Using nanotechnology to improve drug therapy — what is all the fuss about?

Nanoscale science is currently the hot topic in science and medical journals alike. Recent issues of Nature *have featured reports on nanoparticles and nanoelectronics and an editorial in* The Lancet *heralds nanomedicine as a discipline "whose time has come". Harriet Adcock finds out what all the fuss is about*

THE latest buzzword in the scientific community is nanotechnology. A report by the Economic and Social Research Council entitled "The social and economic challenges of nanotechnology" was published last month and draws attention to the increasing controversy over the possible effects of this emerging technology.

Some of its more extreme critics fear this scientific discipline will wreak havoc on the world, turning the surface of the earth into a gooey grey mess. But its most fervent supporters predict it will change the world for the better — making the development of innovative products possible and the production of goods cheaper.

WHAT IS NANOTECHNOLOGY?

Ottilia Saxl, chief executive officer of the Institute of Nanotechnology, based at the University of Stirling Innovation Park, says nanotechnology can be considered an extension of miniaturisation. Essentially, it is the creation of materials, devices and systems at the nanometer scale (see Panel).

"Nanotechnology is offering us the ability to design materials with totally new characteristics. In other words, nanotechnology will fundamentally change the things we make and the way we make them," she says.

But pharmaceutical scientists have been creating small particles for many years. Indeed, Professor Graham Buckton, in his Science Chairman's address at this week's British Pharmaceutical Conference, refers to nanotechnology as "a trendy term for the microparticles that many have been making for years" (see p377). So what has changed? Dr Saxl points out that the development of advanced analytical techniques means that scientists can now see what they are doing and this is allowing matter to be manipulated in precise ways.

CHANGING DRUG CHARACTERISTICS

In terms of application to medicine, nanotechnology looks set to have considerable impact. One company using nanotechnology to manipulate drug particle characteristics is Elan. The company's nanocrystal milling process has allowed drugs like Wyeth's sirolimus (Rapamune) to be developed from an oral solution formulation (requiring relatively complicated administration) to a tablet formulation.

Dr Joseph Fix is executive vice-president of NanoSystems, the drug delivery business unit of Elan. "By making smaller particles we improved the disssolution rate [of sirolimus] enough that we could formulate it as a tablet. The driving force was dosing convenience for patients," he says.

Commercially, this milling technology can only really be applied to poorly soluble drugs but Dr Fix estimates that somewhere between 40 and 50 per cent of all new chemical entities coming out of discovery fit into this category. Furthermore, up to 10 per cent of drugs that are already marketed have some performance issues related to solubility.

Nanotechnology is also permitting drugs such as peptides, conventionally administered by injection to avoid metabolism in the gut, to be delivered in ways that may be more acceptable to patients.

Xstal Bio, a company affiliated to Strathclyde and Glasgow universities, develops protein-coated crystals. Marie Claire Parker, chief executive of Xstal Bio, explains: "Most conventional technologies start with big particles and break them down. Our technology creates the small particle so there isn't any further processing required."

The company is developing an inhaleable formulation of insulin. "Patients simply take a puff of a dry powder formulation of insulin or another protein."

For this route to be effective — and this is where the technology comes in — the particles on which the drug is delivered have to be small enough to avoid clogging up the lungs but large enough to avoid being exhaled. So far, Xstal Bio has taken its inhaleable insulin through the proof of concept stage, but it has yet to be tested in humans.

Nanotechnology is also being applied to earlier, simpler disease detection, improved imaging, and rapid assessment of potential drug candidates, according to Dr Saxl.

The authors of the ESRC report, Professor Stephen Wood and colleagues from the ESRC Centre for Organisation and Innovation, Sheffield, are optimistic about the potential of nanotechnology.

They highlight several medical applications arising from nanoscale science, such as the creation of artificial organs and implants, laboratory-on-a-chip technology for quicker diagnosis and personal health monitors, and advanced drug delivery. "The ultimate combination of the laboratory-on-a-chip and advanced drug delivery technologies would be a device that was implantable in the body, which would continuously monitor the level of various biochemicals in the bloodstream and in response would release appropriate drugs," they say.

GENE THERAPY

Another possible application for nanotechnology is in the delivery of gene therapy. Current vectors — modified viruses — are associated with immune reactions so research is focused on building nanostructures that can carry genes to the required delivery site.

Other delivery and targeting techniques are being investigated to maximise drug action and minimise side effects. In a report published by the Institute of Nanotechnology (www.nano.org.uk), Dr Saxl explains that light-activated coatings can be applied to particulate drugs used to treat bone conditions. "The drugs remain insoluble due to the coating, becoming preferentially concentrated at the joints. The coatings are dissolved by exposure to light, allowing the drugs to be released exactly where needed," she says. Studies are also focusing on using magnetic particles to guide and position drugs at target sites. Coating nano-sized drug particles with polymers such as polyethylene glycol is another technique used to direct drugs to target tissues. This changes the surface characteristics of the drug particles, allowing them to avoid uptake in the liver. "This avenue of research will shortly result in therapeutic procedures," says Dr Saxl.

Nanotechnology may be a trendy term for an established scientific disipline but that should not detract from its potential.

Nanotechnology

Nanotechnology makes use of particles at the nano-length scale — a nanometer is one billionth of a metre. The technology can be approached in one of two ways — from the bottom up or the top down. The top-down approach refers to the construction of nanoscale structures using machining and etching techniques. The bottom-up approach (often referred to as molecular nanotechnology) refers to the creation of structures "atom-by-atom" or "molecule-by-molecule".