RECENT APPROACHES IN MICROSPHERES: A NOVEL DRUG DELIVERY SYSTEM

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ABSTRACT

Microsphere technology has been studied extensively for the sustained delivery of therapeutic agents. Microspheres can be manufactured from various natural and synthetic materials. Glass microspheres, polymer microspheres and ceramic microspheres are commercially available. Recent researches are confined to the discovery of active microspheres in the treatment of cancers. The present paper review the recent approaches in microspheres technology, a novel drug delivers system.

INTRODUCTION

Microsphere is a term used for small spherical particles, (Fig. 1) with diameters in the micrometer range (typically 1μm to 1000μm (1mm)). Microspheres are sometimes referred to as microparticles. Microspheres can be manufactured from various natural and synthetic materials. Glass microspheres, polymer microspheres and ceramic microspheres are commercially available. Solid and hollow microspheres vary a lot in density and therefore, are used for different applications. Hollow microspheres are typically used as additives to lower the density of a material. Solid microspheres have numerous applications depending on whatInvitrogen Life Science. Microspheres vary widely in quality, sphericity, uniformity, particle size and particle size distribution. The appropriate microsphere needs to be chosen for each unique application. [1]

Microscopic, firm spherules which form on the cooling of hot saturated solutions of proteinoids. They were first reported in 1959 by Sidney Fox, K. Harada, and J. Kendrick who proposed that microspheres might represent a significant early stage in precellular evolution. It has been suggested that their greater stability makes them a better proposition in this regard than coacervates. One milligram of proteinoid can yield 100 million microspheres, ranging from 1.4 to about 2.5 microns in diameter. Microspheres have been observed to retain their form for several weeks and, when sectioned, may display a double-walled structure. Recently, Fox argued that microspheres also display characteristics of primitive nerve cells.

Polyethylene and polystyrene microspheres are two most common types of polymer microspheres. Polystyrene microspheres are typically used in biomedical applications due to their ability to facilitate procedures such as cell sorting and immunio precipitation. Proteins and ligands absorb onto polystyrene readily and permanently which makes polystyrene microspheres suitable for medical research and biological laboratory experiments. Polyethylene Microspheres are commonly used as permanent or temporary filler. Lower melting temperature enables polyethylene microspheres to create porous structures in ceramics and other materials. High sphericity of polyethylene microspheres, as well as availability of colored and fluorescent microspheres, makes them highly desirable for flow visualization and fluid flow analysis, microscopy techniques, health sciences, process troubleshooting and numerous research applications. Charged polyethylene microspheres are also used in electronic paper digital displays. [2-4]

TYPES OF MICROSPHERES [3-7]

Glass microspheres

They are primarily used as a filler and volumizer for weight reduction, retro-reflector for highway safety, additive for cosmetics and adhesives, with limited applications in medical technology

Opaque microspheres

Opaque microspheres (Fig. 2) are a superior opacifying agent and provide maximum hiding power with just a monolayer of microspheres as small as 40 micron in diameter. They can be manufactured in any color imaginable and even combinations of two differently colored hemispheres. Opaque microspheres provide an attractive and functional solution to cosmetics, personal care, and skin care industries.

Unique advantage of opaque microspheres in cosmetics is that maximum hiding power is achieved with one invisible and feather-light layer - revolutionizing make-up products. Sphericity and particle size uniformity are responsible for the ball-bearing effect in creams and lotions resulting in luxury feel and silky texture. Exceptional smoothness of spherical microparticles dramatically enhances the tactile experience of a cosmetic product. Opaque microparticles can be used to minimize the appearance of fine lines and wrinkles by both filling them and scattering light. They can be also used as gentle exfoliating agents. Red, green, blue, yellow or even multi-color microspheres make a product that is not only functional but fun and exciting by adding a hint of color, sparkle, or even a changing color effect.

Opaque microspheres are made from low molecular weight polyethylene. The polymer is pigmented to achieve the exact color and opacity level desired by the customer. The spheres are available in particle sizes from 10-1200 micron and are supplied as a dry powder that can be easily mixed into paints, adhesives, creams, lotions, and oils. Just like clear polyethylene microspheres, opaque grades are inert in most solvents and have a sharp melting point at 114C -120C depending on the molecular weight of the material used. High quality opaque polyethylene microspheres are now available in bulk quantities and reasonable prices to scientists and engineers who would like to add color and functionality to new generations of their products.

Ceramic microspheres

They are used primarily as grinding media

Fluorescent Microspheres

FluoSpheres and Trans Fluo Spheres polystyrene fluorescent microspheres (Fig. 3) can be used for a wide range of applications including blood flow determination, tracing, in vivo imaging and calibration of imaging and flow cytometry instruments. Because of dyes incorporated throughout the bead and not just on the surface, they are relatively immune to photobleaching and other environmental factors

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Blood Flow Determination & Tracing

Microspheres for blood flow determination are available in eleven distinguishable fluorescent colors and are compatible with blood flow analyzers (Fig. 4).

Calibration

These fluorescent microspheres provide flow cytometry users the means to calibrate laser alignment, compensation, flow rate, dynamic range and other daily adjustments. Bead dyes are spectrally matched to common lasers and are highly stable (Fig. 5).

