using electron spectroscopy for chemical evaluation can be used **[30]**.

**Entrapment efficiency**

By permitting the washed microspheres to lysate the capture efficiency of the microspheres or the percentage entrapment may be decided. To the willpower of energetic materials as according to monograph requirement the lysate is then subjected. By using the following equation the percentage encapsulation efficiency is calculated:

**% Entrapment = Actual content material/Theoretical content x one hundred three**

**Characterization**

The characterization of the micro particulate provider facilitates to design the right provider for the drug, proteins or antigen transport. These microspheres have exceptional microstructures. The release and the stableness of the provider is decided by means of these microstructures **[31]**.

**In Vivo Methods**

The methods used for reading the permeability of the intact mucosa incorporate of the techniques that take advantage of the biological reaction of the organism systemically or domestically and people who contain direct local measurement of the uptake or the accumulation of the penetrants on the floor. The some of the easy and earliest research of the mucosal permeability utilized the systemic pharmacological results produced by way of the drugs after the application to the oral mucosa. The in vivo research using animal models, buccal absorption checks, and perfusion chambers are but the most extensively used techniques for analyzing the drug permeability **[31]**.

**i] Buccal absorption check**

In 1967, Beckett and Triggs evolved the buccal absorption take a look at. It is the reliable and easy approach for measuring the volume of the drug loss of the human oral hollow space for the unmarried and multicomponent combinations of the medication. The test has been efficiently used whilst the drug is held inside the oral hollow space to investigate the relative importance of the drug structure, initial drug concentration, contact time and pH of the answer **[32]**.

**ii] Animal fashions**

For the screening of the collection of compounds, investigating the mechanisms and usability of permeation enhancers or evaluating a hard and fast of formulations the animal models are specifically used. In the literature the number of animal fashions had been pronounced, but only a few in vivo (animal) animal models consisting of the sheep, hamster, dog, rabbits , rats, cat and pigs were said. The system in widespread includes the anesthetizing the animal

followed via the administration of the dosage form. To save you absorption pathways apart from oral mucosa the oesophagus is ligated, in case of rats. The blood is withdrawn and analyzed at specific time periods **[33-39]**.

**In Vitro Methods**

There is the want for the experimental strategies which allow the permeability and release characteristics of the drug via the membrane to be decided. A quantity of in vitro and in vivo techniques have been stated for this purpose. The in vitro drug release studies have been employed as the fine control procedure in the pharmaceutical manufacturing inside the product development and many others. The sensitive and reproducible release statistics derived from the physic chemically and hydro dynamically described conditions are important. The impact of the technologically described situations and issue in simulating the in vivo conditions has caused the development of the wide variety of in vitro release strategies for the buccal formulations, but no popular in vitro approach but has been evolved. Depending at the shape and application of the dosage form advanced the exceptional people have used equipment of the varying designs and below various situations **[40]**.

**i] Interface diffusion gadget**

Dearden and Tomlinson evolved this technique. It consists of four booths. The compartment A represents the oral hollow space and first of all contained the precise concentration of the drug inside the buffer. The compartment B represents the buccal membrane contained 1-octanol. The compartment C represents the frame 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 every other earlier than use. The samples have been withdrawn with the syringe and back to compartment A **[41]**.

**Ii] Beaker method**

In this approach the dosage form is made to adhere at the lowest of the beaker containing the medium and stirred uniformly by using the overhead stirrer. The stirrer velocity varies from 60 to 300 rpm inside the literature for the research and the quantity of the medium used varies from 50 to 500 ml **[40-42]**.

**iii] Dissolution apparatus**

The preferred USP or BP dissolution equipment have been used to take a look at the in vitro launch profiles through the usage of rotating elements, paddle and basket . The dissolution medium this is used for the study varied from one hundred to 500 ml and speed of the rotation from 50 to a hundred rpm **[43-**

**44]**.

**iv] Modified Keshary Chien Cell**

The specialised apparatus become designed inside the laboratory. It made from the Keshary Chien cell containing the distilled water [50ml] at 370 C as the dissolution medium. The Trans Membrane Drug Delivery System [TMDDS] become placed in the glass tube fitted with the ten# sieve at the lowest which reciprocated in the medium at 30 strokes/min **[45]**.

**In Vitro-In Vivo Correlations**

The correlations among the in vitro dissolution charges and the fee and volume of the supply as decided through the blood attention and or urinary excretion of the drug or metabolites are referred to as the in vitro-in vivo correlations. Such correlations permit one to increase the product specs with bioavailability.

