NZIC Chemistry IN NEW ZEALAND

Volume 76, No.3, July 2012

Articles and Features

Other Columns

Advertising

Cover

Front cover: Representation of the structure of an antimony polyoxometalate (see article by Nicholson and Clark)

Comment from the President

I noticed an April issue of *New Scientist* in our tea room as I was heading to make myself a cup of coffee one evening last week: the banner headline read "**CHEMISTRY'S GREATEST CHALLENGE**" in bold uppercase letters. Turning to the "Cover Story" I discovered that the greatest challenge was the creation of artificial photosynthesis for solar-powered fuels – a subject close to my heart – and I promptly photocopied the article to pass on to my 300-level students. While I agree with the article (my research is on photosynthesis!), I immediately wondered what NZIC members would consider Chemistry's Greatest Challenge – if you email me your answers we will publish the "Top 10 List" in the next issue of *Chemistry in New Zealand* (email: *julian.eaton-rye@otago.ac.nz*).

I suspect that for many of us our own research is high up on our scale of what is important and relevant, and we are dedicated to working on our chosen problem. I think it sometimes goes unnoticed how dedicated researchers are to their work. I doubt if there are many successful academics or researchers who don't put in 50 or more hours a week to keep their research moving forward as they negotiate one deadline after another. Many will have recently completed their Performance-Based Research Fund (PBRF) Portfolio; some, I know, find the exercise frustrating, but this is important for our Departments and Institutions as they position themselves for their portion of the available resources. However, once all the polishing of individual portfolios has been done, I do recommend that you print off your own, read it through and give yourself a good pat on the back for all that you have accomplished and contributed over the last six years.

In addition to the PBRF juggernaut, the 9th of May was the announcement of the Marsden Pre-proposal round. This is a significant day for many of us, and particularly so for younger researchers who are trying to establish their research programmes. Approximately 20% of our members who applied will have received an invitation to submit a full proposal and around a third of those will be popping champagne corks in October. It is important that we congratulate all who are successful and we should celebrate alongside them. However, I believe it is equally important that we recognise the effort we all put into our Marsden Proposals. Even if unsuccessful, the preparation of a grant serves to sharpen and focus our research ideas on topics which we recognise are important and that need answers. That we submit so many pre-proposals, despite the limited funding, is a measure of our dedication and enthusiasm. In the end, Chemistry's Greatest Challenge is that we succeed in passing on that enthusiasm to our students.

Julian Eaton-Rye
NZIC President

New Zealand Institute of Chemistry

supporting chemical sciences

July News

News

NZIC congratulates the following member of their appointments, made on the occasion of the Queen's Birthday and Diamond Jubilee: Professor *Christine* ***Winterbourn***, Companion of the New Zealand Order of Merit; and Dr *Tom* ***Clarkson***, Companion of the Queen's Service Order.

Branch News

AUCKLAND

At a May NZIC branch seminar, Dr *Peter* ***Surman*** from Douglas Pharmaceuticals spoke on the *Pharmaceutical industry in New Zealand: the Douglas story*, and outlined pharmaceutical new product development and some of the technical challenges in New Zealand associated with the development of generic and novel formulations for European and US markets.

University of Auckland

Within the School of Chemical Sciences, Dr *Donald* ***Wlodkowic*** was one of six academics from across the University in 2012 to be awarded an Early Career Research Excellence Award. This recognised Donald's research with a new class of smart microfluidic Lab-on-a-Chip devices for large-scale marine biomonitoring applications. Three Professional Staff Development Awards were also achieved by staff within the School: *Alistair* ***Mead***, who will use the award to present at the Australasian Scientific Glassblowing Symposium in Dunedin; *Michel* ***Nieuwoudt***, to present at the Corrosion and Prevention conference in Melbourne later this year; and *Katrina* ***Graf***, to enable her to accompany the New Zealand Chemistry Olympiad team to Washington DC. The School of Chemical Sciences also held a special celebration on 24 May to mark the achievements of Prof *Margaret* ***Brimble*** this year, particularly her investiture as a Companion of the New Zealand Order of Merit.

In May, the new lecturer in Wine Science, Dr *Bruno* ***Fedrizzi***, from Pado-

va, Italy, took up his position within the School. Bruno is presently working on grape metabolomics and wine quality projects, in particular aroma chemistry. Bruno is accompanied by his wife *Katryna* ***van Leeuwen*** who will continue her PhD research work at Auckland in Analytical Chemistry towards a degree being undertaken through Charles Sturt University in Australia. A recent addition to the Hybrid Polymer group based at the Tamaki campus was Dr *Carla* ***Fonseca-Paris*** on a post-doctoral fellowship, who will apply her background in polymers, surface and interface science to the commercialisation of antimicrobial conducting polymers.

An addition of an instrumental kind will be a four-month placement in 2012 of an advanced surface plasmon resonance instrument (SPR Navi 220A), following the success of Dr *Jenny* ***Malmström***, a post-doctoral fellow working in the group of Assoc Prof *Jadranka* ***Travas-Sejdic***, in winning an international competition run by BioNavis, for a project entitled *Multi-parametric surface plasmon resonance studies of electrically switchable surfaces and related protein adsorption*.

Student achievements and awards began in April on a lighter note, with the School's postgraduate students competing for the most imaginative 'Wish I was...' outfits! on a night out. The prize for best dressed as X-Men's Wolverine went to *Nathan* ***March***, while Clarke Kent (aka *Karthik* ***Kannappan***) scooped the runner-up award. At the time of the May graduation ceremonies, the winner of the L H Briggs Prize was announced, being the person judged to be the most distinguished research worker for a PhD thesis submitted during 2011 in the School of Chemical Sciences. This award went to *Dong Jun (Danny)* ***Lee*** for his thesis on the *Synthesis of Glycopeptides and NeoGlycopeptides using Click Chemistry*, supervised by Prof *Margaret* ***Brimble***. A PhD thesis submitted by *Muhammad* ***Amtiaz Nadeem*** also received exceptional examiners' reports and he was placed on the Dean's list for this achievement. His thesis entitled *Reactions of Ethanol on Bare and Noble Metal Modified TiO_2 Single Crystals and Powders*, was supervised by Prof *Jim* ***Metson***, with co-supervisors Dr *Tilo* ***Soehnel*** and Assoc Prof *Hicham* ***Idriss***.

Each year the current PhD students within the School of Chemical Sciences prepare abstracts for the annual Chemistry Research Showcase. From the best of the abstracts, six students were chosen to present talks at the Showcase in June. The successful students were *Julia* ***Allwood***, *Brendan* ***Harvey***, *Vedran* ***Jovic***, *Meder* ***Kamalov***, *U* ***Bin*** and *Wei* ***Li.*** These six oral presentations join 24 short presentations given by first year PhD students, and more than 70 poster presentations featuring the wide range of research topics covered within the School. Two additional recent student successes were awards for the University of Auckland Spark Entrepreneurship Challenge Ideas competition. In both cases students from the research groups of Assoc Prof *Jadranka* ***Travas-Sejdic*** and Prof *David* ***Williams*** were the winners. *Cosmin* ***Laslau*** received the $2000 Chiasma prize for an idea to commercialise a scanned nanopipette system for biotech applications, while *Anupama* ***Rao Gulur Srinivas*** and *Nathan* ***March*** won a $1000 prize in the commercial category for a proposal for DNA sensors based on conducting polymers and magnetic nanoparticles.

Seminars within the School of Chemical Sciences in recent months have included Dr *James* ***Crowley*** from the Department of Chemistry at the University of Otago, who spoke on *Functional Ligands: It's as easy as 1,2,3 "Click"*; and Prof *John* ***Arnold***, from the University of California at Berkeley, who presented on *Catalytic Hydrogenation with Early Transition Metals: Unusual Structural and Mechanistic Findings*. A seminar was also presented by the School's own Dr *Marija* ***Gizdavic-Nikolaidis***, whose talk entitled *Bioactive Polyaniline Based Conducting Polymers – A New Age of Nanotechnology* covered recent discoveries made at Auckland on a new generation of conducting polymers that combine antioxidant, antimicrobial and additional functionalities in single materials, using microwave assisted and electrospinning methods for their synthesis.

CANTERBURY

The NZIC annual BBQ was held on Monday 12 March, to which were invited all second, third and fourth year Chemistry students (University and Polytechnic), postgraduate students and NZIC members in addition to the passing physics students attracted by the smell of seared mammal flesh who attempted to argue that physics isn't that different from chemistry really. It was exceptionally well attended.

National Chemistry Competition

Following its success last year, the NZIC is running another National Chemistry Competition, this time to be held at Massey University on 26 June. Selection of the local team occurred by a local competition held in March of this year. It involved teams from 12 different schools, from which a team of four from Christ's College emerged victorious. This team will be off to Palmerston North in June to represent our region.

CPIT

Year 12 Chemistry Competition

In mid-May, CPIT held its Year 12 Chemistry competition, which tested both theory and practice for the students. It is great to see so many enthusiastic students in the labs (25 teams each consisting of three students). The winning team was one from Burnside High School, closely followed by Rangiora High School, with Christchurch Girls' High School and Middleton Grange sharing third equal.

University of Canterbury

Comings and goings

The March the Chemistry Department welcomed Professor *John* ***Arnold***, currently Director of the Berkeley Centre for Green Chemistry. He says, in reference to his group's research interests, "Work in my group is focused on chemical questions relating to energy and the environment, from the perspective of inorganic and organo-metallic reactivity. The last three years has seen the group expand into fuel cell chemistry, which has become a major focus area in our research. We are continuing our long-standing interest in early transition metal chem-

istry, with a new focus on catalysts, and are building our efforts in actinide chemistry."

Dr *Barbara* ***Thomson*** is joining Ian Shaw one day a week as a food safety lecturer. Barbara brings experience of analytical chemistry applications to toxicology, forensic science, and environmental and food topics. She graduated from the University of Canterbury in 1978 and 2005 and has worked for ESR and former organisations for over 20 years. Her most recent work features acrylamide, caffeine, and iodine within the food regulatory environment. She has also reviewed aspects of climate change and incidents of chemicals in food for the EU. Barbara has published over 80 peer-reviewed scientific book chapters, journals, conference proceeding, client reports and articles for the popular press. She has presented regularly at local, national and international conferences and appeared on several TV programmes. Barbara is active in the outdoors – tramping, climbing, kayaking, cycling and skiing.

The Department's most recent Erskine Visitor was Dr *Kieran* ***Lim,*** from Deakin University (Australia). Kieran studied at the University of Sydney where his doctoral research with *Bob* ***Gilbert*** used mathematical modeling and molecular dynamics simulations to investigate collisional energy transfer processes, which are the rate-determining steps in many gas-phase reactions. An Archbishop Mannix Traveling Scholarship took Keiran to Stanford University, where he researched gas-phase Sn2 and proton-transfer reaction dynamics using Fourier-transform mass spectroscopy experiments and theoretical methods in Professor *John* ***Brauman's*** group. He was a visiting scientist at University of Goteborg (Sweden), looking at dipole-dipole collision rates with Professor *Sture* ***Nordholm***. Kieran returned to Australia as a lecturer at University of New England and then University of Melbourne before joining Deakin University. Kieran is currently in charge of the Bachelor of Forensic Science programme at Deakin University. His honours course will introduce students to fundamental forensic science principles and discuss the nature of "evidence" and "proof". He has also given presentations on green chemistry and other topics as part of the Universities Outreach Programme to local high-school teachers and students. Kieran is also active in science education research practice. He served on the science advisory panel that developed the new Australian National Curriculum for primary and secondary school years F-10 (New Zealand years 1-11). Kieran is the recipient of the RACI Division of Chemical Education Medal, an Australian Citation for Outstanding Contribution to Student Learning and the RACI Fensham Medal for Outstanding Contribution to Chemical Education. He was with the Department until 8 June.

