Microencapsulation and Controlled Release from Spherical Ceramic Particles Developed for Drug Delivery and Industrial Processes

The Pitch

An increasing range of applications, from the targeting of cancer tumors to protecting material surfaces against bacterial attack, require the production of delivery systems in particulate form. Although a range of organic materials are used to manufacture capsules and particles, only a limited number of inorganic controlled-release systems have been developed for industrial products. This is the case for ceramics, which despite a number of intrinsic advantages such as high mechanical strength, resistance to corrosion, thermal and electrical stability, bio-compatibility, and an environmentally benign nature have remained an untapped resource for the manufacture of controlled release systems. The relative difficulty in manipulating the internal microstructure of ceramics (as compared to polymers) using traditional routes as well as high processing temperatures, which are incompatible with the encapsulation of organic molecules, have limited their use as a controlled release matrix. The Australian company CeramiSphere has overcome both of these limitations by using sol-gel technology (i.e., the suspension of colloidal ceramic particles chemically converted to a gel) to create encapsulating ceramic microspheres.

The Technology

Sol-gel chemistry has revolutionized ceramic production by enabling the ambient temperature, solution-based synthesis of metal oxides with the ability to "tailor" porosity. By combining sol-gel with emulsion chemistry, it is possible to produce spherical particles with a designed microstructure resulting from a judicious choice of solvent/surfactant and sol-gel reaction parameters. By changing the solvent/surfactant combination, the particle size can be varied from 10 nm to 100 μm (see Figure 1). The size of the particles is controlled by the size of the emulsion droplet, which acts as a nanoreactor for the sol-gel reaction. When an active molecule is located in the aqueous droplet, encapsulation occurs as silicon precursors polymerize to build an oxide cage around the active species. Encapsulation efficiencies for hydrophilic molecules are typically >85%, with doping levels typically in the range 5–20 wt%. The release profiles can be tailored, independently of the particle size, by controlling the internal structure of the particles: pore volume, pore size, tortuosity, and surface chemistry. This can be readily achieved by controlling sol-gel processing parameters such as the water to alkoxide ratio, pH, alkoxide concentration, aging, drying time, and temperature. Hence, the release rate of the encapsulated species is controlled by adapting the structure of the internal pore network to the physicochemical properties of the active molecule.

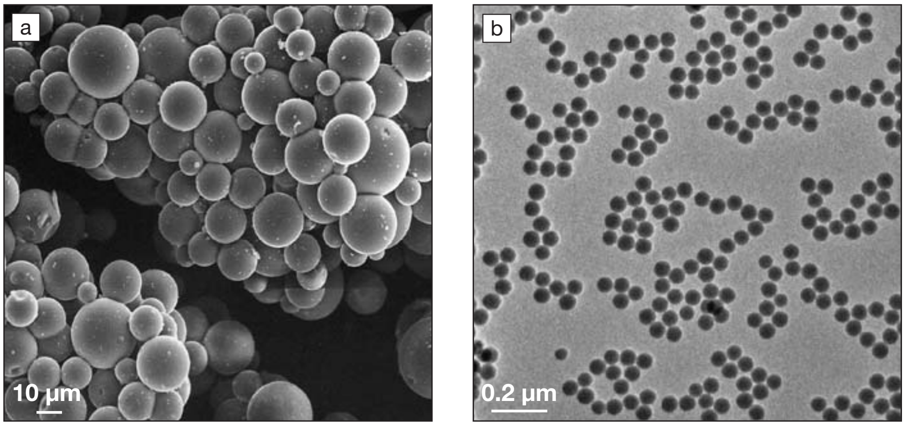

Figure 1. (a) Microparticles (scale bar: 10 μm) and (b) nanoparticles (scale bar: 200 nm) demonstrating the size ranges that can be obtained using CeramiSphere technology.

Although the CeramiSphere technology was originally developed for encapsulation and controlled release of small hydrophilic molecules, the technology has recently been expanded to the encapsulation of biomolecules and poorly soluble molecules and the production of nanoparticles with extended release capacity.

CeramiSphere has developed a procedure by which biomolecules are entrapped in silica microspheres formed from inorganic suspensions of aqueous silica colloids. The release mechanism is diffusion of the biomolecule through the matrix pores. The particles range from 0.5 μm to 10 μm in size with pore size optimized (2–7 nm) to provide an appropriate release rate for the biomolecule of interest (Figure 2). The process is designed to minimize denaturation of the biomolecules during encapsulation.

