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## Review on Microspheres, and its Characterisation of Various Drugs

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### ABSTRACT

Targeted drug delivery is designed in such a way that it concentrate the drug in the targeted tissues and it tends to reduce the concentration of the medication in the other tissues. Hence, surrounding tissues are not affected by the drug. Microspheres are free flowing powders that contain proteins or synthetic polymers that are biodegradable and ideally possess particle size usually less than 200  $\mu\text{m}$ . The best possible means to deliver the drug to the target site with specificity, if modified, and to maintain the desired concentration at the site of interest without untoward effects. These possess importance not only for prolonged release, but also for targeting the anticancer drugs. In future, particularly in diseased cell sorting, gene & genetic materials, diagnostics, safe, targeted and effective *in vivo* delivery as well.

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### INTRODUCTION

Microspheres are usually solid spherical particles with size ranging from 1-1,000  $\mu\text{m}$ . They are free-flowing particles composed of synthetic polymers or proteins that are biodegradable in nature. They contain dispersed drug or drug that is dissolved in a matrix have the potential for specified drug release [1]. They consist polymeric, waxy or other protective materials.

### Materials Used in the Formulation of Microspheres:

Polymers are used in the preparation of microspheres, they are classified as follows:

Synthetic polymers are divided into two types:

#### 1. Non-biodegradable polymers:

Example: Polymethyl methacrylate (PMMA), Epoxy polymers. Acrolein-glycidyl methacrylate.

#### 2. Biodegradable polymers:

Example: poly alkylcyano acrylates, Lactides, glycolides and their copolymers, polyanhydrides.

### Natural Polymers

They are obtained from different sources such as proteins, carbohydrates and chemically modified carbohydrates [2].

Examples: Proteins such as albumin, gelatin and collagen, carbohydrates such as agarose, carrageenan, chitosan, starch, as well as chemically modified carbohydrates such as poly dextran, poly starch are also used [3].

### Types of Microspheres

#### Bio-Adhesive Microspheres

Adhesion will be characterised as adherence to the membrane by the use of the projecting the water soluble chemical compound properties. Bio-adhesive drug delivery system is delivery system uses the bio-adhesion property of a number of the polymers that become adhering on association and can be used for prolonged periods of time to direct drugs to a particular area of the body [4].

### **Floating Microspheres**

Gastroretentive drug delivery ways are floating microspheres on the idea of non-effervescent design. The word used synonymously with floating microspheres is hollow microspheres, microballoons or floating microparticles. These are free flowing cells, varied in scale from 1 to 1000  $\mu\text{m}$  [4].

### **Magnetic Microspheres**

This delivery system is extremely a lot of necessary that initiates the localisation of the drug to the illness site. Carriers receive magnetic responses to a magnetic flux that are incorporated materials and are used for this type are chitosan, dextran etc.

### **Polymeric Microspheres**

Biodegradable chemical compound microspheres Natural chemical compounds such as starch are used with the thought that they are biodegradable [5], biocompatible, and additionally Bioadhesive in nature.

### **Radioactive Microspheres**

The microsphere subgroup that interacts radioactively and is often treated during a comparable manner as non-radioactive microspheres. However, the radioactive microsphere continuously includes one and generally a lot of radio-nuclides are involved in targeting to specified sites [6].

### **Methods of Preparation**

#### **Spray Drying Technique**

This was used to prepare polymer microsphere mixed charged with drug. This requires dispersing the raw substance into liquefied coating liquid [7], after which spraying the mixture into the air for surface solidification accompanied by fast solvent evaporation. This is speedy however can also additionally lose crystallinity because of fast drying.

#### **Freeze Drying Technique**

Freeze drying is used effectively in the manufacture of API protein microspheres. The process is freezing, sublimation, main drying and secondary drying. The freezing step takes into account the eutectic point of the components. Molecules by removing water, creating a glassy matrix, reducing intermolecular interaction by forming hydrogen bonds between molecules or dipole-dipole interactions [8].

#### **Emulsion Solvent Evaporation Technique**

In this, the drug is dissolved in a polymer previously mixed in chloroform and that solution is mixed with aqueous phase containing 0.2% sodium PVP as an emulsifier [9].

This mixture is stirred at 500 rpm and then the drug and the polymer are converted into fine droplets which solidified into rigid microspheres by evaporation of the solvent and kept at room temperature and then collected by filtration and is washed with water. E.g.: Aceclofenac microspheres.

#### **Emulsion Solvent Diffusion Technique**

The drug chemical compound mixture was dissolved during a mixture of ethyl alcohol and dichloromethane (1:1) then the mixture was added dropwise of sodium lauryl sulfate solution.

So, the shaped floating microspheres were washed and dried in a desiccator at room temperature. These microparticles were sieved and collected [10].

#### **Double Emulsification Method**

The Doppel-emulsion strategy needs admixture w / o / w (or) o / w / o process the double emulsion. The solution of the product is distributed in a continuous lipophilic organic phase. The continuous step that consists of a chemical compound solution that encapsulates medication observed in the scattered aqueous layer to make primary emulsion.

