

A review of the science presentations

Joe Chamberlain, science secretary for the British Pharmaceutical Conference from 1990 to 1999 and a former editor of *The Journal of Pharmacy and Pharmacology*, highlights a selection of the work that will be reported in the science sessions at BPC 2004 next week

The theme of this year's British Pharmaceutical Conference is "Medicines: from cell to society" and the range of subject matter in the short science papers presented will underline the role of pharmaceutical scientists in this process.

More than 200 short papers will be presented this year. Apart from sessions for short papers in pharmaceutical analysis and pharmacognosy, jointly organised by the Joint Pharmaceutical Analysis Group, all submitted papers will be presented as posters. However, selected posters will also be presented in special discussion sessions.

The following review groups highlighted papers according to similar research topics. The full abstracts can be downloaded from the BPC section of the Royal Pharmaceutical Society's website (www.rpsgb.org/events).

Pharmaceutics: materials

Li et al (Welsh School of Pharmacy, Aston University and Royal Gwent Hospital, Newport) describe spray-drying as an effective and convenient method of producing appropriately sized respirable particles. Using salbutamol sulphate as a model drug they show that trehalose-based spray-dried powders offer an improvement over lactose-based powders, and that the inclusion of leucine into the formulation before spray-drying can enhance the respirable fraction of the spray-dried powder.

Sharma-Singh and Kirk (AstraZeneca) report on the progress made in assessing the feasibility of applying *in situ* fibre optics to assess the intrinsic dissolution rate of active pharmaceutical ingredients. Their results indicate similar results to off-line high performance liquid chromatography analysis and suggest fibre optics could be routinely applied, enabling considerable time and cost savings.

Drugs formulated in hyaluronan, a naturally occurring polyanionic glycosaminoglycan, and applied topically are retained in the skin with little systemic absorption. **He et al** (King's College London) investigate this mechanism of action of hyaluronan by studying the effect of different molecular weight hyaluronans on diclofenac and ibuprofen. Their work suggests that hyaluronan might affect drug release from the vehicle due to the altered solubility or diffusivity of active drug in the hyaluronan vehicles. Drug design based on receptor targeting tends to recommend lipophilic compounds, in which dissolution characteristics are compromised. This situation has driven the development of strategies to maximise bioavailability by influencing the dissolution process of such compounds.

Rawlinson et al (University of Bradford and Bristol Myers-Squibb) report on studies investigating the formation of an amorphous



Concerns over BSE and vCJD have led **Burke et al** to investigate whether gelatin derived from fish can replace mammalian gelatin in pharmaceutical applications

species of ibuprofen upon combination with cross-linked poly-vinyl-pyrrolidone using simple mixing to facilitate intimate contact. The stabilisation of the amorphous drug species, caused by the partial disordering of ibuprofen, should improve its dissolution characteristics.

Recent concerns over the spread of bovine spongiform encephalopathy and variant Creutzfeldt-Jakob disease, along with a trend to vegetarianism, have led to a search for alternatives to mammalian gelatin for pharmaceutical use. **Burke et al** (Liverpool John Moores University) evaluate the thermal and mechanical properties of a range of softgel ribbons, based on bovine, porcine and fish gelatin. Bovine and porcine gelatin behaved similarly but fish gelatin yielded a more elastic ribbon. These differences may relate to differences in

the structure and composition of the gelatin, and suggest fish gelatin may be a useful replacement for mammalian gelatin in the manufacture of pharmaceutical softgel capsules.

Pharmaceutics: liposomes and niosomes

The solubility and partitioning behaviour of a drug molecule governs its location in the liposome structure; highly hydrophilic drugs ($\log P < 1.7$) are located exclusively in the aqueous compartment of the liposomes while lipophilic drugs ($\log P > 5$) are entrapped in the lipid bilayer. **Mohammed et al** (Aston University and Pfizer UK) enhance the solubility of problematic drugs ($\log P$ between 2 and 4) by exploiting the physicochemical properties of liposomal systems. Incorporation studies demonstrated drug loading could be enhanced by increasing the liposomal hydrophobic volume although the extent of this enhanced drug loading was strongly dictated by the $\log P$ of the drug. Thus both the physicochemical properties of the drug molecules and the lipid bilayer composition must be considered collectively when designing liposome-based solubilisation systems.

