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Solving insoluble drug delivery

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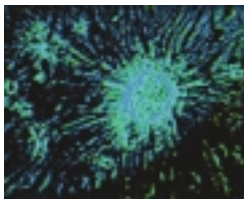

An innovative way of getting macromolecular drugs past the body's natural defences offers a new and promising way of delivering poorly soluble drugs directly to the sites they are required, say pharmaceutical scientists.

Getting through the barriers

With its hostile epithelial barrier and efficient immune system, the human body is well adapted to destroy or clear foreign objects that it encounters, even when those objects are life-saving drugs. Packaging drugs in structures such as liposomes has proved successful for getting water-soluble pharmaceuticals past the immune system. But such structures are not designed to transport poorly soluble drugs – a characteristic of many anti-cancer agents. The delivery of such pharmaceuticals 'continues to represent a challenge', says Vladimir Torchilin, Professor of Pharmaceutical Sciences at Northeastern University, Boston (http://www.neu.edu).

However, Torchilin continues, micelles, which in water assemble with a hydrophobic core, are able to carry sparingly soluble anti-cancer drugs, such as taxol, into the heart of a tumour before the body can recognize and clear it (see review [1]).

Once loaded with a cancer-killing drug, Torchilin says that tumour-specific antibodies can be attached to take the micelles straight to the target tissue. 'Drug-loaded cancer-specific micelles recognize a variety of cancer cells *in vitro* and provoke an increased killing of cancer cells *in vitro* and *in vivo*,' he told BioMedNet News (http://www.bmn.com).

PEGylation

This method has certain advantages over established ways of masking macromolecular drugs, such as pegylation, where the active macromolecule is coated in polyethylene glycol (PEG), thereby masking it from the immune system (see review [2]).

'With the PEG, you have to have a covalent linkage between the protein and the polyethylene glycol,' said Ijeoma Uchegbu, Professor of Pharmaceutical Sciences at the University of Strathclyde, Scotland (http://www.strath.ac.uk). 'Some people don't want to alter their drugs in this way because you could alter the activity and you could be putting the PEG on the active site,' she said.

Liposomes get around this problem, she says, but because of their aqueous inner compartment, they are better suited for transporting aqueous drugs. Although they can carry poorly soluble drugs like taxol, they can only hold them in the membrane and not in the spacious core, she says, which limits the amount of drug that can be transported.

The micelles could be the solution, says Torchilin. 'Our findings may lead to the development of a new, more efficient, and safer delivery system for taxol and other poorly soluble anticancer drugs,' he and his colleagues note in the abstract to a paper they will present at the *30th Annual Meeting of the Controlled Release Society* next month in Glasgow, Scotland (http://www.controlledrelease.org/).

Promise for drug delivery

Uchegbu agrees that this delivery system 'seems to improve cell kill over that seen with the plain drug.' However, she is not convinced that Torchilin's structures should really be called micelles. 'I would love to know how they were classified as such,' she said, 'as it is possible that they could be liposomes or even just plain small solid nanoparticles.' Nevertheless, whatever they actually are, Uchegbu says that Torchilin's packaging structures look like they have promise for the delivery of drugs with limited solubility like taxol and etoposide.

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