The microspheres stuffed with the drug prolonged the unharnessed of the medication 24 hours and were ascertained to be diffusion and erosion regulated [11].

#### **Ionic Gelation Method**

The alginate/chitosan particle system for releasing diclofenac sodium was made using this technique. 25% (w/v) diclofenac sodium was added to a 1.2% (w/v) aqueous solution of sodium alginate continued and then added slowly to a solution containing  $\text{Ca}^{2+}/\text{Al}^{3+}$  and a solution of chitosan in acetic acid. Complete release was obtained at pH 6.47.2, but drug was not released at acidic pH [12].

### **Characteristics of Microspheres**

#### **Particle Size and Shape**

The most widely used methods for visualize microparticles are light microscopy and scanning electron microscopy. Both can be used to determine the shape and external structure of microparticles [13].

SEM allows studies of the surfaces of the microspheres and after the particles have been sectioned.

#### **Thermal Analysis**

Thermal analysis techniques routinely analyse these changes using programmed temperature variations for heating and cooling, and defined sample pressures and atmospheres [13].

**Table 1: Drugs with Different Polymers and its Evaluation Parameters**

Authors	Drugs	Polymers	Excipients Used	Method of Preparation	Conclusion
K.Kannan et al. [14]	Acetazolamide	Acrylate, methacrylate EudragitRL and Eudragit RS	Petroleum ether and light liquid paraffin (40:60)	Solvent evaporation technique	Sustained release of the formulation with Eudragit considering stirring speed and polymer ratio as major criteria. Combination of Eudragit RS & RL shows better release compared to Eudragit RS.
Shikha kesharvani et al. [15]	Metformin hydrochloride	HPMC, Eudragit S100	Ethanol, Dichloromethane	Emulsification solvent evaporation method	The SEM results reveals that the particles are spherical in shape and are effective in controlled release mechanism following case 2 transport.
Sunil Datt Belwal et al. [16]	Aceclofenac	Chitosan, lectins, polyacrylate, deacetylated gellan gum	Ethyl cellulose, Eudragit, PVA, ethanol, span 80, DCM	Emulsion cross-linking method, Solvent evaporation	Solvent evaporation technique has been successfully employed to produce Aceclofenac loaded ethyl cellulose and Eudragit microspheres with optimal drug encapsulation that sustained the drug release over a period of time
S. Sahu et al. [17]	Captopril	Sodium alginate, Sodium CMC & HPMC	Sod. Alginate, Sod CMC, Calcium chloride, phosphate buffer	Ionic gelation technique.	Drug to polymer ratio, stirring speed were major highlights for obtaining spherical particles.
Mulugeta Fentie et al. [18]	Furosemide	Ethylcellulose, HPMC, Tween 80.	Ethanol, dichloromethane, hydrochloric acid, sodium hydroxide.	Solvent evaporation method.	Floating microspheres of furosemide were successfully prepared that shows the sustained release of the drug by altering the ratio of Polymers, and drug.

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Table 1 continued

Authors	Drugs	Polymers	Excipients Used	Method of Preparation	Conclusion
Mahmoud M. Elsayed et al. [19]	Tolmetin sodium	Methylene chloride, glacial acetic acid, light liquid paraffin.	Sodium alginate, Calcium carbonate, potassium dihydrogen orthophosphate.	Internal gelation technique	Coating the alginate microspheres with chitosan delayed the drug release by forming Alg-Ch complex. The microspheres were spherical in shape with large pores at D:P ratio 1:1 while at 1:3 D:P ratio formed microspheres having a smooth surface and small pores. The change in chitosan concentration had a non-significant effect on drug.
L Pachuaue et al. [20]	Salbutamol sulphate and Theophylline	Ethylcellulose, acetone, Tween 80	water, phosphate buffer pH 7	Emulsion solvent evaporation technique.	Considering polymer-drug ratio alternately improves the efficiency and release rate of the microspheres. This helps in controlling asthmatic attacks and are proved successful.
Vikrant K. Nikam et al., [21]	Ketoprofen	Polyvinyl acetate, hydroxypropyl cellulose	Ceresin Wax (gm) Bees Wax (gm)	Melt solidification technique.	The prepared microspheres were spherical and possess smooth surface with excellent micromeritic properties.
Krishna Sailaja A et al. [22]	Ibuprofen	Ethylcellulose	Chloroform, 100ml of aqueous mucilage of 0.5% sodium cmc	Solvent evaporation technique	It can be concluded that F3 formulation with 9:7 to polymer ratio was considered as best formulation for the preparation of ibuprofen loaded ethyl cellulose microspheres.