Awards and appointments

The Chemistry Department held its inaugural Postgraduate Student Research Showcase day on Tuesday 14 February. There were 15 presentations during three sessions given by: *Dmitri* ***Joseph***, *Evan* ***Nimmo***, *Gurpreet* ***Kaur***, *Laura* ***Revell***, *Lauren* ***Raffensperger***, *Nei-Jin* ***Ke***, *Nicola* ***Blackmore***, *Rakesh* ***Puttreddy***, *Robert* ***Currie***, *Rosanna* ***Archer***, *Ryan* ***Golder***, *Sarah* ***Wlso-Coutts***, *Sebastian* ***Reichau***, *Sedigheh* ***Ghadamgahi***, and *Solomon* ***Wasseyehun Kelemu***. At the conclusion of the showcase, presentations were judged to determine the recipient(s) of the Ralph H. Earle Jr. Seminar Prize awarded annually for the best review seminar presentation given in the Department of Chemistry by a second-year PhD student. This year's prize was jointly awarded to Lauren Raffensperger and Sebastian Reichau.

A number of individuals from the Steel, Fitchett and Kruger research groups attended the 7th International Symposium on Macrocyclic and Supramolecular Chemistry, at the University of Otago (29 Jan - 2 Feb). The conference was a great success and brought together many leading researchers from around the world with interests in supramolecular and macromolecular chemistry. A particular highlight of the meeting was the award of Best Poster Prize to Dr. *Alan* ***Ferguson*** (Kruger group) for his paper entitled *Self-assembly of spin crossover* $[Fe_4L_4]^{8+}$ *molecular cages*. The award was sponsored by Springer Publishing and Alan received a book prize.

ESR

On Wednesday 20 June, Darren Saunders gave a presentation at ESR entitled *Spice – the history of an indulgence*, touching on the history of the spice trade and chemical safety issues of spices. This event was co-organised by the NZIFST (NZ Institute of Food Science and Technology) and the Canterbury Branch of the NZIC. Drinks and nibbles (appropriate to the topic) were provided.

MANAWATU

Members of the Manawatu Branch visited the Massey University microbrewery in June. Allan Hardacre, from Massey University's Institute for Food, Nutrition & Human Health, gave a tour of the facilities and provided an explanation of the many subtleties involved in crafting beer. Members were, of course, provided with generous samples of several of the brewery's products.

The National Human Genome Research Institute (NHGRI) and New Zealand Pharmaceuticals are partners on a drug development project. Their goal is to reduce or halt the progression of a rare disorder, Hereditary Inclusion Body Myopathy (HIBM), by treating affected patients with a small-molecule therapeutic drug. HIBM primarily affects distal muscle tissue, and owing to dramatically decreased muscle strength most HIBM patients must use a wheelchair by the time they are in their thirties. NZP has licensed NHGRI's portfolio of patents related to treating HIBM and other muscle wasting diseases – as well as kidney diseases related to hyposialylation – with a monosaccharide *N*-acetyl-D-mannosamine known as DEX-M74. This compound is one of the first molecules to enter development in the Therapeutics for Rare and Neglected Diseases (TRND) programme at the National Institutes of Health (NIH). NZP and TRND are currently collaborating to complete needed pre-clinical studies for treating HIBM with DEX-M74. These studies will be the basis of an investigational new drug application to be submitted to the Food and Drug Administration this year. Once the ap-

plication goes into effect, a phase I/II clinical trial is scheduled to begin at the NIH Clinical Centre. The study will be led by HIBM expert and NHGRI Clinical Director, William Gahl.

Massey University, Institute of Fundamental Sciences

Peter ***Derrick*** attended the Fourth International Conference on Hybrid and Organic Photovoltaics in May. The conference was held in Uppsala, Sweden, and was also attended by *Emad* ***Al-Imarah***, who presented a poster. Peter used the opportunity to collaborate with staff from the University of Uppsala as well as Stockholm and Copenhagen Universities. Peter was also present at the 60th ASMS Conference on Mass Spectrometry and Allied Topics in Vancouver, Canada.

Mark ***Waterland*** is visiting the laboratories of Professor Vikas Berry at Kansas State University, USA.

Vyacheslav ***Filichev*** and *Paul* ***Pleiger*** have made it through to the second round of the Marsden fund. Their projects are entitled, respectively: *DNA triplexes to paint genes on intact chromosomes* and *The good without the bad, selective chelators for beryllium*.

Ajay Pannu has joined the Pleiger group as a postdoctoral fellow. The subject of his research will be nanomagnets. Mehdi Jazi also joins the Pleiger group as a PhD student researching anion sensors. *Nishani* ***Thennakoon*** has completed her PGDipSci under Paul Pleiger's supervision and has since taken a position as a technician in the laboratory of Gareth Rowlands. Laura Troussicot and William Bunouf from Oleans University, France have also joined Gareth Rowland's research group.

Vyacheslav Filichev visited an NMR facility led by Prof. Carlos Gonzalez, a Vice-Director of the Instituto de Química Física 'Rocasolano', Spain. The facility is part of the Spanish Council for Scientific Research. Other than eating tapas and drinking Spanish red wine, Vyacheslav performed numerous NMR experiments on chemically modified nucleic acid secondary structures, and gave a talk entitled *Intercalating nucleic acids and targeting of double-stranded DNA*. He also spent two days in Seville visiting Dr Juan Carlos Morales in the Instituto de Investigaciones Quimicas in Seville where he gave another presentation. The trip was supported by the International Mobility Fund and the Royal Society of New Zealand.

Visitors to Massey's Chemistry department include Yoshihiko Takeda from the Quantum Beam Unit of the National Institute for Materials Science, Japan, who gave a talk entitled *Characterization on wavelength dispersion of third order optical susceptibility and optical nonlinearity of metal nanoparticles*. *Robin* ***Fulton*** from Victoria University presented her work on the activation of carbon dioxide by group 14 complexes. Annie Powell from the Universität Karlsruhe, Germany, presented a talk on the use of a co-ordination cluster as a building block for nanomaterials. Victoria Rose from the University of Oregon, USA, discussed her work on RNA chemistry. *Jane* ***Allison*** from the Institute of Natural Sciences at Massey University's Albany campus gave a talk entitled *Shake, rattle and roll: using simulations to explore how proteins move*. *Alexander* ***Goroncy***, a postdoctoral researcher in the Institute of Fundamental Sciences, presented a talk on the subject of the characterisation of biomolecules by NMR.

OTAGO

University of Otago, Department of Chemistry

Humphrey ***Feltham*** successfully defended his PhD thesis in late March. His thesis was formally deemed to be 'exceptional' by the three examiners and the Pro-Vice-Chancellor of Sciences (top 10%). He has since taken up a MacDiarmid research fellowship in Brooker's Bunch and recently visited Prof Downard at Canterbury University for a week, then IRL (Lower Hutt) to collect magnetic data. *Sally* ***Brooker*** presented the last of her 2011 RSC Australasian Lectureship Award lectures at Canterbury in May. *Alain* ***Valery***, a master's student from Toulouse University, is currently a visiting researcher in Brooker's Bunch, and is working closely with third year PhD student *Rajni* ***Wilson*** on porphyrin-like N_4-donor macrocycles. Brooker's Bunch honours students *Ross* ***Hogue*** and *Michael* ***Bennington*** gave great talks on their projects at the one-day honours student symposium in late April. PhD student *Sebastien* ***Dhers*** is making a remarkable recovery from his broken leg, and is frequently observed hobbling round the corridors in the department. He is looking forward to discarding the remaining crutch and returning to the lab next month. We recently received good news from ex-Brooker's Bunch PhD graduate, *Dr Juan* ***Olguín***, who has been awarded an IRCSET postdoctoral fellowship to extend his current one year position with Prof Martin Albrecht at University College Dublin for another two years.

Egor ***Tchesnokov*** is a recipient of a Canadian Health Research Fellowship which will allow him to continue his postdoctoral work in *Guy* ***Jameson***'s laboratory for a further two and a half years. In addition, Egor received a Maurice and Phyllis Paykel Trust Travel Award to support his travel to the Second Penn State Bioinorganic Workshop held in June.

In May *Greg* ***Rankin*** (Larsen group) successfully defended his PhD thesis on the *Synthesis and Structural Elucidation of Fully Lipidated Phosphatidylinositol Dimannosides*. Based on the recommendations of the examiners, Greg's thesis was placed on the Divisional List of exceptional PhD theses.

Elaine ***Burgess***, summer student *Jermy* ***Lei*** and *Nigel* ***Perry*** were on the radio recently with Alison Ballance speaking about Nutrigenomics New Zealand, a joint project between Plant and Food Research, AgResearch and the University of Auckland that aims to develop targeted foods or groups of foods to prevent, ameliorate or cure inflammatory diseases. *Luke* ***Youard***, a PhD student with Nigel Perry and Janice Lord (Botany), passed the oral examination on his thesis *The function of secondary metabolites in the leaves of Pseudowintera colorata*.

A small group from the chemistry department recently spent a day working with staff from Natural History New Zealand, who have a 'Phantom Camera' which can record at up to 1000

frames per second (in HD). They were keen to get some super slow motion images of smashing objects frozen in liquid nitrogen (including a sheep's brain!). We were happy to oblige, but also took along a number of other experiments to record, including igniting hydrogen balloons, burning phosphorus and liquid oxygen-soaked cotton wool sheep and 'foam snakes'. Some fantastic images were collected which NHNZ will allow us to use for Outreach activities. Our thanks go to *Matthew* ***Smart*** and *Steve* ***Ting*** for organising this, and also to the large number of people from NHNZ who gave up their time and expertise to help.

Following their winning the Prime Minister's Science Prize in December, the Centre for Chemical & Physical Oceanography-NIWA collaborative research centre were announced as inaugural recipients of the University of Otago's Research Group Award. *Katie* ***Baer-Jones***, a PhD student in the centre, has been awarded the NZ Marine Science Society student travel award to attend the joint NZMSS-AMSA conference in Tasmania in July.

Philipp ***Nasemann***, who completed his MSc at the Leibniz University of Hannover, has commenced PhD studies at Otago under the supervision of *Sylvia* ***Sander*** and *Claudine* ***Stirling***. As part of his research, Philipp and his colleagues will set up a method to measure the iron isotopic composition of seawater and hydrothermal fluids in order to gain new insights into the marine iron-cycle, by tracing its major sources.