The encapsulation of active hydrophobic molecules is a key component of their use in various industries such as pharmaceuticals, cosmetics, and food. The encapsulation in silica offers good protection for sensitive molecules such as retinol against chemical attack, oxidation, or decomposition. In addition, the release rate of the molecules can be optimized for specific compounds.

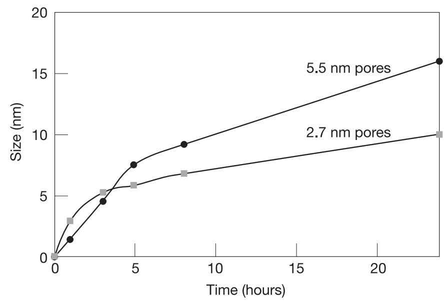

Figure 2. Release of ovalbumin (45 kDa), encapsulated in two different pore size (2.7 nm and 5.5 nm) silica particles into phosphate-buffered saline at 37°C.

The encapsulation of active pharmaceutical ingredients into nanoparticles enables new routes of administration and treatment. Using room-temperature sol-gel polymerization in reverse emulsions, active pharmaceuticals can be encapsulated inside silica nanoparticles. The particle size can be precisely tailored from 10 nm to 250 nm, and the release rate can be controlled from days to months. The particle surface can be functionalized to minimize protein interaction and enhance blood circulation for active targeting.

CeramiSphere has also developed a method for encapsulating different active molecules in separate layers of the silica nanoparticle while preserving the particle monodispersity. This enables the production of particles with delayed, sequential, or pulsed release capabilities. It also

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enables the encapsulation in the same particle of incompatible or reactive molecules. The ability to encapsulate various molecules in different layers in the particle also offers a range of novel potential applications such as optical storage, data encryption, and security ink.

In vitro experiments demonstrate that the encapsulating particles degrade relatively rapidly (from hours to weeks) in physiological media. In addition, they show good biocompatibility, only interfering with cellular processes at very high doses (20 mg/ml). This, combined with the regulatory approval by the U.S. Food and Drug Administration of ceramics such as silica in oral, topical, and mucosal applications, makes this technology an interesting candidate for drug delivery.

The microreactor approach should make it possible to scale-up the process to produce up to 10,000 ton/year cost effectively for the applications that have been investigated to date.

Opportunities

CeramiSphere is seeking to incorporate their technology into the products of commercial partners as well as potentially to manufacture and supply their own powders. The company is currently exploring, in collaboration with industrials partners, the potential for their technology to be applied for drug delivery, the protection of surfaces (release of biocides and anticorrosion), and the encapsulation and release of cosmeceuticals and nutraceuticals.

Source: Chris Barbé, CeramiSphere Pty Ltd., ANSTO, Bldg 58, PMB1, Menai NSW 2234 Australia; tel. +61-2-9717-3824, fax +61-2-9717-9106, and web http://www.ceramisphere.com.

Electrodeposition of Large-Area Thin Films Provides Inexpensive Single-Crystal Substrates

The Pitch

Single-crystal substrates in the form of free-standing thin films can be produced cost effectively using a method developed by researchers at Brown University. Analogous to a printing press, the process transfers the crystalline structure of an original template material to a final layer and leaves the template available to create more material. Inexpensive electrodeposition methods produce the single-crystal films in long ribbons or sheets that can serve as substrates for other technologies such as photovoltaics or high-temperature superconductors (HTS). Compared with conventional methods, this method is inexpensive; can produce large-area formats; consumes less starting material; and requires no cutting, polishing, or other post-depositional processing of the material.

The availability of relatively inexpensive single-crystal substrates could impact a number of emerging technologies. HTS, for example, depend strongly on the crystallographic alignment of the superconducting layers. The projected $5 billion market for HTS products is driven by the need for higher energy efficiency and performance (e.g., transmission cables, generators, motors, fault circuit limiters, and magnets). Single-crystal substrates have the potential to induce improved crystallinity and higher performance than the high-textured polycrystalline substrates now used. Similarly, many photovoltaic-device materials also have improved performance as single crystals. Other potential applications include device structures that can benefit from single-crystal properties such as no grain boundaries and long-range order (e.g., catalytic processes such as in fuel cells or catalytic converters, low-stress substrates for microelectromechanical systems, or magnetic storage media).

