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A REVIEW ON FEATURES OF POLYMER COLLOIDS AND MICROSPHERES

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ABSTRACT

Functional polymer microsphere needed different features of polymer colloids such as small size & volume, strong flexibity & agility, uniformity & variety. Functional polymer microsphere exhibits some important medicinal pharmaceutical applications such as Immunoassay and affinity-diagnosis, DNA diagnosis, blood flow measurement, embolization & phagocytosis. There are a few polymer molecules which have a drug feature, but in most instances, when polymers are used in drug delivery systems, they act as drug carrier. Polymeric materials are expected to make a major contribution to the drug delivery systems (DDS) for the subsequent reasons: the large size of the molecules allowing them to remain for a long time at the shipped site; drugs can be released gradually or in a regulated manner by carrier-polymer diffusion, or by the degradation of the carrier itself; and in addition to drugs, the carrier polymer can be combined with functional components to target the drugs or to monitor the release rate.

Keywords: DNA diagnosis, Embolization, Phagocytosis, Embolic Microsphere

INTRODUCTION

One of the most important research areas of pharmaceutical sciences is the development of new delivery mechanisms for controlled release of drugs. A well engineered managed drug delivery system can solve some of the traditional therapy problems and increase the therapeutic efficacy of a given medication. To achieve maximum therapeutic efficacy, it becomes necessary in the right time to deliver the agent to the target tissue in the optimum amount by causing little toxicity and minimal side

effects there. There are different approaches to supplying a medicinal drug in a sustained controlled manner for release to the target site. The targeting process and site-specific delivery can be achieved with absolute accuracy by attaching bioactive molecule to liposome, bioerodible polymer, implants, monoclonal antibodies and various particulates. One such solution is to use microspheresas drug carriers.

Microspheres: A spherical shell typically made of a biodegradable or resorbable plastic polymer with a very small diameter, generally in the micron or nanometer scale, often filled with a material (as a drug or an antibody) for release as the shell is degraded **[1]**. It is a small spherical microparticle, with usually 1 μm to 1000 μm (1 mm) diameters.

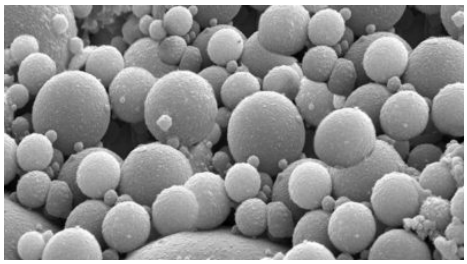

Figure 1: Microspheres [2]

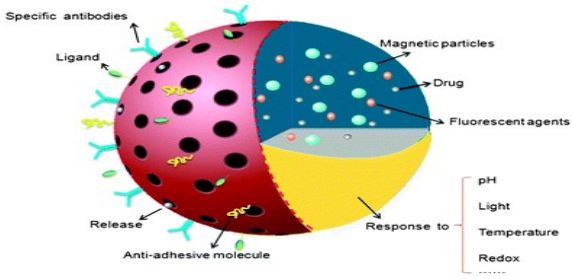

Figure 2: Nanoporous microsphere [3]

The advantages offered by microsphere-based protein and peptide delivery systems include shielding the proteins and peptides from GIT's harsh environment such as enzymatic hydrolysis and acidic pH. Microspheres may also facilitate the absorption of the therapeutic protein or peptide that is integrated in the delivery system via the paracellular pathway in particular. Another benefit of the microsphere-based delivery system is the possibility to monitor the release of the therapeutic protein or peptide integrated in different areas of the GIT using pH-sensitive polymers [**4**]. For one study, apart from healthy rat models, the ability of microsphere delivery systems to distribute the insulin hormone orally was tested on diabetic rat models. The insulin was loaded into polymer (methacrylic-g-ethylene glycol) microspheres. The findings showed that the microsphere effectively protected the integrated insulin molecules against enzymatic degradation in the stomach's acidic environment and no microspheric swallowing occurred. At the other hand, with the subsequent release of the integrated insulin molecules in the intestine, swallowing of the microspheres occurred in the basic intestine setting. The hypoglycemic function of the administered microsphere insulin delivery systems was

evaluated and the hypoglycemic effect was observed in both the diabetic rat models and the dose-dependent balanced rat models within 2 h of administration **[5]**.

Certain possible disadvantages include cleavages in the structure of oxidation, aggregation, and bonds leading to structural changes in proteins or peptides and ultimately a loss of biological activity. Structurally distorted proteins can also cause immunogenic responses to be initiated upon administration, because they can be immunogenic. The poor loading potential of protein microspheres may also be a limiting factor for their utility and oral protein delivery systems **[6]**.

Functional polymer microspheres

The word 'polymer colloid' refers to a polymer microsphere suspension or dispersion. Diameter in sub-micron order to a few microns. The medium of dispersion is in general water. Non-aqueous dispersion (NAD) is a dispersion whose medium is not water.