WELLINGTON

The Branch was saddened by the death of former Hon. Gen. Secretary Alan A. Turner on Tuesday 17 April. A full obituary appears in this issue (p. 101)

A turn to forensic science saw the March Branch meeting entitled *The Things I Learned from CSI* or *Television Toxicology*. We were given a fascinating address by Dr *Helen* ***Poulsen*** of ESR that served to illustrate the things that the media will do to pretty-up science-based TV drama series. Unfortunately, the April meeting had to be cancelled due to the last minute unavailability of our speaker, Dr *Matthias* ***Lein*** of SCPS. However, he did not get away from us, as he was re-scheduled into the May slot and spoke about his research under the title *The Supercomputer in my pocket: How the digital revolution changed chemistry*. He started by putting us chemists in place by citing Richard Feynman, one of the more illustrious physicists who is attributed with the statement: *All theoretical chemistry is really physics; and all theoretical chemists know it*, and then went on to show why this assumption was made and what lay behind it. Matthias's work lies at the boundary between chemistry and physics, and he showed us how technological advances have transformed theoretical chemistry into computational chemistry. This has added value to the whole discipline where it was previously thought that any effort was doomed to be futile. He outlined a collection of fundamental and applied questions that are commonly asked of theoreticians and demonstrated how they are usually approached, outlining the current limits of theoretical understanding and computation.

Industrial Research Ltd.

Dr *Lawrence* ***Harris*** has completed a three-month sabbatical at the Innovative Technology Centre in Cambridge, UK, the brainchild of Professor Steve Ley. While there, Lawrence learned many of the engineering techniques and the equipment required to make 'Flow Chemistry' technology practicable when it comes to its application to organic synthesis. Drs *Olga* ***Zubkova*** and *Gary* ***Evans*** formed part of a delegation (from the Maurice Wilkins Centre for Molecular Biodiscovery) to take part in the Fourth National Forum on New Technologies in Drug Discovery and Sino-New Zealand Drug Discovery, which was held in Shanghai on 27 April. The delegates also used the opportunity to visit a number of Chinese CROs, the National Centre for Drug Screening, and the Chinese National Compound Library while in Shanghai. Drs *Gary* ***Evans***, *Richard* ***Furneaux***, and *Peter* ***Tyler*** attended the NZ Society for Oncology 2012 Conference in Wellington over 2-4 May, where Richard presented the Carbohydrate Chemistry group's latest oncology research results.

Victoria University – SCPS

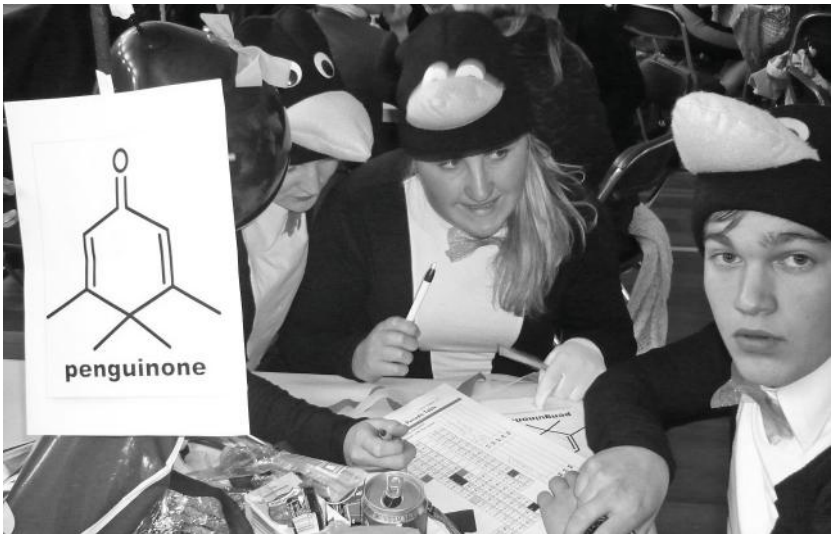
The staff of the SCPS were especially saddened by the death of Professor Sir Paul Callaghan. Although a physicist, he was a much appreciated and supportive colleague and friend. An obituary appears in this issue (p. 99). We were also much saddened by the sudden death of our genial and more than helpful IT support man, Scott Forbes, who died on 2 May.

Early March saw Prof *Terry* ***Gustavson*** (Ohio State University) visit the MacDiarmid Institute and speak on *Femtoseconds to Chemistry: Dynamical Studies of Molecules for Energy Conversion* to a teleconference including the Auckland and Canterbury MacDiarmid groups. Much of what Terry had to say revolved around the energy absorption-emission of metal co-ordinated organic ligands and especially cyano- and alkyne-linked anthracene moieties. It provided a useful refresher on absorption, intersystem crossing and emission events coupled to ultimate energy conversion. Dr *Carla* ***Meledandri*** (Otago University) also visited in early March to meet the material scientists and give a School seminar on *Magnetic nanocomposite materials with tunable magnetic resonance relaxation enhancements.* The lecture focused on the development and characterization of different classes of iron oxide-based magnetic nanocomposite materials with controlled size and tunable properties. Such materials are comprised of nanoparticles and/or nanoparticle assemblies functionalized with fatty acids, polymers, phospholipids, and/or the subsequent addition of gold nanoparticles to form hierarchical core@shell-type assemblies. These features attract increasing attention in biomedical applications, notably for improved medical diagnosis and targeted drug delivery. Current applications include magnetic resonance imaging (MRI) contrast agents where iron oxide nanoparticles are used to produce strong magnetic resonance relaxation enhancements. An ability to control particle and cluster size, architecture and surface composition is critical for biomedical application of the nanocomposite materials, as they largely determine the bio-distribution and the extent of contrast enhancement.

Prof *Annie* ***Powell*** (KIT, Karlsruhe) spent Tuesday 20 March in the SPCS and gave a seminar on *the coordination cluster as a building block for nanomaterial*, whereby it is regarded as a co-operatively coupled aggregation of metal ions held within a shell of ligands. Such a cluster can show very high spins states, not possible for a co-ordination complex containing a single metal centre. Annie discussed the use of such clusters to construct nanomaterials such as molecular nano-magnets. Prof *Micha* ***Polak*** (Ben-Gurion University, Beer-Sheva, Israel) visited on 4 May from IRL, where he has been on leave for some time. Apart from meeting materials science-based chemists and theoreticians he gave a lecture on *Prediction of separation-like phase transitions in binary and ternary nanoalloys*. He showed that modeling studies developed by his group for deriving the 'Coordination-dependence of Bond-Energy Variations' (CBEV), combined with the highly efficient statistical-mechanical 'Free-energy Concentration Expansion Method' (FCEM) predicted compositional structure thermal variations in Pt-Ir, Pt-Pd and Pt-Pd-Ir nanoparticle-equilibrated systems. Depending upon the nanoparticle size and overall composition, distinct intra-core and inter-particle separation-like phase transitions were revealed for all three systems. They exhibit critical temperatures significantly lower than the corresponding alloy bulk ones. The role played by preferential strengthening of surface-subsurface elemental bonds has been elucidated. The results he described have enable the construction of the first nano-alloy phase separation diagrams.

PhD student *Nayeem* ***Mullungal***, under the supervision of *Russell* ***Frew*** and *Robert* ***van Hale***, has won the best poster award in the physical sciences division at the International Congress of Environmental Research, Surat, India. *Cleo* ***Davie-Martin*** of the Hageman group gave the winning talk at the Otago Institute Travel Award Competition. She received $1500 to help her attend the American Chemical Society Conference in Philadelphia, in August 2012. The title of her talk was *Modelling the vapour drift potential of current-use pesticides*.

The 2012 Wellington Branch *High Schools Chemistry Quiz* was held at Victoria University on June 13, this time in the Recreation Centre gym. Almost 200 Year 12 and 13 students made up 48 teams and competed through 11 rounds of questions. Chemistry-inspired pop music and the allocation of spot prizes provided the breaks. The winning team, by just two points, was *One Reaction* (Cameron Inglis, Vinesh Nair, Nick On and Anthony Wong) from Wellington College. A great night was enjoyed by all, helpers and participants. Sponsorship from the VUW Faculty of Science and the provision of spot prizes were donated by The Carter Observatory, Burger King, Burger Wisconsin, the Embassy Theatre, the MacDiarmid Institute, The Met Shop and Vic Books is gratefully acknowledged.



The Penguinones - one of the student groups at the Wellington quiz.

New Zealand to host world's largest radio telescope

After a meeting in the Netherlands at the end of May, it was announced that New Zealand and Australia along with South Africa have won the rights to host the Square Kilometre array (SKA) and that the $2.5 billion project will be split between all three countries. South Africa and Australia already have infrastructure in place and this includes radio telescopes dishes, which will now be incorporated into the SKA project.

Satellite dishes will be installed at the top of the South Island of New Zealand, in Western Australia and in the Northern Cape of Africa with the aim that construction should begin in 2016 and be completed in 2024.

The telescope will consist of 3000 satellite dishes each of which will measure 15 metres in width and will cover a surface area of one square kilometre. It will be able to scan the sky 10,000 times faster than any other telescope. It should also give a clear view of the tectonic plate activity deep beneath New Zealand.

Sergei Gulyae who is the head of Auckland University of Technology's Institute for Radio Astronomy and Space Research has stated "By observing quasars on the border of the universe, we create a fundamental reference frame in which we can study all the irregularities of the rotation of the Earth, ocean, tides, and solid earth, and the way an island like New Zealand is breathing." He says that said the radio telescope could use "quasars" - stable points on the edge of the universe - as a frame of reference for measuring the most minute changes on Earth.

Michiel van Haarlem, director general of the consortium, said "The SKA will transform our view of the universe; with it we will see back to the moments after the Big Bang and discover previously unexplored parts of the cosmos."

For more information see: *www.skatelescope.org*

Article

Oligosaccharide profiles of Asian commercial honeys

Mérine Dumté and Merilyn Manley-Harris

Department of Chemistry, University of Waikato, Private Bag 3105, Hamilton 3240, New Zealand (e-mail: *manleyha@waikato.ac.nz*)

Keywords: Asian commercial honey; oligosaccharides; moisture and monosaccharide content

As part of the development of a method to detect honey in imported materials, a database of the oligosaccharide composition of a range of Asian commercial honeys has been prepared. Low maltose contents were detected compared with literature values for honey from Europe, North Africa and South America; with this exception oligosaccharide contents were similar to those in the literature. Moisture contents were slightly high compared with literature values for Europe and North America but comparable with literature values for Asia. Moisture, monosaccharide and sucrose contents were generally within the limits applied by the Codex. Four honeys were apparently adulterated.

Introduction

In New Zealand an Import Health Standard (IHS) for processed bee products exists pursuant to Section 22 of the Biosecurity Act 1993. This IHS specifies the requirements to be met for the effective management of risks associated with the importation of specified processed bee products.[1, 2] Foods, confectionary, dietary supplements and medical preparations containing greater than 2% of honey require an import permit. To assist in the enforcement of this IHS by the Ministry of Agriculture and Forestry (MAF) it has been necessary to develop a method for the detection of honey at low levels in such materials. The method described here is based upon the detection and quantification of the relatively uncommon oligosaccharides that derive from reversion in honey during maturation. As part of the validation of the method we have undertaken a survey of oligosaccharides in commercial honeys of Asian origin.