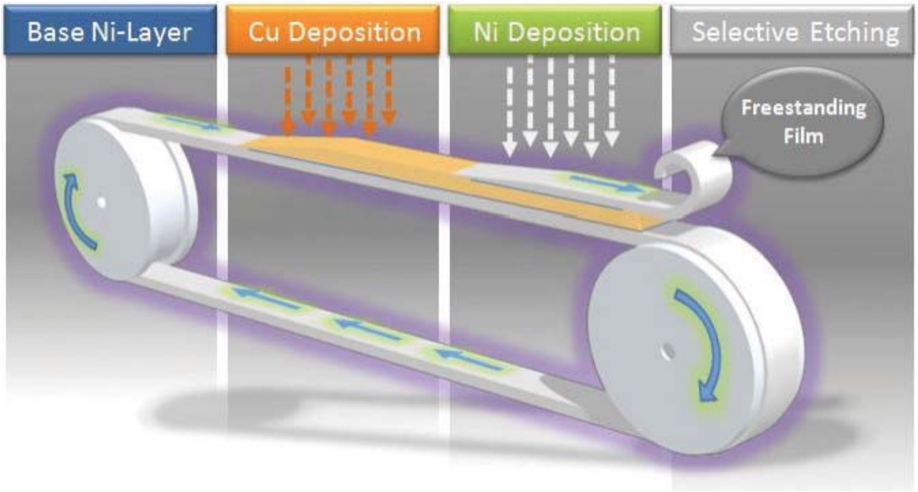

Figure 1. Schematic of process developed at Brown University to form large-area single-crystal substrates using electrochemical deposition and etching.

The Technology

The Brown University method is based on a combination of electrochemical deposition and etching steps for the production of nickel substrates (shown schematically in Figure 1). The starting material is a loop made of single-crystal nickel. In the first stage, a thin copper layer is electrodeposited epitaxially onto the base nickel layer (both have the same crystalline orientation), so that it also forms a single crystal. In the next stage, a thicker single-crystal nickel layer is electrodeposited onto the copper layer. In the final stage, the nickel layer is separated from the base by selectively etching the copper layer electrochemically without damaging the nickel layers. The resulting continuous ribbon of free-standing nickel foil can be used as a single-crystal substrate for subsequent deposition of other materials such as superconductors.

The as-produced substrate is smooth (rms roughness <3 nm) with an in-plane misorientation as good as that measured on the starting crystalline substrate (0.1°). Although process development has focused on producing nickel and nickel-tungsten alloy films, the process can be adapted to produce single crystals of other metals such as gold, iron, or platinum. Individual samples are being routinely produced, and a prototype machine for producing continuous ribbons is currently being built at Brown University.

Opportunities

The researchers at Brown University are seeking investments or partners for further development, licensees, and contracts for their single-crystal substrate technology.

Sources: For technical information: Eric Chason, Brown University Box D, Providence, RI 02912, USA; tel. 401-863-2317 and e-mail Eric_Chason_PhD@Brown.edu. For business development, investment, or licensing: Adam Standley, tel. 207-299-2192 and e-mail Adam_Standley@Brown.edu.

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Phase-Separated, Low-Cost, Superhydrophobic Glass Powder Developed

The Pitch

A super-water-repellent (superhydrophobic) glass powder coating material that causes water or water-based solutions to bounce off virtually any coated surface has been developed at Oak Ridge National Laboratory (ORNL). The basic concept of this new coating material is nanoscale surface texturing. The coating pins air on its surface, thus preventing water from adhering to that surface. By pinning a layer of air on the surface, these coatings change the normal water-to-solid interface to a water-to-air-to-solid interface. This technology has the potential to markedly improve the performance of existing products and create new products that interact with water. A few of the possible product candidates include watercraft, drain pipes, rain gear, any metal subject to corrosion, and any electronic circuitry subject to water damage.

To make a high-quality superhydrophobic surface, the surface must either be coated with nanoparticles or be textured on a nanoscale. Existing high-quality superhydrophobic materials are generally relegated to university research laboratories because they are difficult and expensive to produce, not scalable to large volumes, and not amenable to being made into commercially viable coatings. ORNL's new nanoscale-textured superhydrophobic coating materials cost less to fabricate than previous alternatives. They have high levels of superhydrophobic performance and are readily scalable to industrial production.

