news

Beyond PEGylation

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Polymers are playing an increasingly important role in drug formulation and delivery, but the pharma industry has so far done little more than dip its toe into polymer technology. The average shampoo contains more sophisticated polymers than those found in pharmaceutical products. But some specialist polymer producers are now turning their attention to pharma as a potential new market for their expertise.

PEGylating to protect

The rising number of drugs based on large biological molecules like proteins and peptides has stimulated pharma's interest in polymers, which are one way of solving these macromolecules' inherent delivery and pharmacokinetic problems. Many are denatured in the stomach if taken orally, and when injected their half-life in the body is often very short. Anchoring them to a large polymer molecule protects them from attack by enzymes, slows their clearance by the kidney, and can also provide controlled release properties. To do this, drug formulators rely on PEGylation – attaching strands of polyethylene glycol to the drug molecule.

To date, PEG is the only polymer used in this way. To some polymer chemists, this seems odd. 'It seems that pharma has found something that worked, and stuck with it,' says David Haddleton, Professor of Chemistry at Warwick University (www.warwick.ac.uk) and founder of Warwick Effect Polymers (WEP; www.wep-ltd.co.uk), which supplies specialized polymers to various industries including pharma and biotech . You can understand that because it's FDA-approved, and it's been very successful. But as a polymer chemist I thought "you're only using one water-soluble polymer, and I've got 500. Surely one of those is going to work better." PEG is just the simplest nonionic surfactant. The cleaning and personal care industries probably don't even use it anymore, because it's the least sophisticated of maybe 200 others they can choose from.'

Living radical polymerization

WEP is targeting the pharmaceutical industry with its living radical polymerization (LRP) technology [1,2]. This allows the hundreds of commercially available individual monomers to be put together in a precisely controlled way to achieve the desired functionality. 'If natural monomers are put together in the right way they can make anything from hair to insulin,' Haddleton says. LRP uses addition polymerization and can therefore achieve higher molecular weights than the conventional ring-opening or condensation polymerization. It also eliminates variation in functionality among individual polymer chains. Polymers can be designed as drug conjugates, or can have small-molecule drugs incorporated into them along with functional groups that bind with target sites.

'Materials made by LRP have tunable structures, properties and functions,' says Karen Wooley, Professor in the Department of Chemistry at Washington University in Saint Louis, and Editor of the *Journal of Polymer Science*. 'They have significant promise in many applications, including pharmaceutical delivery or as pharmaceuticals themselves. Particularly interesting are materials that combine biological activity, imparted by selective chain-end functionality, with biocompatible, stealth-like behaviour imparted by side chain PEG units, and compartmentalization, offered by the programmed assembly of amphiphilic block copolymers'.

Would using these sophisticated polymers push up the cost of drug manufacture? Haddleton says not, pointing to the high price of existing PEGylation agents. But any new polymers will have to offer significant benefits to justify the cost of obtaining regulatory clearance.

References

1 Lecolley, F. *et al.* (2004) A new approach to bioconjugates for proteins and peptides ('pegylation') utilising living radical polymerisation. *Chem. Commun.* 18, 2026–2027
2 Tao, L. *et al.* (2004) α-aldehyde terminally functional methacrylic polymers from living radical polymerization: application in protein conjugation pegylation. *J. Am. Chem. Soc.* 126, 13220–1322