Vangala and Perrie (Aston University) evaluate the physicochemical characteristics of DNA-loaded dehydration-rehydration vesicle niosomes in the presence of sucrose and trehalose as cryoprotectants. The disaccharides could efficiently be employed without significantly influencing encapsulation efficiency; a pronounced effect was observed on vesicle size yielding submicron sizes, which could further be lowered by increasing surfactant hydrophobicity and thereby reducing the overall surface free energy.

Pharmaceutics: particles

Whitaker et al (Critical Pharmaceuticals Ltd and University of Nottingham) address the outstanding problems of formulating proteins in a microparticle system, particularly the problem of heat denaturation of the protein during polymer mobilisation. Supercritical carbon dioxide was used as a processing medium for the fabrication of poly(DL-lactic acid) microparticles that encapsulate a protein material where the processing can be performed at 35°C and in the complete absence of conventional organic solvents.

As part of an investigation into understanding the nature of the interaction between stabilising polymers and drug nanoparticles, **Goodwin et al** (King's College London and GlaxoSmithKline) studied the effect of polymer molecular weight on size reduction. More than four hours of wet-milling was required to obtain nabumetone particles in the submicron size range using undegraded hydroxypropylcellulose. However, nanoparticles were formed

after less than two hours using hydroxypropylcellulose which had been exposed to ultrasonic degradation. This more rapid reduction in drug particle size could be explained by a greater milling efficiency due to a lower viscosity or by lower molecular weight polymers having a faster ability to diffuse to the newly generated drug particle surfaces.

Biopharmaceutics: microbiological issues

Keegan et al (University of Brighton, University of Portsmouth and GlaxoSmithKline Research & Development) aim to develop zinc/polycarboxylate complexes that are retained within the oral cavity to provide sustained antimicrobial protection against oral pathogens. An association forms between the polycarboxylate and zinc ions, and the presence of sodium and calcium ions in saliva will allow displacement of the zinc. Thus these complexes have the potential to form a bio-responsive antimicrobial delivery system that will preferentially release the antimicrobial agent in lower pH environments, such as those generated in the oral cavity by cariogenic microorganisms.

The difficulty in eradicating established microbial biofilm using parenteral antibiotics has led to the assessment of nebulised gentamicin as a preventive strategy for ventilator-associated pneumonia. In an effort to enhance the attachment of gentamicin to the surface of the endotracheal tube, **McCroly et al** (Queen's University of Belfast) describe a macroporous hydrogel system loaded with gentamicin to coat the tube to reduce bacterial colonisation. A greater gentamicin loading was obtained with drug incorporated before polymerisation as opposed to soaking the hydrogels in a buffered gentamicin solution after polymerisation.

Similarly, **McBride et al** (Queen's University of Belfast) have studied the adherence and persistence of activity of antimicrobial-incorporated teraocylododecoxysilane silicones. The antimicrobial-incorporated elastomers showed significantly lower adherence and a significantly longer persistence of activity, compared with the control silicone. The incorporation of the antimicrobials did not significantly affect the tensile strength or the contact angle of the silicone. The coefficient of friction of the novel material was significantly lower than the control silicone, due to the production and release of the oily alcohol, octyldodecanol. There are potential benefits of the antimicrobial-incorporated teraocylododecoxysilane silicones over existing silicones through the production of this renewable lubricious surface.

Biopharmaceutics: drug metabolism

Siddique et al (University of Strathclyde, University of Glasgow and AstraZeneca) describe the use of amphiphilic conjugates of doxorubicin in a programme to alleviate the side effects of such drugs, by modifying drug pharmacokinetics and biodistribution. The conjugates initially accumulate in the cell membrane and within small spherical com-

partments within the cell indicating endocytosis, potentially bypassing the P-glycoprotein pump. The conjugates were similar in cytotoxicity and showed an increase in dose tolerance in comparison with doxorubicin.