Although an extensive literature describes the oligosaccharide profiles of honeys from Europe, North and South America, and North Africa, few articles describe samples of Asian origin. Studies about adulteration analysed three commercial Chinese acacia honeys but did not actually tabulate the results, as the honeys were intended only to test a validation method.[3, 4] Another study described 81 samples from three different honeybee species of Nepalese origin but only tabulated the results for sucrose, turanose and maltose, grouping the other disaccharides together without a statistical analysis,[5] while a study of honeys from the Phillipines measured only fructose, glucose and sucrose.[6]

Materials and Methods

Materials

IRC-50 resin standard grade was purchased from BDH Chemicals Ltd. $NaBH_4$ was obtained from Alfa Aesar - A Johnson Matthey Company. Tri Sil HTP reagent was obtained from Thermo Fisher Scientific Inc. Methanol was of HPLC grade and supplied by either Scharlau or Ajax Finechem Pty Ltd. Pyridine (99+%, A.C.S. reagent) was purchased from Sigma-Aldrich Co. and dried over molecular sieve. Water was obtained from a Crystal Pure Ultra Pure Water System. Glacial acetic acid (analytical reagent) was purchased from Ajax Finechem Pty Ltd.

Fructose, sucrose, turanose, maltose, nigerose, -trehalose, palatinose, melibiose, gentiobiose, isomaltose, melezitose, raffinose, maltotriose, panose, isomaltotriose, xylitol and kojibiose were obtained from Sigma-Aldrich Co.; glucose was purchased from BDH AnalaR; cellobiose was purchased from BDH Biochemical; maltulose was from CMS Chemicals Ltd.; 1-kestose was isolated from oligofructose kindly supplied by Salkat New Zealand, using HPLC and confirmed by NMR spectroscopy.

Honey samples, which had been intercepted at the New Zealand border, were supplied by MAF Biosecurity (New Zealand) and were stored at 4 °C until required. The country of origin was recorded by MAF personnel and as indicated by labelling. Samples were warmed to 40 °C and stirred to remove crystallisation before analysis.

Determination of moisture content

Moisture content of the samples was determined using a Misco Palm Abbe PA203 Digital refractometer. Measurements for each sample were taken every 10 seconds until three consecutive stable values were obtained.

Preparation of standards

Three individual solutions of xylitol were prepared as internal standards. Each of the triplicate measurement of samples and standards used a separate internal standard.

$NaBH_4$ (5 mg per mg of standard) was weighed into a glass vial (7 mL) and the required amount of sugar standard added. Deionised water (1 mL) was added. The vial was heated (50 °C, 4 h) then cooled and freshly washed IRC-50 resin added to remove excess $NaBH_4$ until no more gas was evolved. The standards were filtered and evaporated under reduced pressure until nearly all the solvent had evaporated. The remaining liquid was transferred quantitatively into a glass vial (7 mL) and evaporated under a stream of dry nitrogen (40 °C) followed by co-evaporation six times with acidified methanol (2 mL) to remove residual borate. Xylitol internal standard (100 µL) was added and the solution evaporated under a stream of dry nitrogen (40 °C) until no liquid was visible, then dried overnight in a vacuum oven (40 °C).

Reduced sugars were per-*O*-trimethylsilylated by adding dry pyridine (900 µL) and sonicating (5 min). Tri Sil HTP (100 µL) was added and the vials heated (10 min, 75 °C).

The vials were left to cool and subsequently centrifuged (3 min, 3000 rpm). The supernatant (0.5 mL) was transferred to a clean GC vial, diluted appropriately using dry pyridine (~1 mL) and subsequently analysed by GC-FID. Non-reducing sugars were per-*O*-trimethylsilylated without the prior reduction step.

Response factors were determined by analysing each available standard in triplicate with varying amounts of compound and a consistent amount of internal standard. The response factor was taken from the gradient of a linear fit to the graph of the ratio peak area standard: peak area xylitol versus the ratio weight standard: weight xylitol. Sugars for which standards were not available were quantified using the mean response factor for di-or trisaccharides as appropriate.

Preparation of samples

Samples were prepared in triplicate. Honey (approximately 15 mg) and $NaBH_4$ (60-70 mg) were weighed into a glass vial (7 mL) and deionised water (1 mL) was added. The vial was heated (50 °C, 4 h) then cooled and freshly washed IRC-50 resin added to the vial to remove excess $NaBH_4$ until no more gas evolved. The samples were filtered, then evaporated under reduced pressure until nearly all the solvent was removed. The remaining liquid was transferred quantitatively into a glass vial (7 mL), evaporated under a stream of dry nitrogen (40 °C) and co-evaporated six times with acidified methanol (2 mL) to remove residual borate. Xylitol internal standard (100 µL) was added and the solvent evaporated to near dryness. The vials were then dried overnight in a vacuum oven (40 °C). Reduced samples were per-*O*-trimethylsilylated by adding Tri Sil HTP (1.5 mL), sonicating for 10 mins and heating (10 min, 75 °C). The vials were left to cool and subsequently centrifuged (3 min, 3000 rpm). The supernatant (0.5 mL) was transferred to a clean GC vial and subsequently analysed by GC-FID.

Gas Chromatography with flame ionisation detection (GC-FID)

GC-FID was carried out using a gas chromatograph (Model 6890N Series, Agilent Technologies) equipped with an autosampler (Model G2614A Series Autosampler, Agilent Technologies) and injector unit (Model 7683 Series Injector, Agilent Technologies). Analyses were carried out with an on-column injector and using a 30 m × 0.32 mm × 0.25 µm Zebron ZB-5 capillary column (phase: 5%-phenyl-95%-dimethylpolysiloxane) and FID detection. Carrier gas was hydrogen at 2.6 mL/min. Two microliter samples were injected into the column, with the injector temperature tracking the oven temperature. Detector temperature was maintained at 325 °C. The oven temperature program was 150 °C (5 min) + 3 °C/min to 300 °C + 1 °C/min to 325 °C (10 min).

Results and discussion

The moisture contents of the honey samples are given in Table 1.

Compared with the average moisture content of USA floral honeys of 17.2% (range: 12.2 – 22.9%),[7] or the average moisture content of honeys from the Madrid province of Spain of 16.13% (range:13.00-18.30%),[8] the moisture contents of Asian honeys (average: 18.3% , range: 16.5-20.4%) are slightly higher. The Codex Alimentarius Commission for honey prescribes a limit of 20% moisture, except for *Calluna* honey at not more than 23%.[9] Eight of the samples supplied had moisture contents higher than the 20% limit and these are listed separately in Table 2.

Table 1. Moisture contents of Asian honey samples.

Country of origin (number of samples)	Average moisture content (range) (%)
China (n = 6)	17.8 (17.2 – 19.1)
India (n = 7)	19.4 (17.8 – 20.3)
Indonesia (n = 1)	18.4
Japan (n = 2)	17.4 (16.5 – 18.2)
Malaysia (n = 2)	16.8 (16.7 – 16.8)
Russia (n = 1)	18.1
South Korea (n = 1)	18.4
Vietnam (n = 2)	19.9 (19.3 – 20.4)
Average (n = 22)	18.3 (16.5 – 20.4)

Table 2. Moisture contents of some honeys that exceeded 20% as recommended in the Codex Alimentarius.

Sample origin	Moisture content (%)
China	22.9
India	21.2
Vietnam 1	22.4
Vietnam 2	27.4
Vietnam 3	28.7
S. Korea	20.9
Sri Lanka 1	21.0
Sri Lanka 2	20.5

A comparison of moisture content of honeys by honey bee in Nepal gave 21.51 ± 2.38, 20.12 ± 2.66 and 17.14 ± 2.56 for *Apis dorsata*, *A. cerana* and *A. mellifera* respectively;[5] a similar comparison in the Phillipines gave 23.1 ± 2.3, 22.0 ± 3.7 and 19.5 ± 1.6, respectively.[6] The latter study gave possible causes for the higher range of values as bee species, handling practices and environmental humidity, although the former study narrowed the possibilities to the bee species, by collecting on the same day and from the same district. It is likely that some of the honeys in the present study may have originated from the indigenous Asian honeybees *A. dorsata* and *A. cerana* and so, with the exception of two samples from Vietnam, the moisture content difference is appropriate. Nevertheless, honeys for which the moisture content exceeded 20% have been separated in case the moisture content is due to some type of adulteration.

Because of the problems of chromatographic resolution of the very large number of di- and tri-saccharides present in honey and the difficulty and expense of obtaining

standards, many studies quantify only a representative sample of sugars. Gas chromatography of per-*O*-trimethylsilylated alditols gives good resolution but suffers from two drawbacks. Firstly, reduction of sugars with a fructose reducing end results in an epimeric pair of sugar alditols, thus complicating the chromatography. Secondly, because of symmetry considerations, reduction gives rise to three pairs of identical species which it is not possible to resolve. These are nigerose and the first peak of turanose, the second peak of turanose and the first peak of maltulose, and the second peak of maltulose and maltose. These pairs of peaks are therefore grouped in subsequent tables. Fructose and glucose cannot be distinguished by this method and so are combined and listed as monosaccharides.

The mean weight % of the sugars found in the Asian honey samples by country are given in Table 3, together with the global means and ranges.

Table 4 lists the sugar contents for honeys whose moisture contents exceeded 20%.

Several of these honeys also fell below the range specified by the Codex Alimentarius for monosaccharides of not less than 60g/100g;[9] two honeys whose moisture contents were within the specified range but whose monosaccharide sugar content fell below 60% are listed separately in Table 5.

Comparison of the data in Table 3 with the literature for honey samples from Europe, principally Spain,[8, 10, 11, 12, 13] North Africa,[14, 15] North America,[16] and South America[17] shows that the ranges for cellobiose, laminaribiose, gentiobiose and palatinose are displaced slightly higher than the literature and isomaltose and raffinose are slightly lower. A proper comparison is not possible as not all authors list all sugars and there is also considerable variation in the literature. 1-kestose, erlose and melezitose are lower than some of the literature; the latter two sugars are associated with honeydew honey,[18] and the lower values may indicate a lower contribution of this type of honey. The greatest difference is in the value for maltose: assuming that maltose is the sole contributor to the maltose + maltulose(2) peak, maltose has a mean value of 1.49 and a range of 1.04-2.03. This is considerably lower than observed in the literature with the exception of honeys from North America determined by HPLC.[16] The reasons for this are unclear, since methodologies in the literature vary; significantly lower levels of maltose were found in honeys from *A. dorsata* and *A. cerana* than in *A. mellifera*.[5] It is also possible that it relates to the current ready availability of corn syrups for feeding in Europe and the

Table 3. Mono- and oligosaccharides in Asian honey samples.