Features of polymer colloids and microspheres

1) **Small size and volume**

Polymer molecules typically have a molecular weight greater than 10,000 Da and, thus, a particular size cannot be less than 5 nm even though only one polymer molecule is composed of a atom. A polymer microsphere is around 30 nm in diameter if it consists of 1000 molecules of 10,000 Molecular Weights. However, polymer microspheres are small enough to show the current positions and can be used as a label or marker **[7]**.

2) **Broad surface area calculated**

The total surface area of around 60 m2 is 1 g of microspheres with a diameter of 0.1 mm. The surface area total is inversely proportional to the diameter. A wide area of surface is essential for adsorption and desorption sites, chemical reactions, light dispersal, etc.

3) **Strong flexibility and agility**

Low viscosity and high fluidity of polymer colloids relative to solutions that contain the same volume of solid. The viscosity of polymer colloids is a basic feature of the apparent volume fraction of Polymer colloid and microsphere characteristics. The apparent volume fraction of microspheres can be modified for some polymer colloids by environmental conditions including pH and temperature [**8]**. In a dispersion the microspheres can move by gravity, electric field, etc. and microscopically by Brownian motion through the medium. Such motions create a fresh connection between the medium and the microspheres.

4) **Uniformity**

The 1980s experienced several attempts by polymer colloid chemists to prepare

monodisperse microsphere [**9, 10]**. As a result, this technology has been tremendously developed to offer microspheres smaller than 1.005 with monodispersities (a weight-average diameter ratio to number-average diameter). The use of monodisperse microspheres enables their applications to produce sharp, accurate, and reproducible results or outputs. Attention must be paid not only to their scale uniformity but also to that of the microspheres' chemistry and morphology. Technologies to satisfy these conditions were also established with an understanding of the principles for particle nucleation and growth in polymerizations that shape particles. But, in general, inorganic surface chemistry the required uniformities are still missing for polymer composite microspheres [**11, 12]**.

5) Variety

Physical methods such as emulsification, coacervation and spray drying, and chemical methods such as heterogeneous polymerisation, will prepare polymer microspheres. Such preparatory methods in terms of scale, surface chemistry, composition, surface texture and morphology offer a variety of microsphere. Most polymer colloids or polymer latices are made by polymerization of the emulsion, yielding products for paints, adhesives, binders, rubbers, etc. The microspheres have been optimized for each purpose in terms of consistency and functionality, as well as manufacturability. Microgels, for example, were developed to reinforce coatings and amphoteric microspheres to increase their absorption into paper **[13]**. The microspheres do not maintain their identity and form in solution in the above-mentioned applications but they become a continuous film or bulk. Recently, another field where microspheres are used attracts attention, i.e. where microspheres exhibit their own functions while maintaining their original functions **[14, 15]**.

Medical & biological function of Microspheres

1] Immunoassay and affinity-diagnosis

- **Immunoassay using microspheres -** The antibody is a protein that is produced by lymphocytes when intruding into species a certain foreign substance called 'antigen.' Antibody's function is to protect the species from the antigen that invades them. It can be realized in the process whereby the antibody binds to catch and/or kill it with their antigen. The approach to this method is the dynamic creation of a high efficiency and selectivity between complementary antigen and antibody. Therefore, if there are

ample antibody molecules in a closed space, whole antigen molecules may be attached to antibody molecules. For such a system, the amount of antigen± antibody complex produced is proportional to the number of antigen molecules. The amount of complex antigen-antibody produced in such system is proportional to the number of molecules of antigene. When the resort has specific properties, e.g. the antigen- and antibody-identifiable absorbance, the amount of antigen in the original mixture can be calculated by adjusting the properties. Nephelometry is one of the methods by which antigen concentration is measured by calculating the light dispersion that is caused by the development of an antigen±antibody complex.

- **DNA diagnosis-** To prepare medicines with biospecific resistance, biocomponents other than antibodies are also immobilised. Such biocomponents include DNA, Hormones, Ligands, etc. particles which carry DNA are used in the diagnosis of DNA. DNA-carrying particles can be used for the detection of DNA linked to an disease. For examples, mutations of the K-ras genes are commonly found in primary pancreatic, colorectal and lung carcinomas and, thus, identifying this genetic abnormality for early detection of cancers is very important.

2] Microspheres in Blood

- ***Blood Flow Measurements-*** Cardiac output and regional blood flow, which are major factors in the decision to transport oxygen and oxygenate tissues, were calculated by methods using labeled microspheres pioneered in 1967 by Rudloph and Heymann **[16]**. Radioactive labelled microspheres have a diameter of approx. in most traditional measures of blood flow. 10±30 mm, i.e. approximately the same or slightly smaller than the red blood cells, is used and tissue radioactivity was obstructed **[17-19]**. For example, measuring blood flow in an aging rat posterior canal crystal using these microspheres revealed a substantial age-related decrease in blood flow accompanied by a decrease in capillary lumen in the mean capillary diameter and volume fraction caused by impaired end-organ function [**20]**. Because the use of radioactive microspheres

for calculating blood flow poses a safety issue, methods of replacement have been identified. For example, colored polystyrene (15 mm diameter) was injected into organs of interest to calculate and distribute the regional myocardial blood flow.