Carlsson et al (AstraZeneca R&D and Uppsala University, Sweden) verify enzyme-mediated degradation in intestinal fluid of a model drug and compare the degradation in human intestinal fluid and dog intestinal fluid. The parent drug, an ester, and the expected degradation product, the corresponding acid, are determined by HPLC. Enzyme-mediated degradation in the intestine can be determined by *in vitro* testing in real intestinal fluids, and should thus be a useful tool in early drug development. The dog seems to be a reasonably good model for man, although the degradation capacity seems to be somewhat higher possibly due to a higher enzyme concentration.

Drug delivery: adhesion

Mortazavi (Shaheed Beheshti University of Medical Sciences, Iran) investigates the influence of wet granulation on the mucoadhesive properties of tablets prepared from cellulose derivatives. Tablets prepared by completely granulating cellulose mixtures had lower mucoadhesive strengths than their corresponding formulations which were partially granulated. However, the duration of mucoadhesion of tablets was found to improve by granulation. Increasing the concentration of extra-granular sodium carboxymethylcellulose helped to increase the mucoadhesive strength of the resulting tablets, although the duration of mucoadhesion of the test tablet was reduced. In contrast, increasing the amount of hydroxypropylmethylcellulose in the tablet, and in particular within the granules, resulted in an increased duration of mucoadhesion, despite lowering the mucoadhesive strength of the formulation.

Russell et al (Aston University) extend their previous work on the adhesion of polyacrylic acids to the oesophagus by studying the potential of the polyacrylic acid Noveon AA1 for efficient delivery of isosorbide dinitrate and nifedipine as model drugs. They compare the *in vitro* oesophageal retention of Noveon AA1 and simple emulsions and measure the rate of drug release from these formulations. Drug release for isosorbide dinitrate is significantly greater than that for nifedipine from all formulations. For both drugs, drug release from Noveon AA1 is related to viscosity, with significantly improved release from the lower viscosity pH 4.7 solution. At high concentrations, isosorbide dinitrate is released more rapidly from light mineral oil emulsion compared with heavy mineral oil emulsion, yet the reverse is true for nifedipine. Both Noveon AA1 and the emulsions tested demonstrate potential for bioadhesion to the oesophagus *in vitro*. Drugs are successfully released within a short time and the systems have potential for oesophageal delivery.

Suresh et al (Al-Ameen College of Pharmacy, Bangalore, India, and University of East Anglia) investigate the use of alginate mi-

cro-particles as a sustained delivery system for oesophageal delivery. The retention of alginate microparticles on the oesophageal tissue is significantly higher than that of an equivalent alginate solution. For both formulations, the greatest loss is observed in the first 20 minutes, although the solution continues to show greater loss thereafter. It may be possible to develop an alginate microparticulate formulation that is retained on the surface of the oesophagus for prolonged periods, thus enabling the incorporated or attached drug to be adsorbed onto or absorbed into the oesophageal tissue.

Drug delivery: oral delivery

The mechanism by which oil-free polyethylenimine formulations promote the oral absorption of the hydrophobic immune suppressant ciclosporin is currently unknown.

Cheng and Uchegbu (University of Strathclyde) set out to examine whether the inhibition of the intestinal P-glycoprotein efflux pump or the opening of paracellular transport pathways is involved in the absorption enhancement observed with these solubilising polyethylenimine amphiphiles. They find that increasing the number of amine groups increases the cytotoxicity of the polyamines and that amine substitution reduces the cytotoxicity of the long chain polyamines. However, at biocompatible concentrations, the polyethylenimine amphiphiles do not act by either a modulation of the P-glycoprotein pump or by altering the paracellular junctions.