	China (n = 6)	India (n = 7)	Japan (n = 2)	Malaysia (n = 2)	Vietnam (n = 2)	Indonesia (n = 1)	Russia (n = 1)	Thailand (n=1)	South Korea (n = 1)	Mean	Std Dev	Range
Sugar	%w/w											
Monosaccharides	68.84	68.84	72.13	66.92	69.53	68.3	85.05	59.91	77.79	70.81	7.10	59.91–85.05
Sucrose	0.73	0.73	0.15	0.06	0.11	0.27	0.12	0.04	0.02	0.25	0.28	0.01–0.73
Trehalose	0.1	0.1	0.08	0.1	0.09	ND	0.05	0.12	0.02	0.08	0.03	0–0.12
Cellobiose	0.38	0.38	0.3	0.47	0.39	0.49	0.4	0.66	0.42	0.43	0.10	0.3–0.66
Laminaribiose	0.35	0.35	0.25	0.6	0.43	0.17	0.25	0.23	0.12	0.31	0.15	0.12–0.6
Nigerose + Turanose1	1.16	1.16	0.8	0.52	0.66	0.83	1.92	2.17	1.55	1.20	0.57	0.52–2.17
Turanose2 + Maltulose1	0.66	0.66	0.44	0.28	0.36	0.14	1.26	1.32	0.95	0.67	0.42	0.14–1.32
Maltulose2 + Maltose	1.39	1.39	1.45	1.31	1.38	1.04	1.66	2.03	1.76	1.49	0.29	1.04–2.03
Kojibiose	0.32	0.32	0.15	0.21	0.18	0.09	0.49	0.69	0.56	0.33	0.20	0.09–0.69
Melibiose	0.4	0.4	0.13	0.33	0.23	0.2	0.79	1.13	1	0.51	0.37	0.13–1.13
Gentiobiose	0.21	0.21	0.05	0.28	0.17	0.13	0.11	0.37	0.4	0.21	0.12	0.05–0.4
Palatinose	0.56	0.56	0.24	0.51	0.38	0.25	1.15	1.65	1.58	0.76	0.55	0.24–1.65
Isomaltose	0.37	0.37	0.56	0.77	0.67	ND	ND	0.09	ND	0.47	0.25	0–0.77
Raffinose	0.03	0.03	0.01	ND	0.01	ND	0.01	ND	ND	0.02	0.01	0–0.03
Kestose	0.12	0.12	0.08	0.02	0.05	0.01	0.18	0.11	0.15	0.09	0.06	0.01–0.18
Erlose	0.32	0.32	0.17	0.02	0.10	0.01	0.73	0.25	0.16	0.23	0.22	0.01–0.73
Melezitose	0.03	0.03	0.01	0.02	0.02	ND	0.07	0.05	0.05	0.03	0.02	0.01–0.07
Maltotriose	0.09	0.09	0.05	0.12	0.09	0.04	0.17	0.17	0.1	0.10	0.05	0.04–0.17
Panose	0.08	0.08	0.13	0.16	0.15	0.18	0.18	0.24	0.2	0.16	0.05	0.08–0.24
Isomaltotriose	0.01	0.01	0.01	0.03	0.02	0.04	0.04	0.03	0.02	0.02	0.01	0.01–0.04

Table 4. Mono- and oligosaccharides in Asian honey samples whose moisture content exceeded 20%.

	China	India	Vietnam 1	Vietnam 2	Vietnam 3	S. Korea[1,2]	Sri Lanka 1[2]	Sri Lanka 2[2]
Sugar								
Monosaccharides	57.43	57.43	57.79	63.29	56.16	52.82	77.30	85.75
Sucrose	0.96	0.96	0.22	0.10	0.03	1.19	0.06	0.06
Trehalose	0.03	0.03	0.08	0.03	0.02	0.06	ND	0.14
Cellobiose	0.15	0.15	0.32	0.16	0.26	0.35	0.47	0.71
Laminaribiose	0.21	0.21	0.13	0.29	0.05	0.26	0.18	0.78
Nigerose + Turanose1	0.50	0.50	0.59	0.60	1.13	0.78	2.63	2.00
Turanose2 + Maltulose1	0.22	0.22	0.08	0.34	0.57	0.49	1.67	1.41
Maltulose2 + Maltose	1.20	1.20	0.53	1.50	1.04	2.33	2.20	2.79
Kojibiose	0.14	0.14	0.05	0.28	0.28	0.28	0.82	0.56
Melibiose	0.18	0.18	0.08	0.20	0.24	0.47	1.03	0.71
Gentiobiose	0.07	0.07	0.07	0.08	0.08	0.21	0.11	0.34
Palatinose	0.28	0.28	0.11	0.44	0.01	0.46	1.70	0.79
Isomaltose	ND	ND	ND	0.32	ND	ND	ND	ND
Raffinose	0.01	ND	0.01	0.00	0.01	0.02	ND	ND
Kestose	0.14	ND	0.01	0.09	0.04	0.33	0.09	ND
Erlose	0.49	ND	0.02	0.05	ND	2.37	0.26	0.17
Melezitose	0.03	ND	ND	ND	0.00	0.11	0.09	0.03
Maltotriose	0.12	ND	0.02	0.07	0.03	0.29	0.18	0.24
Panose	0.04	ND	ND	0.14	0.05	0.16	0.21	0.15
Isomaltotriose	0.00	ND	ND	0.01	ND	ND	0.04	ND

[1] possibly a honeydew honey as it has elevated erlose content.

[2] These honeys have maltose contents that fall outside the range for other Asian honeys but not outside values quoted in the literature for Europe, N. Africa and S. America.

Americas and that the North American paper predates this practice.

Four of the samples were apparently adulterated: two from China and one (possibly) from the Phillipines, either by inappropriate feeding with sucrose or addition of sucrose syrup; this was deduced from the presence in these samples of a large sucrose peak.[4, 10] The sample from the Phillipines (which was labelled "pure honey") may possibly be a honeydew honey as it has an elevated erlose content, but the sucrose content (9.94%) is considerably higher than the 5% permitted by the Codex.[9] It should be noted, however, that a mean of 9.51% was found from colonies of *A. cerana* in the Phillipines;[6] and that in another study sucrose ranged to higher levels in the two Asian honeybees compared with *A. mellifera*.[5] One sample from Malaysia was adulterated and exhibited enlarged peaks for maltose (-6 % w/w) and maltotriose (~5%) probably due to addition of, or inappropriate feeding with starch syrups.[4, 19, 20] The presence of adulteration makes it difficult to accurately quantify minor oligosaccharides. The mean weight % of sugars in apparently adulterated samples by country is given in Table 6.

Acknowledgements

The authors would like to thank Zoran Sinovcic of MAF Biosecurity (New Zealand) for kindly supplying the honey samples.

References

1. Biosecurity New Zealand, *Import Risk Analysis: Honey Bee Products*, Ministry of Agriculture and Forestry: Wellington, New Zealand, 2004.

2. Ministry of Agriculture and Forestry, *Import Health Standard for Specified Processed Bee Products*: Wellington, New Zealand, 13 November 2006: Wellington.

3. Cotte J.F., Casabianca, H., Chardon, S., Lheritier, J., Grenier-Loustalot, M.F. *J.Chromatogr. A*, **2003**, *1021,* 145-155.

4. Cotte, J.F., Casabianca, H., Chardon, S., Lheritier, J., Grenier-Loustalot, M.F. *Anal. Bioanal. Chem.* **2004**, *380*, 698-705.

5. Joshi, S.R., Pechhacker, H., Willam, A., von der Ohe, W. *Apidologie* **2000**, *31*, 367-375.

6. Laude, V.T., Naegel, L., Horn, H. *Apidologie* **1991**, *22*, 371-380.

7. White, J.W. Jr. "Honey". In J.M. Graham, (Ed.), *The Hive and the Honey Bee* (pp. 869-925), Dadant & Sons: Hamilton, Illinois, 1992.

8. Sanz, M.L., González, M., de Lorenzo, C., Sanz, J., Martínez-Castro, I. *J.Sci.Food Agric.* **2004**, *84*, 1577-1584.

9. Codex Alimentarius Commission, *Revised Codex Standard for Honey. Codex STAN 12-1981*, FAO and WHO: Rome, 2001.

10. Ruiz-Matute, A.I., Weiss, M., Sammataro, D., Finely, J., Sanz, M.L. *J. Agric. Food Chem.* **2010**, *58*, 7317-7322; Ruiz-Matute, A.I., Brokl, M., Soria, A.C., Sanz, M.L., Martínez-Castro, I. *Food Chem.*

Table 5. Mono- and oligosaccharides in Asian honey samples whose monosaccharide content was less than the 60% prescribed by the Codex alimentarius but whose moisture content was within the specified range.

	China	Thailand
Sugar		
Monosaccharides	54.06	53.08
Sucrose	0.30	0.02
Trehalose	0.16	0.03
Cellobiose	0.19	0.60
Laminaribiose	0.23	0.24
Nigerose + Turanose1	0.76	2.13
Turanose2 + Maltulose1	0.64	1.21
Maltulose2 + Maltose	0.88	1.56
Kojibiose	0.14	0.62
Melibiose	0.20	1.03
Gentiobiose	0.03	0.38
Palatinose	0.23	1.57
Isomaltose	ND	ND
Raffinose	0.01	ND
Kestose	0.08	0.09
Erlose	0.94	0.06
Melezitose	0.09	0.03
Maltotriose	0.10	0.18
Panose	0.02	0.29
Isomaltotriose	0.00	0.05
Moisture content	18.9	17.6

Table 6. Mono- and oligosaccharides in Asian honey samples which were apparently adulterated

	China	China	Malaysia	Philippines[1]
Sugar	**% w/w**			
Monosaccharides	50.02	41.46	51.43	61.74
Sucrose	22.98	30.06	0.27	9.94
Trehalose	0.19	0.24	0.05	0.33
Cellobiose	0.24	0.27	0.53	0.13
Laminaribiose	0.09	0.26	0.17	0.37
Nigerose + Turanose1	0.21	0.31	0.72	1.59
Turanose2 + Maltulose1	0.18	0.20	0.35	1.11
Maltulose2 + Maltose	0.36	0.41	6.12	3.57
Kojibiose	0.09	0.08	0.17	0.27
Melibiose	0.18	0.17	0.30	0.26
Gentiobiose	0.15	0.16	0.29	0.10
Palatinose	0.15	0.19	0.43	0.32
Isomaltose	ND	ND	ND	ND
Raffinose	0.10	0.13	0.01	0.09
Kestose	0.08	0.11	0.01	0.69
Erlose	0.15	0.79	0.04	5.53
Melezitose	0.02	0.03	ND	0.11
Maltotriose	0.01	0.01	5.29	0.27
Panose	0.01	0.00	0.03	0.09
Isomaltotriose	ND	ND	ND	ND
Moisture content:	17.7	17.7	15.9	21.7

[1] Possibly a honeydew honey and possibly an *A. cerana* honey; see section 4.

2010, *120*, 637-642.

11. Sanz , M.L., Gonzalez, M., de Lorenzo, C., Sanz, J., Martínez-Castro, I. *Food Chem.* **2005**, *91*, 313-317.

12. Bentabol Manzanares, A., Hernández García, Z., Rodríguez Galdón, B., Rodríguez Rodríguez, E., Díaz Romero, C. *Food Chem.* **2011**, *126*, 664-672.

13. de la Fuente, E., Ruiz-Matute, A.I., Valencia-Barrera, R.M., Sanz, J., Martínez Castro, I. *Food Chem.***2011**,*129*, 1483-1489.