The Technology

ORNL's patent-pending process for making superhydrophobic glass powder is based on the differential etching of two glass phases from phase-separated glass. Starting with borosilicate phase-separating glass as the base material, the glass is phase separated by heat treating, then crushed into a powder. Next, it is differentially etched to completely remove the interconnected borate glass phase and partially remove the interconnected silica glass phase. Differential etching makes the powder very porous and also creates nanoscale enhanced features (shown in Figure 1). Lastly, the etched powder is treated with a hydrophobic solution to change the glass surface chemistry from hydrophilic to hydrophobic. The porosity and nanoscale-enhanced features of the powder amplify the effect of the surface tension and cause the powder to become unwettable (i.e., superhydrophobic). The inset in Figure 1 shows a water drop on a piece of fabric coated with superhydrophobic powder.

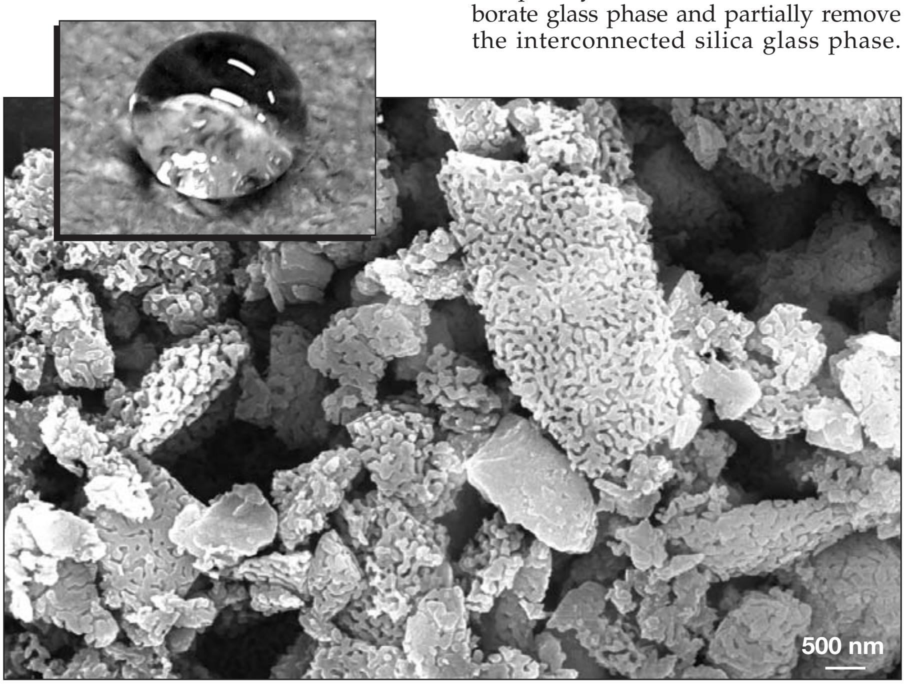

Figure 1. Scanning electron micrograph of nanotextured glass powder grains. The inset shows a water drop on a piece of fabric.

The advantages of ORNL's superhydrophobic powder include ease of manufacturing, low cost, and scalability. The preservation of the spinodal (coral-like) nanoscale features as the powder grain size is reduced enables the fabrication of very small superhydrophobic powder grains (<300-nm-diameter grains). This implies that a small volume of low-cost superhydrophobic powder could potentially coat a relatively large surface area. Another important feature of this powder is its thermal insulation properties. Because the powder grains are superhydrophobic, water does not enter the grain pores, resulting in a dry, breathable coating with trapped insulating air throughout. Because the powder consists almost entirely of porous amorphous silica, it can also serve as a very good electrical insulator, particularly as it also repels water and water-based solutions effectively. Finally, water-based corrosion of the substrate is greatly reduced, if not entirely eliminated, because of the air layer between the coated substrate and any water on its surface.

Opportunities

The researchers and ORNL are seeking development partners and licensees for their superhydrophobic material technologies.

Sources: For technical information: John T. Simpson, Oak Ridge National Laboratory, Oak Ridge, TN 37831-6054, USA; tel. 865-574-5565 and e-mail simpsonjt@ornl.gov. For licensing: Mark Reeves, ORNL Technology Transfer Department, Oak Ridge National Laboratory, Oak Ridge, TN 37831, USA; tel. 865-576-2577 and e-mail reevesme@ornl.gov.

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