**Table 1: List of Marketed Microspheres Drug Products [46]**

| Sr. No. | Drug | Technology | Commercial name |
|---|---|---|---|
| 01 | Bromocriptine | Spray drying | Parlodel LAR$^{TM}$ |
| 02 | Triptorelin | Phase separation | Trelstar Depot, Decapeptyl$^{R}$ SR |
| 03 | Octreotide | Phase separation | SandostatinR LAR |
| 04 | Naltrexon | Double emulsion (o/w) | Vivitrol$^{R}$ |
| 05 | Lanreotide | Phase separation | Somatuline$^{R}$ LA |
| 06 | Somatropin | Spray drying | Nutropin$^{R}$ |
| 07 | Leuprolide | Double emulsion (o/w/o) | Leupron Depot$^{R}$ |
| 08 | Risperidone | Double emulsion (o/w) | Risperdal$^{R}$, Consta$^{R}$ |

## APPLICATIONS OF MICROSPHERES

**The fluorescent microspheres**

The fluorescent microspheres are made of polystyrene or poly vinyl toluene mono disperse gadget ranging within the length from 20nm- 4µm. The training of the fluorescent microspheres comprising swelling the polymeric microsphere in order that the fluorescent dyes might also input the microsphere pores. Unswelling the polymeric microspheres in order that a fluorescent dyes end up physically entrapped in to the pores.

**The microspheres for Lymph targeting**

To provide an powerful anticancer chemotherapy to save you the metastasis of tumor cells by using collecting the drug within the regional lymph node is the primary purpose of the lymph targeting.

**The microspheres for Ocular delivery**

Most of the programs of the drug loaded ophthalmic shipping structures are for the glaucoma remedy specially the cholinergic agonists like the pilocarpine. From the very short time [1 to 3 minutes] the short elimation 1/2-existence of the aqueous eye drops can be prolonged to extended time [15-20 minutes] the use of the microspheres that have the biodegradable homes. For eg- Poly alkyl cyano acrylate.

**The microspheres for DNA Delivery**

For the transfer of plasmid DNA the microspheres were recently used as the delivery car which ends up in improve the transfer of the plasmid DNA and their stability within the bio- environment38. In 1998, Truong-Le and co-workers evolved the radical machine for the gene shipping primarily based on the use of DNA-gelatin nanoparticles/microspheres formed by using the salt induced complicated coacervation of the gelatin and plasmid DNA.

**The adjuvant impact for vaccines**

In numerous research on the materials or the oral administration an adjuvant effect of the nanoparticles/microspheres with both matrix entrapped or the floor adsorbed vaccines were proven. The Kreuter and co-workers determined that the poly methyl methacrylate microspheres containing the influenza antigen triggered extensive antibody reaction. The oral transport of the antigens with the microspheres may be an elegant approach of manufacturing an boom response of Ig A [Immunoglobin A] antibody **[47]**.

**The microspheres in chemotherapy**

One of the most promising utility of the microspheres are viable to use because the vendors for the anti- tumor retailers. The superior endocytic pastime and the leaky vasculature administrated microspheres. By coating with the soluble polyoxy ethylene the stealth microspheres are organized. For the most cancers chemotherapy the buildup of the non-stealth microspheres in RES [Reticulo Endothelial System] may also be exploited **[48-50]**.

**CONCLUSION**

Because in their blessings of sustained and controlled release movement, progressed the steadiness, decreased the dose frequency, dissolution fee and bioavailability the microspheres drug delivery system is the most popular drug delivery machine. The microparticles are round microspheres and are used to supply the drug at the goal website with specificity if changed and to preserve the preferred awareness on the website of interest without the untoward consequences. The microspheres has the drug placed centrally in the particle wherein it's miles encased within the unique polymeric membrane. The microspheres are the better choice of DDS [drug delivery system] than many different types of the drug shipping machine. By combining various other techniques, in future the microspheres will find the vast and central vicinity inside the novel drug transport mainly inside the diagnostics, diseased cell sorting, gene and genetic materials, centered, secure, powerful and unique in vitro shipping and supplements

as the miniature variations of the diseased tissues and organ in the frame.

**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 and 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 Chem Tech 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/Bio adhesive microspheres- 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, Biomacro-molecules: 200: 6: 1280- 1288.

**[21]** Dutta P, Struti J, Niranajan 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): 76-82.

**[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 spheronization. Curr. Drug Delivery: 2005: 2: 1- 8.

**[29]** Bodmeier R, Chen H. Preparation and characterization of micro-spheres containing the anti-inflammatory agents, Indomethacin, ibuprofen and kitoprofen. 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]** Rathone, 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 and 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 cetypyridinium chloride". J. pharm. sci: 1990: 79 (2): 116-120.

**[43]** Parodi, B.; Russo, E.; Caviglioli, G.; Cafaggi, S, Binardi, G: "Development and characterization of a buccoadhesive dosage form of Oxydodone hydrochloride". Drug Dev. Ind. pharm: 1996: 22(5): 445-450.

**[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.