14. Terrab, A., Vega-Pérez, J.M., Diez, M.J., Heredia, F.J. *J.Sci.Food Agric.* **2001**, *82,* 179-185.

15. Ouchemoukh, S., Schweitzer, P., Bachir Bey, M., Djoudad-Kadji, H., Louaileche, H. *Food Chem.* **2010**, *121*, 561-568.

16. Swallow, K.W., Nicholas H., Low, N.H. *J.Agric.Food Chem.* ***1990***, *38*, 1828-1832.

17. Da Costa Leite, J.M., Trugo, L.C., Costa, L.S.M., Quinteiro, L.M.C., Barth, O.M., Dutra, V.M.L., De Maria, C.A.B. *Food Chem.***2000**, *70*, 93-98.

18. Astwood, K., Lee,B., Manley-Harris, M. *J. Agric. Food Chem.* **1998**, *46*, 4958-4962.

19. Cordella, C., Militão, J.S.L.T., Clément, M-C., Drajnudel, P., *Anal. Chim. Acta* **2005**, *531*, 239-248.

20 Megherbi, M., Herbreteau, B., Faure, R., Salvador, A. *J. Agric. Food Chem.* **2009**, *57*, 2105-2111.

Melt-extruded polyethylene oxide (PEO) rods as drug delivery vehicles: Formulation, performance as controlled release devices and the influence of co-extruded excipients on drug release profiles

Michael R. Mucalo [1] and Michael J. Rathbone[2]

[1]Chemistry Department, Faculty of Science and Engineering, University of Waikato, Private Bag 3105, Hamilton 3240. (Email: *m.mucalo@waikato.ac.nz*). Author to whom correspondence should be addressed.

[2]International Medical University, No. 126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia.

Introduction

The utility of controlled release medication formulations lies in their ability to keep drugs at steady levels in the blood plasma of recipients and within the termini of the maximum and minimum effective therapeutic levels. This avoids the "ups" and "downs" of medication levels within the body which would have been the result had conventional immediate release tablets been administered instead. In the veterinary field, controlled release medications are essential[1] because of the logistical difficulties of administering drugs on a regular (e.g., daily) basis to animals. The chief advantages of controlled release veterinary medications lie in the ease with which they can be administered; decrease in stress for animals, owing to less need for rounding up and frequent dosing; and, most importantly for farmers, the reduced cost of treatment relative to that for a multiple dosage regime.

Polyethylene oxide (PEO) is considered a valuable material in controlled release drug delivery science in the human field of medicine because drugs can diffuse through the viscoelastic mass that PEO forms upon gelation by water. In addition to this important property, PEO can also be used as a flocculent, viscosity-inducing agent, as a lubricant as well as a dispersant and water retention agent.[2] The basic structural unit of the PEO polymer is the ethylene glycol skeleton, which can be written as HO-(CH_2-CH_2-O)$_n$-H. PEO grades (and the nomenclature for these) are determined by the molecular weight of the polymer. Below 25,000 Da, PEOs are termed polyethylene glycols or "PEGs".

The use of PEOs and PEGs in pharmaceutical products is increasing because of their widening acceptance by pharmaceutical regulation agencies. This is attributed to PEOs and PEGs having good physical and chemical stability, dissolving easily in water over time, and possessing the ability to be compressed. Owing to their relatively low melting point (*ca.* 70 ºC) , the higher molecular weight PEO polymers like PEO-303 (as supplied by DOW Chemicals), which has a molecular weight of approximately 7,000,000 Da, are amenable to hot melt extrusion (HME) to produce cylinders or tablets which can incorporate other materials like the active drug and excipients. Pharmaceutical hot melt extrusion (HME), a widely used method in the plastics processing industry, involves the physical mixing of a drug and carrier at the fusion temperatures of the carrier (usually a polymer). Several publications have focussed on this use.[3-8] Some reports involving HME focus on addressing the challenges of increasing the dissolution rate of poorly water-soluble drugs in developing dosage forms[6]. Other reports discuss the advantages of HME being a more efficient and cost effective method for manufacturing various dosage forms.[7] A previous study looked more at manufacturing issues, such as the pursuit of uniform cylindrical shape and homogeneous density.[8] It also looked at additives which could influence mechanical and dissolution properties of the extruded substance which have a bearing on its usefulness as a controlled release drug delivery device.

In the present study, we have sought generally to investigate the innovative use of melt-extruded PEO rods containing commonly used drug substances, with a view to its potential application in extended release drug delivery for the treatment of bovine mastitis in the veterinary sector. Mastitis is an intramammary infection common in lactating cows[9] which is of particular concern in the agricultural sector of countries with major dairy farming-based economies. In New Zealand, this is particularly so because the clinical and subclinical forms of mastitis can bring about significant financial losses caused by lower milk production (from rejected milk), lower milk quality (leading to lower value due to degradation), loss of valuable bovine breeding stock (owing to the need to eliminate infected animals), as well as the associated medical and labour costs with treatment or management of the condition in a commercial dairy herd.

Teat treatment options have been widely reported in the science literature. For example, patents from the mid 1970s[10] have described "bovine teat dip" or "aqueous compositions to aid in the prevention of bovine mastitis". "Teat seals" are contemporarily used and are usually applied to cows that have dried off. In such a treatment, the teat of the cow is infused with two syringes: one which contains an antibiotic like cloxacillin and the second containing some inorganic salts in an oily base which serve to seal the teat so blocking off access to the udder by mastitis bacteria during the dry period. Teat seals containing either reduced antibiotic levels or no antibiotic levels have been reported to be successful at combating the incidence of mastitis in dairy herds in past studies.[11] The drive for reducing the antibiotic levels has emerged from concerns for the overuse of antibacterials in combating mastitis.[11] The use of viscoelastic gels such as PEO or PEG for teat

seals has obvious advantages in that not only can the gel function as a physically soft barrier seal but also it potentially provides a matrix for the extended release of various medications such as antibiotics or other types of medication into the mammary gland. In particular, the melt extrusion process can produce lengths of PEO/drug rods directly that could possibly be used for teat sealing purposes by direct insertion into the teat channel.

It is thus of interest to investigate the conditions under which such extruded PEO rods can be produced, and the factors influencing the release of drugs from such matrices when they are placed in or exposed to aqueous, though physiological-mimicking, milieu. In the present work, we have thus conducted a feasibility study of the manufacture of the extruded rods using simple benchtop extruders from dry drug/PEO mixtures and the carrying out of a UV-based assay of drug release from the rods into an aqueous alcoholic medium. Studies focussed initially on the general behaviour of release from PEO rods containing drug alone. They were then extended to probe the effect of excipients co-extruded with the PEO and drug to determine if a significantly greater extent of controlled release could be achieved. Note that this aim, qualitatively assessed by inspection of the UV-measured drug release profiles over a 24 hour period (see later), was the primary focus of this study rather than an in-depth assessment of the kinetics of release from these particular rods, which should only be attempted in a carefully designed and considered study involving larger data sets for release of drug than have been used in the present study.

In the course of the work some important manufacturing issues were also identified when certain excipients were incorporated. These have also been covered, as they were regarded as useful observations for future development of this field. A wide range of excipients was considered for inclusion in the PEO/drug extrudates with the express intention of creating a useful material from a veterinary point of view (i.e., a device that could offer controlled release over many hours or even days if possible), compared to several hours. In attempting to cover all feasible options to achieve this goal, a wider range of excipients than might have been considered in earlier literature on PEO HME-related topics had to be employed. This has led to some useful observations on their actual or apparent effects in trying to retard PEO gelation, with one aspect not directly discussed in this publication but covered in a presentation in the 2011 NZIC conference held in Hamilton,[12] being studied further for commercial application.

Materials and Methods

Most chemicals (polyethylene oxide-303, molecular weight of 7,000,000 (PEO-303, DOW), the individual drugs, buffer salts, excipients and ethanol) were sourced from commercial suppliers as either Analytical grade or laboratory grade reagents. Diazepam, hydrochlorothiazide, naproxen sodium, and chlorpheniramine maleate) were kindly donated by Douglas Pharmaceuticals, West Auckland, New Zealand) and were used without further purification.

Determination and testing (for adherence to Beer's Law behaviour) of candidate drugs that could be co-extruded with PEO for release studies

By consulting pharmacopoeia,[13] a range of drugs was decided upon for incorporation into PEO by melt extrusion. These are summarised in Table 1. After sourcing the drugs, they were checked for their solubility in either water (initially for some drugs) or in 40% (v/v) AR grade (Rhone Poulenc) ethanol, and accurately known concentrations of them were prepared and then scanned using a Biochrom Libra S12 UV spectrophotometer. This was done to determine: 1) the characteristic UV/Vis spectrum of the drug over 200-400 nm to check if it conformed with that shown in the pharmacopoeia and 2) to check that a reasonably linear Beer's Law plot of UV absorbance (at a chosen absorption maximum in the drug's spectrum) versus concentration of the drug was obtained within certain concentration limits. The results of 2) also led to a graphical slope value which could be

Table 1. Drugs used in the release studies from extruded PEO rods[13].

Drug	UV absorption maximum (λ_{max}) / nm in 40% EtOH	Melting point/ °C	Therapeutic use
Sodium Salicylate	296	300 °C ,	Analgesic
Progesterone	246	126-131 °C	Progestational steroid
Hydrochlorothiazide	271	268 °C (decomposes)	Diuretic
Diazepam	254	131-135 °C	Tranquilliser
Chloropheniramine Maleate	263	130-135 °C	Allergy treatment
Methyl Paraben	257	125-128 °C	Preservative
Ethyl Paraben	257	115-118 °C	Preservative
Propyl Paraben	257	95-98 °C	Preservative
Bromazepam	235, 260	247 °C	Tranquilliser
Metoprolol Succinate	222, 274	120 °C	β-Adrenoceptor blocking agent
Naproxen Sodium	226, 263, 267, 271, 317, 331	156 °C	Analgesic

used in future studies for calculating concentrations of the drug in receptor media in which it had been released from gelled PEO extruded rods.

A list of the drugs used in this study together with their melting points and UV absorption maxima is given in Table 1. Although this research was done with a view to applying it to the manufacture of teat seals and for the treatment of mastitis in cows, the drugs chosen for study were not ones which would be considered for treating mastitis. This was because we wanted to know in general the extent to which the gelation chemistry of melt-extruded PEO could be modified to influence release. Hence the choice of drugs used in the study was chiefly based on their different molecular characteristics (e.g., difference in polarities), with the main aim being to test how well they were released from the rods into a receptor medium when they were co-extruded with PEO either on their own or with various excipients. They were also chosen on the basis of their solubilities in the 40% v/v ethanolic release solvent used (see later).