The design, synthesis and characterisation of a series of dendrimer-based prodrugs for the enhancement of drug solubility and permeability are described by **Najlah et al** (University of Manchester). Naproxen is selected as a model low-solubility drug and conjugated to dendrimers by an amide bond or an ester bond. The results indicate a high chemical and enzymatic stability of the amide-linked conjugate with slow release of the parent drug in human plasma making these conjugates suitable for further study as prodrugs.

From the same group, **Jevprasesphant et al** (University of Manchester) investigate the transport mechanisms of dendrimers and surface-modified dendrimer conjugates across Caco-2 cell monolayers, and also the use of dendrimer-drug conjugates to enhance the solubility of poorly soluble drugs and bypass the P-glycoprotein efflux transporter. Dendrimer and lauroyl-dendrimer conjugates were chemically bound to propranolol base, a model P-glycoprotein substrate and low-solubility drug. The results suggest that dendrimer carriers bypass the P-glycoprotein efflux transporter by a method involving endocytosis. No difference in the permeability of propranolol-dendrimer conjugates is apparent in the presence and absence of ciclosporin A, indicating that the conjugates are not P-glycoprotein substrates.

Drug delivery: other routes

Jahan et al (School of Pharmacy, University of London) extend previous work on the *in vivo*

electroresponsive release of a model drug diclofenac in rats, from chitosan hydrogels. Diclofenac could be released from chitosan hydrogel in a pulsatile fashion in response to repeated pulses of electrical stimuli. Some release of drug during the "off" period is also observed, probably due to drug diffusion along a concentration gradient. The electro-stimulated release may be attributed to syneresis of the gel, with concomitant drug expulsion or to electrophoresis of the negatively charged drug towards the anode.

In a separate paper, the same group describe electro-responsive release of diclofenac from chitosan microspheres. A burst release of drug is observed, after which diclofenac levels rise slowly in both electro-stimulated and control rats, although the burst release and the subsequent gradual drug release are greater in rats that have been electrostimulated; enhanced drug release is probably via electrophoresis of the drug towards the anode. This is the first report of electro-responsive drug release from gel microspheres *in vivo*.

Donnelly et al (Queen's University of Belfast) note that the zwitterionic nature of aminolevulinic acid, widely used in topical photodynamic therapy, impairs drug penetration, being ionised at both high and low pH. Topically applied aminolevulinic acid, therefore, penetrates intact stratum corneum poorly. Bioadhesive patches containing ¹⁴C-labelled aminolevulinic acid are prepared containing 0–5 per cent of either dimethyl sulphoxide or oleic acid. Patch segments are applied to equal areas of neonate porcine skin and allowed to remain in place for four hours at 37°C. Sectioned skin samples are assessed by liquid scintillation spectroscopy. Neither dimethyl sulphoxide nor oleic acid have significantly useful influences on aminolevulinic acid concentration at a depth of 2.375mm.

Ammar et al (Cairo University) present a comprehensive study on the development of a transdermal delivery system for glipizide which would circumvent the problems associated with oral therapy of the antidiabetic. They prepared inclusion complexes of the drug in a range of beta-cyclodextrins and developed several percutaneous formulations for the drug and the prepared complexes in different bases. The results reveal sustained effect of the drug for about 48 hours, as well as suppression of hypoglycaemia induced in glucose-loaded rats. The best biological performance was shown by a glipizide-dimethyl-beta-cyclodextrin complex in Carbopol gel base in the presence of urea and by glipizide in the same base in the presence of propylene glycol together with oleic acid.

Drug delivery: gene delivery

Microneedle arrays are a novel intra/transdermal delivery device that provides access to the viable cells of the epidermis through the creation of microchannels within the stratum corneum. **Coulman et al** (Cardiff University and Royal Gwent Hospital) aim to combine the cutaneous delivery potential of a microneedle device with the rational design of

non-viral gene therapy formulations to create a controllable therapeutic gene delivery system. The visualisation of microconduits within the stratum corneum, approximately 15µm in diameter, is followed by the microneedle-mediated delivery of fluorescent colloidal nanoparticles to the viable cells within the human epidermis. These studies confirm the capability of a microneedle array to create a route of delivery for macromolecular gene therapy formulations.