Imaging Calibration

There are six different types of reference standards designed to facilitate adjustment and calibration of both conventional fluorescence microscopes and confocal laser-scanning microscopes (Fig. 6)

In vivo Imaging

Microspheres specifically designed for vascular imaging, graft migration, neuronal tracing, pulmonary ventilation, phagocytosis and time-resolved detection of rare targets in tissues (Fig. 7).

APPLICATIONS [4-8]

Some recent researches in applications for microspheres are:

Assay - Coated microspheres provide measuring tool in biology and drug research.

Buoyancy - Hollow microspheres are used to decrease material density in plastics (glass and polymer).

Ceramics - Used to create porous ceramics used for filters(microspheres melt out during firing, Polyethylene Microspheres).

Cosmetics - Opaque microspheres used to hide wrinkles and give color, Clear microspheres provide "smooth ball bearing" texture during application (Polyethylene Microspheres).

Drug Delivery - Miniature time release drug capsule (polymer).

Electronic paper - Dual Functional microspheres used in Gyricon electronic paper.

Personal Care - Added to Scrubs as an exfoliating agent (Polyethylene Microspheres).

Spacers - Used in LCD screens to provide a precision spacing between glass panel s (glass).

Standards - Monodispere microspheres are used to calibrate particle sieves, and particle counting apparatus.
Retroreflective - Added on top of paint used on roads and signs to increase night visibility of road stripes and signs (glass).
Thickening Agent - Added to paints and epoxies to modifyviscosity and buoyancy

BIOLOGICAL PROTOCELLS [5-8]

Microspheres or protein protocells as small spherical units postulated by some scientists as a key stage in the origin of life. In 1953, Stanley Miller and Harold Urey demonstrated that many simple biomolecules could be formed spontaneously from inorganic precursor compounds under laboratory conditions designed to mimic those found on Earth before the evolution of life. Of particular interest was the substantial yield of amino acids obtained, since amino acids are the building blocks for proteins.

In 1957, Sidney Fox demonstrated that dry mixtures of amino acids could be encouraged to polymerize upon exposure to moderate heat. When the resulting polypeptides, or proteinoids, were dissolved in hot water and the solution allowed to cool, they formed small spherical shells about 2 µm in diameter—microspheres Under appropriate conditions, microspheres will bud new spheres at their surfaces.

Although roughly cellular in appearance, microspheres in and of themselves are not alive. Although they do reproduce asexually by budding, they do not pass on any type of genetic material. However they may have been important in the development of life, providing a membrane-enclosed volume which is similar to that of a cell. Microspheres, like cells, can grow and contain a double membrane which undergoes diffusion of materials and osmosis. Sidney Fox postulated that as these microspheres became more complex, they would carry on more lifelike functions. They would become heterotrophs, organisms with the ability to absorb nutrients from the environment for energy and growth. As the amount of nutrients in the environment decreased, competition for those precious resources increased. Heterotrophs with more complex biochemical reactions would have an advantage in this competition.

CANCER RESEARCH [8]

Various useful discovery made from the research of microspheres is a way to fight cancer on a molecular level. According to Wake Oncologists, "SIR-Spheres microspheres are radioactive polymer spheres that emit beta radiation. Physicians insert a catheter through the groin into the hepatic artery and deliver millions of micropheres directly to the tumor site. The SIR-Spheres microspheres target the liver tumors and spare healthy liver tissue. Approximately 55 physicians in the United States use Sirtex's SIR-Spheres microspheres in more than 60 medical centers.

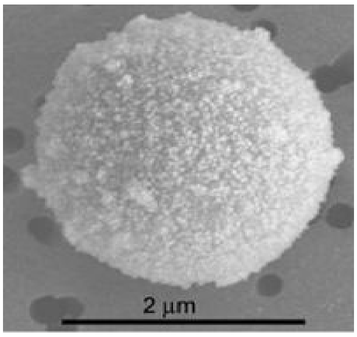

Fig.1

Fig. 2

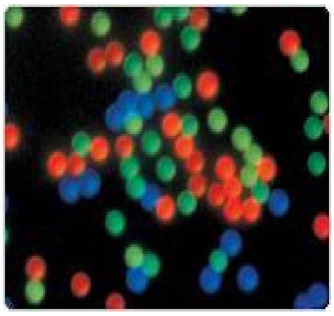

Fig. 3

Fig. 4

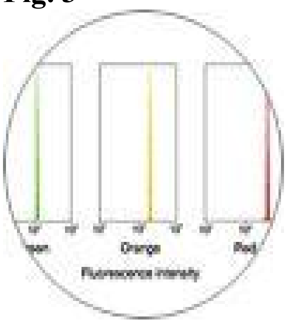

Fig. 5

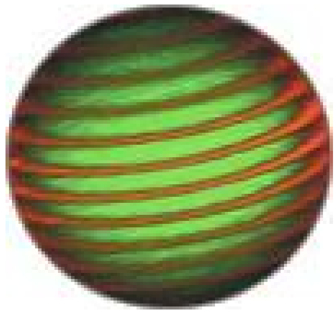

Fig. 6

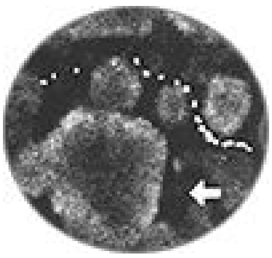

Fig. 7

Photographs showing different aspects of Microspheres

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