

DRUG DELIVERY

Nanostructured Silicon Wires Up Controlled Delivery

Purposely introducing silicon wires into a pharmaceutical tablet or powdered suspension is not typically a formulator's objective. After all, silicon is the primary material in computer processor chips and wafers. Researchers at pSivida Ltd. (Perth WA, Australia), however, have patented a nanostructuring technology that modifies the structure of silicon such that the material is biodegradable and dissolves well in the body, which can make it an ideal alternative to other biomaterials such as polymers.

The nanostructuring procedure, discovered by physicist Leigh Canham (pSimedica, a company subsidiary), produces BioSilicon—a biocompatible, honeycomb-shaped material. Microparticle powders (typically 30 μm in size) and even three-dimensional implants (1-cm in size) are internally modified to enclose this porous structure. Just 5–10 atoms across, the silicon nanowires make up the honeycomb's walls, which surround the drug-filled cells (typically 50–100 nm wide).

Although the BioSilicon structure can be used with various drugs, the company is initially focusing on cancer therapies, treatments for central nervous system diseases, peptides, and small proteins. "We like to use hydrophobic drugs because they are not absorbed very well by the body," says Aston. Putting these drugs into the nanostructure, he explains, increases the solubility "quite substantially."

The key to controlling the delivery is the method by which the nanowires are etched. The company uses a well-established hydrofluoric acid-driven process to dissolve (or etch) the silicon and control its biodissolution, thereby control-

ling the rate of drug release (see Figure 1). Roger Aston, pSivida's commercial strategy director, says the company doesn't physically handle the wires, but rather takes large pieces of silicon and etches the silicon walls to a particular

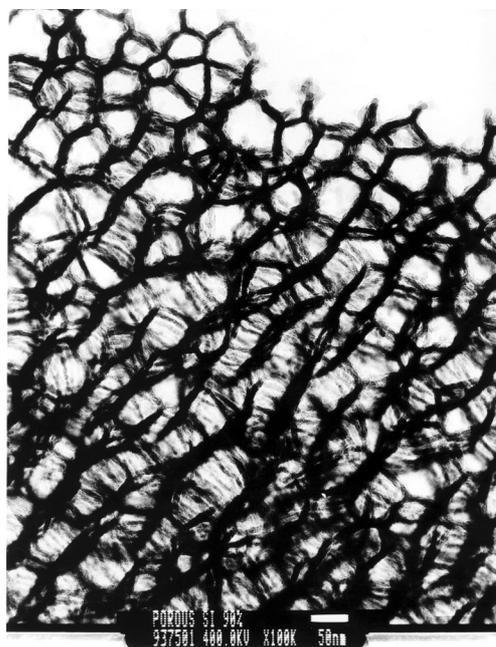


Figure 1: Transmission electron microscope photo of nanostructured silicon. Black regions are the nanowires, measuring approximately 5 to 10 atoms across, and the white regions are the cells into which the drug would be loaded (measuring 50 to 100 nm across).

width and the cells (honeycomb cavities) to a particular size. Etching fine nanowires and big holes leads to rapid dissolution, while etching big nanowires with small holes leads to longer dissolution rates (see Figure 2). Thus, the release rate can be "tuned" during manufacturing so that the mesh releases its contents over periods ranging from two

to three days up to three months, according to zero-order release kinetics.

Aston points to several advantages of using biodegradable silicon over other biomaterials such as polymers. A major difference is that developing a polymer matrix typically involves chemical reactions among the various monomers and also between the monomers and the drug. When polymer matrices dissolve, some amount of free drug is released. What may also be released, however, is drug linked with the monomers and

even drug linked with the polymer, which, depending on the polymer being used, may result in some toxicological effects.

In contrast, using biodegradable silicon does not involve reactions between the carrier structure and the drug. The drug is not changed or chemically modified in the process. According to Aston, when the BioSilicon material dissolves in the body, it produces SiOH_4 , which is the nutritional form of silicon and a dietary requirement for normal bone or collagen growth. This substance is quickly excreted through the kidneys.

With such promising characteristics in their new material, pSivida researchers are hoping that BioSilicon will enable new therapeutic applications where other biomaterials cannot. Earlier this year, the company began Phase IIa clinical trials of its "BrachySil" microparticles for the treatment of inoperable tumors of the liver (primary liver cancer). The project takes advantage of another key characteristic of silicon: it is "radioactively hard."

That is, silicon can survive an irradiation process, whereas polymers cannot.

For the BrachySil project, the silicon is doped with phosphorus-31. When exposed to a high neutron flux, phosphorus-31 becomes the radioactive phosphorus-32 while the silicon remains intact. Using a fine needle and an ultra-

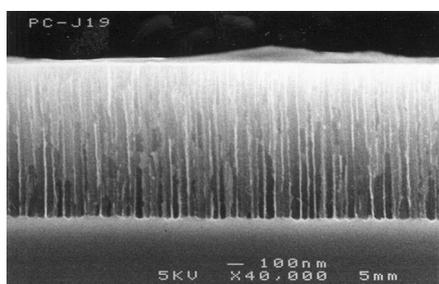


Figure 2: Cross section of nanowires.

sonic image, the drug is nonsurgically injected through the abdomen directly into each tumor. The phosphorus-32 powdered silicon suspension is held localized to the tumor. Phosphorus-32 emits beta particles that kill the cancer cells and regress the tumor. Without the silicon, the drug cannot be injected directly into the tumor because, as a soluble drug, it would rapidly come out of the tumor and be absorbed into the body's circulation, likely causing toxicity problems in the lung or brain. The company hopes to report the first results of the trial by the end of this month, with projected market launch by 2007.

Last month, pSiMedia was awarded a European patent relating to the application of BioSilicon in orally administered drugs and even chip-based "smart drugs" that would offer processor-based targeted delivery. The company is also looking into using BioSilicon for orthopedic devices (e.g., biodegradable screws, pins, braces, rings). Says Aston, "As a company, we are looking for specialist applications that nanostructured silicon can offer over and above other biomaterials."

-Maribel Rios