Omid et al (Welsh School of Pharmacy, Tabriz University of Medical Sciences, Iran and University of Setif, Algeria) assess the toxicogenomics of starburst polyamidoamine dendrimers and polypropylenimine diamino-butane dendrimers and demonstrate that these dendrimeric delivery systems for gene therapy intrinsically alter gene expression in human epithelial cells. The nature of the genes whose expression is induced by these dendrimeric nanostructures is diverse and includes some common genes, among which are those related to apoptosis and stress as well as membrane receptors and transcription factors. Thus, certain dendrimers can induce diverse gene expression changes in cells and cannot truly be considered to be genocompatible.

Lam et al (University of Nottingham, University of Sussex and Biocompatibles International) describe a novel diblock copolymer as a potential vector for gene delivery. Evaluation of the diblock copolymer showed that the presence of a methacryloyloxyethyl phosphorylcholine block prevents aggregation of the DNA condensates by providing steric stabilisation, creating condensates with sub-200nm average diameter. However, the steric stabilisation effect of the block has to be balanced against the decreased ability of the copolymers to provide efficient DNA condensation as the length of the methacryloyloxyethyl phosphorylcholine moiety increases. The reduced level of DNA condensation is directly related to the decreased level of DNA protection from enzymatic degradation *in vitro*. Careful design of the copolymer architecture is required to balance the stabilising and DNA condensing properties of the copolymers.

Barlow et al (King's College London and Laue Langevin Institute, Grenoble) aim to establish the existence and extent of the interactions of calcium with zwitterions using neutron reflectivity, examining the effects of DNA, in the presence and absence of calcium, on a monolayer formed at the air-water interface by the zwitterionic phospholipid 1,2-distearoyl-*sn*-glycero-3-phosphocholine. Structural changes to the phospholipid monolayer are observed in the presence of calcium that are a direct result of interaction with DNA. Although the thickness of the lipid hydrocarbon layer remains constant (at ~25Å) after the addition of DNA, there is a marked decrease in the scattering length density of the adsorbed layer. This indicates insertion of hydrogenous material into the layer, or a structural rearrangement of the molecules within the layer to occupy a greater interfacial area.

Changes of a similar nature are observed in the absence of calcium but occur much more slowly and are of a much smaller magnitude. Thus calcium promotes interactions between zwitterionic phospholipids and DNA, and these systems might make suitable (non-toxic) vectors for gene delivery.

Pharmacognosy: analysis

Herbal medicine is gaining interest because of supposed reduced side effects, but safety and efficacy data are limited. **Langyan and Ahuja** (Hisar University, India) study the accumulation of nickel and cobalt in some Indian herbal preparations (churna, guggulu, bati, ras, pishti and arishtas). Eleven marketed products show varying amounts of nickel and cobalt. These metal ions may have entered through the raw material or during processing. Some herbal remedies do contain metal ions as their therapeutically active ingredients but the authors suggest they should not be considered as dietary supplements for these compounds.

Putalun et al (Khon Kaen University, Thailand, and Kyushu University, Japan) seek a rapid determination method for glycyrrhizin, suitable for use in plant samples and report the development of a rapid immunochromatographic assay for the detection of glycyrrhizin. This qualitative assay is based on a competitive immunoassay in which the detector reagent consists of colloidal gold particles coated with anti-glycyrrhizin monoclonal antibodies. The detection limit for the strip test is 250ng/ml. The appropriate sample volume size was 200µl, and the assay can be performed in about 10 minutes. The immunochromatographic strip assay is suitable as a rapid and simple procedure for screening glycyrrhizin concentrations in plants, biological fluid and food samples.

Reid et al (Robert Gordon University, Aberdeen) report the separation and quantification of the main alkaloids found in opium samples and poppy straw using capillary electrophoresis, an improvement on previous chromatographic methods. Distinct profiles of different opium samples (Persian, Indian, Turkish and Yugoslavian), along with those for different poppy straws have been generated. The method has been extensively validated with a detection limit of 100ng/ml for morphine. Quantitative scoring of capillary electrophoresis peak areas and retention times for the profiles may be used to authenticate and assess sample quality.