Manufacturing of the Extruded Rods

It was important for this research to develop a reliable bench scale manufacturing method for the melt extruded rods from polyethylene (oxide). This was achieved using a small bench-sized (in-house manufactured) extruder which had a heating unit wrapped around a stainless steel augur screw that was heated through a programmable ATHENA temperature controller (Fig.1)

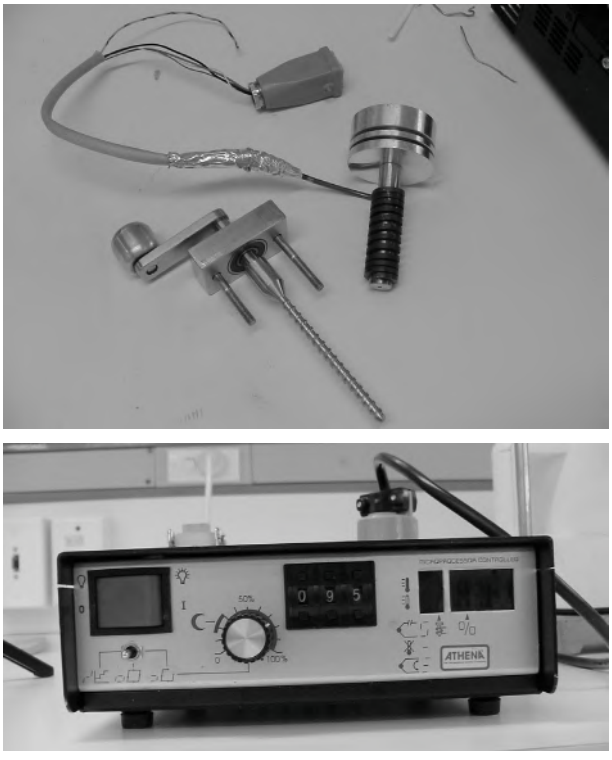


Fig.1. *Upper:* The extruder and heating jacket (dark-coloured screw attached to barrel with wires). *Lower:* The ATHENA extruder temperature control unit.

The methodology for using the extruder to form the extruded rods was as follows. By means of a vice clamped to the edge of a lab bench, the augur screw and heating unit shown in the upper part of Fig. 1 was assembled by inserting the augur screw into the cylinder shaped barrel with heating jacket and held firmly in place with the clamp. The heating jacket was plugged into the heating unit (with heating initiated by setting to 80-100 ^{o}C) and a well-mixed powder consisting of PEO (plus drugs and any excipients) was introduced via a spatula at the top of the barrel in which the augur screw had been inserted. The "crank handle" attached to the augur screw was then turned vigorously clockwise. This action caused the powder to be carried down into the screw and beyond into the heated barrel where the PEO melted and was extruded as a thin rod (Fig. 2) through the small exit point at the end of the barrel. The residence time of the powder mix in the augur screw was thus brief, being less than a minute.

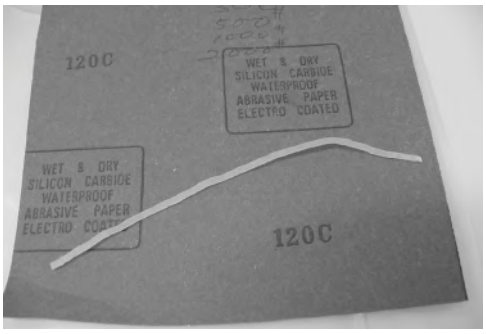


Fig. 2. Typical appearance of a PEO extruded rod. The width of the rod was *ca.* 2.1-2.4 mm. These were initially extruded limp to the touch, but hardened rapidly on cooling to the firmness of a hard plastic rod.

When the actual drugs and/or excipients (added to delay the onset of PEO gelation) were co-extruded with the PEO to form the rods, PEO powder mixes containing these were prepared in 30 g batches on a % (w/w) basis by accurate weighing to give *ca.* 1% (w/w) drug/PEO rods. When mixes were formulated with excipient inclusion in particular, this was done with either 5% or 20% (w/w) excipient. In experiments where the influence of %(w/w) excipient on drug release was being investigated, 10% (w/w) NaCl was included as an additional excipient. Before extrusion, the drug and/or excipient components of the powder mix were well pre-mixed by shaking in a pottle or a large plastic bag to maximise homogeneity. In using this simple extrusion methodology, the physical form of some of the excipients (e.g. chunky sodium chloride or calcium chloride, lumps of paraffin, etc) often provided a challenge to achieving homogeneous PEO/drug/excipient powder mixes (see later discussion). However, the methodology was maintained because the % cumulative concentration versus soaking time plots generated (see later) tended to be independent of the different relative loadings of drugs across samples, and it was the gross trends in drug release that were of main interest in this study for assessing the drug release behaviour from the extruded PEO rods with or without the addition of the various excipients.

Samples were also prepared in which a randomly selected melt-extruded PEO/drug rod system (i.e., 1% metoprolol succinate) was also subjected to physical barrier coating treatments for controlling the rate of PEO gelation in the 40% alcohol/water release medium. A barrier coating sys-

tem containing a 25 % (w/w) combination of SPAN80 (sorbitan mono-oleate), an excipient used for orally taken medical preparations, together with a tabletting excipient called hexaglycerol distearate or "HGDS", was prepared. Coating of the co-extruded PEO/metoprolol succinate drug rods involved the brief dipping of the rods into the hot SPAN80/HGDS melt followed by air cooling until the coating solidified. Samples were generated where completely coated rods were generated but also samples where the bottom only or the bottom and top parts of the rod were left exposed (by scratching off the soft coating after application at ends of the rods). This led to a subset of 4 samples for this particular experiment, i.e., fully coated, coated with one end of rod exposed, coated with both ends exposed and uncoated rods. Two samples per coating permutation were prepared. These systems were assessed for drug release in the receptor medium following the same methodology described below.

In vitro *drug release test methodology*

For assessing the release of drugs from the extruded PEO/drug/excipient rods, the extruded rods were cut into approximately 2-cm lengths and weighed on a 3-decimal place balance (Mettler). They were then affixed using superglue (and a wire to keep the rod approximately straight) to the ends of plastic spikes that had previously been threaded through the centre of plastic 100 mL pottle lids and glued in place with hotmelt-gun glue (see upper part of Fig. 3). The lids with attached spikes plus affixed rods could then be screwed onto the accompanying plastic 100 mL pottle where fresh receptor medium (in most cases 40% (v/v) A.R. (Rhone-Poulenc) ethanol/water) was added and made up to the 100 mL mark on the pottle. This particular solvent medium was chosen in this study not only to act as a "sink" but also to simulate a biological membrane,[14] which would possess both hydrophobic and hydrophilic character (such as the inside of a cow's teat or a bovine vaginal membrane) so that an implant such as a melt-extruded rod of PEO could, in practical veterinary treatment situations, be pressed against for release of drugs across that membrane.

When rods containing a certain formulation of PEO/drug or PEO/drug/ excipient were assessed for release, the test was done in duplicate using two separate samples made from the same rod. The pottles with rods and receptor medium were then placed inside sample holders on a 37.5 °C shaker water bath which moved from side to side (see lower part of Fig. 3).

A total of four withdrawals of 10 mL of release medium per replicate sample from pottles for each replicate was done with a syringe to assess release. These were done roughly at one hour (1 h), two hours (2 h), three hours (3 h) and twenty four (24 h) hours after initiation of soaking. The 10 mL withdrawn at each time point was then replaced with an equivalent volume of solvent (40% ethanol) to keep the volume at a constant 100 mL during the release experiment. Owing to the number of samples being processed (i.e., withdrawn and replaced by an equivalent volume of fresh release medium) at a given time period, it was challenging to sample at exact times

Fig. 3. *Upper:* Mode of attachment of extruded PEO rods to release media pottle lids. *Lower:* Pottles in the water bath for testing release of drug from PEO extruded rods into 40% (v/v) ethanol/water.

such as 1 h, 2 h and 3 h for exposure time for each sample so these times are nominal only. The 1 h, 2 h, 3 h, and 24 h soaking times could be thought of as the first, second, third and fourth sampling points for testing release of drug from the extruded rods. The first three sampling points (1 h, 2 h, 3 h), for instance, correspond in practice to soaking times of between 1 and 5 hours after exposing the rods to the release media. The final time point corresponds to an exposure of the sample to the release medium for at least 24 hours.

All 10 mL portions of withdrawn samples were placed into separate sealable pottles, allowed to cool and then analysed by UV/Vis spectrophotometry by taking absorbance readings at the λ_{max} values of the particular drug released from the PEO/drug/excipient rod. The whole spectrum of the receptor medium containing the drug from 200-400 nm was usually scanned before measurements to ensure there were no significant spectral interferences from excipients or PEO etc. Drug concentrations in mg/L (ppm) were then calculated using the relevant Beer's Law plot measured for the drug being tested and % cumulative concentration release profiles were then plotted. The % values were based on the 24 h release concentration which was taken to be the time by which 100% release of the drug from the extruded rods might be expected to have occurred. This assumption was justified by the observation that the PEO portion of the extruded rods had completely disintegrated after immersion for 24 hours in the release medium used, i.e., 40% ethanol/water (see later). Often this 24 h release

value was used as a benchmark to assess how much the rod had released relative to the calculated 100% release value into the 100 mL release medium which was determined from the weight and % (w/w) of drug incorporated in the rod.

In addition to soaking of extruded rods from all PEO/drug/excipient combinations studied, an experimental release trial was carried out to test homogeneity of powder mixing of PEO/drug mixes with and without excipients added. The drug tested for release for this experiment was sodium salicylate which was added to give a value of ca. 1% (w/w) in powder mixes of PEO combined with either "cellulose CMC", paraffin or no excipients (i.e., PEO alone with the drug) . Accurately weighed amounts (0.1-0.6 g)of these powders (i.e. they were not extruded into rods) were added to pottles into which 100 mL of 40% EtOH/H2O was then added. These were sealed and left to stand in the dark at room temperature for 48 hours. At the conclusion of this experiment the solutions were subjected to a single UV analysis at 296 nm after shaking to homogenise the contents of the pottles. To ensure complete dissolution of the powders in the release medium, soaking for 48 h was used instead of for 24 h.

Results

Initial Experiments involving the extrusion of PEO (alone) with a wide range of drugs and soaking in 40% EtOH to determine release behaviour

Initial experiments involving the extrusion of PEO(alone)/1% (w/w) drug powder mixtures involving diazepam, hydrochlorothiazide, sodium salicylate, naproxen sodium, bromazepam, methyl (as well as ethyl and propyl) paraben, metoprolol succinate, chlorpheniramine maleate and progesterone gave favourable results with all extruding well at 80-95 ºC. The lengths of rod tested for release were generally in the range of 1.98 to 2.08 cm, width 0.20 to 0.24 cm and weighing from 0.081 to 0.140 g. The glue used to affix the rods to the pottle caps was confirmed not to dissolve in the 40% EtOH release solvent used to give any background in U.V./Vis. spectra.

Generally by the first sampling point ("1 h"), the PEO/drug rods were observed to go limp and progressively dissolve over the next two sampling points, albeit while still being attached to the pottle lids. By the time more than 24 hours of soaking had elapsed, the rods had dissolved and deformed to such an extent that they had become detached from the pottle lid with a diffuse mass of PEO in the approximate form of the rod observed to be lying on the bottom of the release pottle. This approximately 24 hour sampling point was where the highest UV absorbance due to the released drug was usually observed. In fact, the concentration detected was visually levelling off in % cumulative concentration *vs*. soaking time graphs plotted of the release at that point (see later). It was this point (owing to the degraded and dissolved state of the extruded rod) that the cumulative concentration % release plots were calculated (the last point at which is invariably "100%"). The use of this time point at the 100% release was deemed mostly justifiable because a significant proportion of the drug co-extruded into the rod had released after only the third time point for measuring release (i.e., up to 90 % of the expected amount based on the % (w/w) of drug in the extruded rod for some drugs). Hence there is likely to be less than 10% of the original drug amount still resident in the diffuse mass of PEO gel lying at the bottom of the release pottle after 24 h of soaking.