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Table 1 continued

Authors	Drugs	Polymers	Excipients Used	Method of Preparation	Conclusion
S. Mohapatra et al. [23]	Glipizide	Sodium alginate, HPMC K4M, PEG4000 and Ethyl cellulose	Glipizide, Sodium Alginate, PEG 4000 Ethyl Cellulose HPMC K4M	Ionic gelation method	Improved bioavailability and reducing the frequency of administration thus minimizing the side effects along with patient compliance.
Manikandan Palanivelu et al. [24]	Ranitidine Hydrochloride	Carbopol 934, Chitosan, sodium alginate	Dichloromethane, Calcium carbonate, Tween 80, Glacial acetic acid, Conc Hydrochloric acid, Potassium bromide	Ionotropic Gelation Method, Solvent Evaporation Method.	Among all the formulation optimized (RF3) formulation shown the very good drug release and fulfil all the evaluation parameters effectively.
Satish Balakrishnabhise et al. [25]	Rifampicin	Ethanol, Eudragit RLPO, Dichloromethane	RIF, Glyceryl monostearate, Eudragit RLPO, Ethanol AR and Dichloromethane (HPLC grade)	Emulsion solvent diffusion method	The stability of RIF is improved by using this technique and the drug release profile was up to 3 hrs. DSC studies proved that the drug was mostly in amorphous form.
R. N. Saha et al. [26]	Diclofenac Sodium	Poly-lactic-co-glycolic acid, Ethylcellulose	Ethylcellulose, cyclohexane,	Phase separation-coacervation method	The mean particle size was found to be in between 49.94mm and 52.72 mm. In vivo pharmacodynamic studies proved the sustained release of the drug. Microsphere depot formulation is convenient technique for preparation of Parenteral formulations.

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Table 1 continued

Authors	Drugs	Polymers	Excipients Used	Method of Preparation	Conclusion
Sabdat O Ekama et al. [27]	Maraviroc and tenofovir	Chitosan, MRS Agar,	Sodium tri polyphosphate, acetic acid,	Ionic gelation technique	The combination of both drugs shows efficient action on HIV-1BaL virus. The anti-retroviral drugs were predominantly released from the carrier polymer and didn't disrupt the growth of Lactic acid bacterial microflora.
A. Mishra et al. [28]	Amlodipine Besylate	Ethylcellulose, Hydroxy propyl methyl cellulose, ethanol dichloromethane.	HPMC, Polysaccharides, ethyl cellulose, Dichloromethane.	Solvent evaporation method.	Availability of various dosage forms of AD also provides an option for prescribing depending on patients condition.
Pushpendra Kumar Khangar et al. [29]	Sulfasalazine	Chitosan, light liquid paraffin, glutaraldehyde. heavy liquid paraffin, Span 85, isopropyl alcohol	Ethanol, methanol, 0.1N HCL, 0.1N NaOH, chloroform and 7.4 pH buffer, isopropyl alcohol.	Simple emulsification phase-separation technique, cross-linking method.	The microspheres showed favorable release profiles in simulated colonic fluid. Further evaluation of the carriers are needed to improve the treatment options for colonic diseases.
Naoki nagahara et al. [30]	Amoxicillin	Carboxyvinyl, methylcellulose,	Hydrogenated castor oil, phosphate buffer.	Spray-chilling method.	The prepared ones are effective in clearing H. pylori than amoxicillin administered as amoxicillin suspension. Use of amoxicillin microspheres reduces toxicity

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Table 1 continued

Authors	Drugs	Polymers	Excipients Used	Method of Preparation	Conclusion
Pavani S, Mounika K et al. [31]	Acyclovir	Chitosan and sodium alginate	Acyclovir, HCL, calcium chloride, glacial acetic acid.	Ionic gelation techniques	UV analysis of ACV and melting point were complied with standards. From the study it is evident that promising sustained release microspheres of ACV may be developed from ionic gelation techniques by using polymers chitosan and sodium alginate.
G. P. Agrawaleet al. [32]	Albendazole	Chitosan, or b 2-amino-2-deoxy-d-glucose, liquid paraffin, toluene.	Chitosan hydrochloride, Glutaraldehyde	Emulsion method.	The effect of polymer concentration, stirring rate and concentration of cross-linking agent on the particle size of the microspheres which resulted in larger emulsion droplets and finally greater microsphere size.
Patil P.B. et al. [33]	Atenolol and Propranolol	Chitosan, hydroxypropyl cellulose, poly (ethylene glycol), polyethylene glycol macromer, poloxamer, (PVP).	Sorbitan monooleate, PVP, PAA	Solvent diffusion method, Interpolymer complexation method.	It may be feasible to use PAA/PVP mucoadhesive microspheres as a gastro-retentive DDS for antihypertensive effect. The release rate of the Beta-blockers agents is reduced because of Slower dissolution rate of the polymer taken.

## Drug Content

The combination need to be held apart to permit the debris to sediment and then wash. 1mL changed into moved into volumetric flask from the filtrate, and the extent changed into balanced with 0.1N NaOH [Table 1]. Drug changed into measured spectrophotometrically after the perfect dilution [34].

## CONCLUSION

Microspheres are the drug carriers in novel drug delivery system and are effective in cancer therapy or in any other disease treatment like a pulmonary related, cardiac related, and nervous system.

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## Conflict of Interest

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