Pharmacognosy: activity

Ali et al (King's College London) investigate the potential anti-diabetic properties of Malaysian local plants using *in vitro* models, and isolate the compounds responsible for the activity using bioassay-guided fractionation techniques. The most active extract is the hexane extract of *Phyllanthus amarus*, which has a significant inhibitory effect. The hexane extract is fractionated by preparative thin layer chromatography. Five fractions are collected and tested in the bioassay to obtain the most active component.

Fang and Houghton (King's College London) select five traditional Chinese medicines, four plants and one animal, for research into their reputed anti-cancer effects. Chloroform extracts of *Illicium verum* fruits, *Lonicera japonica* flowers and *Aristolochia manshuriensis* stem show considerable cytotoxicity; the chloroform extract of *I verum* is selectively cytotoxic for lung cancer.

McCurrie et al (University of Bradford) note that populations consuming diets rich in phytoestrogens appear to have reduced cardiovascular disease risks, and they investigate the possible mechanism by which phytoestrogens relax blood vessels. A comparison is made of relaxant actions of genistein, a tyrosine kinase inhibitor and its analogue daidzein with those of the endogenous oestradiol. The authors conclude that relaxation elicited by phytoestrogens does not depend on the presence of endothelium in all types of blood vessel.

Cheung et al (King's College London and Institute of Soil Science and Plant Cultivation, Pulawy, Poland) report for the first time on the activity of saponins from *Medicago* species against dermatophytes. Total saponins were separately obtained from roots and aerial parts of *M sativa*, *M murex*, *M arabica* and *M hybrida*. Four isolated glycosides of medicagenic acid, one of hederagenin and one of soyasapogenol were also available and all eight extracts and six compounds were tested against three species of dermatophytic fungi. *Trichophyton tonsurans* appears to be the most sensitive of the dermatophytes to the active compounds. Glycosides of medicagenic acid are the most active compounds, especially the 3-O-glucoside. TLC analysis of the extracts shows no clear correlation between content of identifiable compounds and activity although many compounds present are unidentified.

Simulation and computing

Naylor et al (GlaxoSmithKline and TNO Pharma, The Netherlands) describe and evaluate the TNO Intestinal Model (TIM), an *in vitro* model that can mimic the dynamic conditions found within the stomach and small intestine. The model can simulate fed conditions by introducing the meal into the system itself and setting enzymic secretion conditions. A dosage form is introduced into the model and samples are taken throughout the run. Development work is carried out utilising the TIM and an immediate-release paroxetine formulation. A prediction of the plasma profile is carried out using the commercially available program GastroPLUS with TIM data as input, providing an excellent tool to aid the selection of a formulation in pharmaceutical development.

Burke et al (University of Sunderland and Robert Gordon University, Aberdeen) are designing more efficient chiral stationary phases by modelling the interaction of hexahelicenes with chiral analytes. The energies obtained from the modelling show good agreement with the experimentally derived data and the most favourable energy corresponded to com-

pounds with the longest retention times. The promise of delivery of drugs by the transdermal route remains largely unrealised because for many drug molecules the skin constitutes a significant barrier. A greater understanding of the mechanism of action of penetration enhancers could assist in their rational design.

Notman et al (King's College London and Unilever Research & Development) investigate the possible mechanisms of action of oleic acid in a lipid system using molecular simulation and confirm that the oleic acid molecules do indeed interact with the hydrocarbon chains of the lipid bilayer. Oleic acid disperses throughout the bilayer without forming a separate lipid phase. Although a range of solubility-enhancing formulation types exists, there is little published information about how to choose the most suitable formulation types for a given drug.