- ***Embolization and embolic microspheres*** When the blood current carries undissolved material of a certain thickness, it can occlude certain parts of the vascular system. This embolic effect is often used for therapy and surgery, e.g. preoperative embolization promotes surgical removal by reducing tumor volume and vascularity, and decreasing blood loss during surgery. Many synthetic and natural polymer microspheres, as well as thrombi, tissue fragments, bacterial clumps, gas bubbles, etc., have been used as emboluses. Embolic materials are normally inserted into micrtocatheters and thus the materials' slippery or non-adherence is a required condition for forcing them to pass through the catheter. It has been established that spherical hydrogel microspheres have poor adhesion and bioinertness **[21]**. Polyurethane microspheres charging Tantamium have been prepared by polymerization of condensation and modified by poly (methacrylic acid) grafting [**22]**. Tantanium has strong radiopacificity and grease in this device hydrophilicity imparted, and non-adherence. Now, biodegradable materials benefit as promising emboluses. A recent research has inserted starch microspheres into the brain to examine the clinical and histophathological effects of arterial embolization **[23]**. Microspheres of the poly (d, l) lactide were also examined **[24]**. Polymers that are thermosensitive, such as poly (N-isopropylacrylamide) can be a new artificial embolus candidate [**25]**. It precipitates over the so-called lower critical solution temperature at temperatures, and occludes capillary vessels. When cooled, this thermosensitive polymer dissolves once more.
- **Phagocytosis and phagocytized microspheres** Phagocytosis is a feature of unique cells, phagocytes, which defend their host by engulfing and digesting them from invaders. The main phagocytes include macrophages and leukocytes. Phagocyte behavior can be measured by evaluating the

capacity of the cells to phagocytize foreign material. This measurement is conducted using particles from latex as foreign material. For example, a reliable measure of phagocytic activity was provided by microspheres carrying special groups that emit fuorescence when digested in phagocytes [**26]**. Phagocytes can be classified using microspheres in a mixture of cells, as was done for phagocytic macrophages with fluorescent microspheres in blood monocyte cultures **[27]**.

If we plan to use microspheres as an embolus or drug carrier as a drug delivery system, assessment of the phagocytosis sensitivity of microspheres must be performed first.

When a drug is aimed at phagocytic cells, it is required that the drug carriers be phagocytized efficiently, while in the opposite case drug-carrying microspheres are allowed to avoid the phagocytosis and stay in the blood flow for a longer time.

Drug delivery system and carrier microspheres

There are a few polymer molecules which have a drug feature, but in most instances, when polymers are used in drug delivery systems, they act as drug carrier.

Polymeric materials are expected to make a major contribution to the drug delivery systems (DDS) for the subsequent reasons:

a) the large size of the molecules allowing them to remain for a long time at the shipped site;

b) drugs can be released gradually or in a regulated manner by carrier-polymer diffusion, or by the degradation of the carrier itself; and

c) in addition to drugs, the carrier polymer can be combined with functional components to target the drugs or to monitor the release rate.

Dissolved molecules hydrogelbulks, microcapsules, are the textures of drug-carrying polymers Microspheres, and lyposomes. Lyposomes, a kind of lipid bilayer microcapsules, received a booming reputation and were investigated as the perfect drug carrier. Yet the mechanical endurance of lyposomes held them away from their practical usage except in a few cases where the lyposomes provided some reinforcement [**28]**. That is the case for traditional microcapsules, too. Microspheres, on the contrary, carry adequate energy and longevity. Different polymeric materials were used to produce microspheres, and the likelihood of a drug carrier was investigated [**29-32]**.

Normally, the studies are carried out according to the following procedure:

1. Strategy setup (system collection, process, and kinetics).
2. Preparation of a microsphere (material use and preparatory methods).
3. Incorporation of medications (sometimes compared to 2).
4. Research in vitro / in vivo (for release and/or distribution);

As far as the system is concerned, it must be determined which priority is given to secure distribution, prolonged release and targeting. The mechanisms are divided into the following categories: the release of drugs through microsphere diffusion, and that of microsphere degradation or corrosion. This hinges on the consistency of the carrier microsphere and the drug-carrier combination. The discharge function could be the materials used for carrier microspheres have been primarily biodegradable, including biopolymers such as albumin, gelatin, etc., and synthetic polymers such as poly (lactic acid), poly (glycolic acid), poly (cyanoacrylate), etc.

CONCLUSION

The science and technology of polymeric microspheres and their dispersions have been rapidly developed over the last three decades, and development seems to be growing more and more as the era needs fine materials, mesoscopic research, nanotechnology, etc. and all the colloids. This also suggests a new method for preparing and characterizing microspheres one after another. What is especially noteworthy among them is the creation and characterization of monodisperse particles. Consisting of a single molecule, the design of fine particle morphology, the application of intelligent particles particulate matter, soft aggregation power, organized particle assembly etc.

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