Branchu et al (AstraZeneca R&D) build a data set from AstraZeneca proprietary drugs as well as substances and suitable formulations taken from the literature. The properties included pKa, molecular weight, melting point, octanol/water distribution coefficient, number of hydrogen-bond donor and acceptor groups, dose and dose-to-solubility ratio. The data set was then examined using principal component analysis resulting in the identification of latent variables highlighting the presence of structure in the data. Certain compounds, such as nifedipine, played little part in influencing the principal components. Other compounds, such as chlorzoxazone, made a greater contribution. The study suggests that empirical approaches combining multivariate projection and case-based reasoning may be applicable in dosage form development. Interest in the use of artificial neural networks for the modelling of pharmaceutical formulations has increased during the past decade, and numerous commercial programs are available.

Plumb et al (University of Bradford and UMIST) study the effect of varying the training algorithm on the predictive ability of three programs: InForm (Intelligensys), CAD/Chem (AI Ware) and the Neural Network Toolbox (The MathWorks). An immediate release tablet formulation data set comprising 205 records is used. Choice of training algorithm and hidden layer architecture is shown to exert a significant effect on predictive ability. Nevertheless different packages are capable of generating equivalent models provided that both training algorithm and hidden layer architecture are optimised.

Buggins and Taylor (Welsh School of Pharmacy) make an ambitious attempt to correlate calculated solubility and molecular connectivity indices of some phenothiazines and angiotensin converting enzyme inhibitors with their absorption, distribution and elimination. Both solubility and connectivity indices appear to have potential, as several correlations are found with the pharmacokinetic parameters. However, the same correlations are not seen for both groups of drugs, suggesting that consideration of several physicochemical and molecular parameters is

the best strategy for determining quantitative structure-pharmacokinetic relationships.

Spectroscopy: near-infrared

Near-infrared spectroscopy provides a quick and accurate alternative to a reference analytical method such as HPLC, which allows for increased testing frequency and greater process knowledge and understanding, and facilitates the move of quality systems towards continuous verification. **Smith et al** (School of Pharmacy, University of London, and Pfizer Ltd) demonstrate the feasibility of a single-tablet near-infrared assay for atorvastatin in Lipitor tablets, a significant challenge due to the low concentration of atorvastatin present.

Morton et al (Abbott Laboratories and School of Pharmacy, University of London) report the use of near-infrared spectroscopy to measure the limit of detection of caffeine in sucrose powders. The limit of detection is dependent on the variability of particle size fractions of the substrate and strategies to improve this can enable lower values to be obtained.

Spectroscopy: Raman spectroscopy

Owen et al (Imperial College London) developed a novel biophotonics technique using Raman spectroscopy to monitor the interaction of chemicals with cells non-invasively and *in situ* over a period of days. The technique is demonstrated using etoposide. No changes were observed in the concentrations of the components except for a decrease in DNA. Raman spectroscopy was capable of modelling cellular changes in real-time and the potential to analyse any cellular component makes the technique a powerful drug-screening technology. The biophotonics cell monitoring system can speed up pharmaceutical R&D by rapidly eliminating drug candidates that are deleterious to human cells. It may eventually offer an alternative to some forms of animal testing.

The simplest form of univariate imaging is not an option for unknown mixtures so **Sašić et al** (Pfizer Global Research and Development, Sandwich and University of Greenwich) analyse Raman images of pharmaceutical products by sample-sample 2D correlation spectroscopy. Comparison of this method with principal component analysis was found satisfactory, encouraging the use of the technique as an initial approach for producing chemical images of pharmaceutical samples.

Spectroscopy: ultrasonic spectroscopy

High-resolution ultrasonic spectroscopy is a new technique for material analysis based on the measurement of high-frequency sound waves propagating through samples, allowing direct probing of micro-structural organisation and intermolecular forces. **Dwyer et al** (Ultrasonic Scientific, Dublin, and University College Dublin) describe the application for direct real-time monitoring of crystallisation of lysozyme, formation of micro-emulsions, and the hydrolysis of maltodextrin by alpha-amylase. The technology is extremely sensitive, non-destructive, requires no markers and can be used in non-transparent samples.