Graphs of cumulative % concentration of drug released vs. *soaking time for drugs co-extruded solely with PE.*

A wide range of commonly used drugs (as shown in Table 1) were co-extruded with PEO alone at a loading level of approximately 1% (w/w). Two cumulative concentration % vs. time and % release vs. time plots for drugs with differing solubility properties in aqueous solutions are shown in Fig. 4, namely diazepam, which is largely insoluble; and Naproxen sodium, which is soluble. Both drugs, however, dissolved in the 40% EtOH/water release medium to produce UV-analysable solutions. Two curves per drug are shown in Fig. 4 for the diazepam/PEO system and serve to show the consistency of release behaviour for each of the two replicates per drug tested. The shape of the curve, to which a logarithmic trend-line is best fitted, is strongly representative of the typical drug release behaviour observed throughout this study from the extruded rods, namely, a steep increase in drug release at the first, second and third time (sampling) points followed by a plateauing or leveling off by the "24 h" timepoint. This release behaviour is obviously dominated by the fact that the rods swell rapidly via hydration to the point that they drop off the pottle lids to rest at the bottom of the sampling containers.[15] The same curve shape is observed when the actual UV measured concentration data from each replicate rod are plotted *vs.* the time of soaking, implying that this shape is not an artefact of using cumulative concentration as a unit. Hence, the speed at which gelation occurs for PEO co-extruded for drugs without any added excipients is leading to rapid loss of drug from the rods. Indeed in a study where a related polymer PEG6000 was co-extruded with a poorly soluble drug, 17β-estradiol hemihydrates,[16] the PEG6000 (and other polymers co-extruded in separate samples) were found to be facilitating the transport of this relatively insoluble drug into solution.

In the present study, although the cumulative concentration % release versus time plots gave very similar appearances over all drugs trialled, the actual cumulative concentration % release values at the first three sampling points did exhibit some variation, depending on which drugs were tested. The range of release concentrations is illustrated in Fig. 5 for all replicates tested of the drugs studied. This shows the wide variation in concentrations at the 1h, 2h and 3h sampling points. Progesterone, sodium salicylate and naproxen sodium exhibit the highest release over that time period, probably because of their higher solubilities in the release media. Values for the % cumulative concentration range for all the drugs tested range from the about 45% to 70%.

Visually the PEO extruded rods went limp very quick-

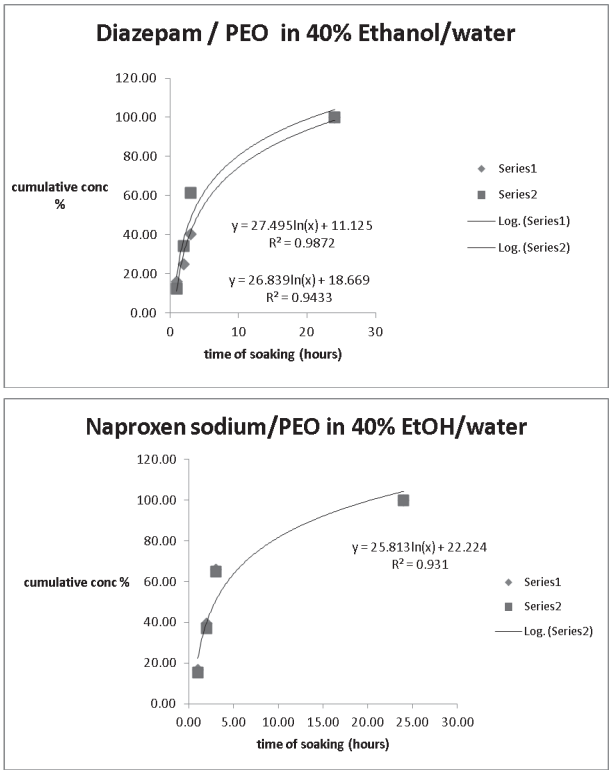


Fig. 4. Cumulative concentration versus time of soaking for (upper) Diazepam/PEO (plots for both replicates shown), and (lower) Naproxen sodium/PEO co-extruded rods in 40% ethanol at 37ºC.

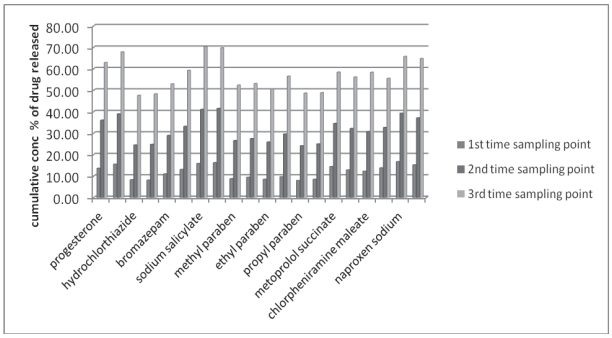


Fig. 5. UV-assayed % cumulative concentrations measured at 1 h, 2 h and 3 h soaking times (in 40% EtOH/H_2O at 37 ºC) for release of drug from melt extruded rods of PEO (alone) with various drugs. Sampling points for each group of 3 bars per replicate sample for drugs should be read from left to right.

ly when immersed in the release medium, as is evident in Fig. 6. In terms of how "accurate" the 100% release assumption at 24 hour sampling was concerned, Fig. 7 shows a plot of the comparison of observed 24 hour release concentrations (in ppm) for all replicates of drugs illustrated in Fig. 5, with their calculated 100% release value based on the weight of the rod and weight percent of drug inside each rod and, furthermore, assuming 100% release of that into the 100 mL of release solvent. As is evident, there is a large variation of agreement between the calculated 100% and observed release values. Most of the % variance in agreement was positive, so larger concentrations than expected from calculated 100% release concentrations were actually observed. Some systems like PEO/chlorpheniramine maleate and PEO/metoprolol succinate gave extremely large positive variances, while a few like PEO/bromazepam and PEO/ethyl paraben gave negative variations for their concentrations at 24 hour sampling periods. The many reasons for these variations include inhomogeneities in drug concentration throughout the PEO/drug extruded rod, sampling technique or dilution errors building up in the values calculated for the concentration with time owing to the need to correct the observed concentrations for dilution. However, with most %variance between -20 and +20 %, the results were seen as indicative. With the exception of bromazepam, the replicates for each extruded drug/PEO combination behaved consistently with each other.

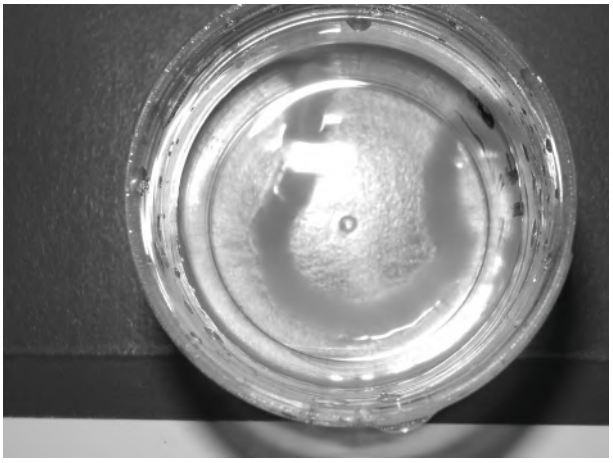


Fig. 6. A melt-extruded PEO rod (U-shaped shadow) and its appearance after soaking in 40% EtOH/H_2O for 1 hour. Lengthening and swelling of the rod as illustrated occurs rapidly within the first hour of soaking.

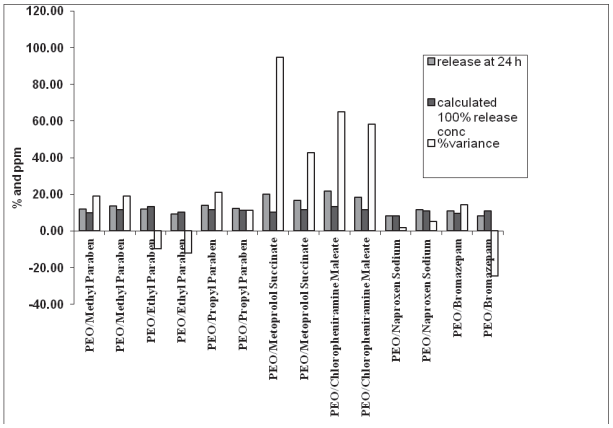


Fig. 7. Comparison of the UV-assayed release profiles of drugs from extruded PEO(alone)/drug rods soaking in 40% EtOH/H_2O solutions at 37 ºC with the concentrations for the calculated 100% release of drugs from rods into 100 mL of release solvent. Release at 24 h, calculated 100% release of drug concentrations and % variance should be read from the left to right columns respectively per replicate sample tested for the drugs.

Experiments in which PEO is co-extruded with sodium salicylate and excipients to achieve a greater extent of controlled release

It was obvious from experiments involving extrusion of drugs with PEO alone that the level of release into the 40% EtOH/H_2O medium was very rapid, to the extent that its use as a controlled release material for delivering a drug over a matter of days would be limited, owing to rapid dissipation from the gelating PEO matrix which

visibly leads to its rapid disintegration. PEO forms a hydrogel in aqueous solution. Hydrogels are well known for producing networks which can release drugs rapidly over periods of hours or days. Much work has been done with molecularly based strategies for limiting release such as through crosslinking.[17] However, given that there is an interest in finding simpler ways to do this for veterinary applications where the veterinary industry supplying these pharmaceuticals and the clientele using them prefer lower unit cost of materials utilized for such purposes, physical methods for delaying drug release from the PEO hydrogel were sought instead. Various strategies along these lines have been tried in the past, such as charge interactions between ionic type polymers and charged drugs (not applicable with PEO) and surface diffusion control, where a reduced permeability film resides at the surface along with a thermosensitive switch that may facilitate diffusion given changes in temperatures. The approach taken in this study was simpler in concept and concentrated more on the use of excipients co-extruded with the PEO and drug. Historically, excipients were defined[18] as additives to a pharmaceutical that ensured it had the correct weight, consistency and volume so that administration could proceed in the way intended. This was the role expected of an excipient when the drug delivery vehicle was restricted to the traditional tablet or pill. Nowadays, with more diverse forms of drug delivery vehicles available, the traditional definition has been extended with excipients often performing multiple roles when included in a pharmaceutical formulation. In the present study, it was desired to rein in the fast release characteristics of the PEO when it, alone, was extruded along with the drug. Hence, excipients were chosen so that they might compete with the PEO for water after immersing the extruded rods in the release medium (see Table 2). This, it was envisaged, should then slow down the rate of gelation of the PEO, hence slowing the release of drug from the rods.

Thus, it was necessary to design experiments where various excipients were added to the PEO/drug powder mix before extrusion, so that rods containing these could be manufactured and trialled for their ability to delay release by subjecting them to the identical protocol used for the systems where PEO alone was co-extruded with drug. In testing this simple physical method for controlling release, it was decided to trial a very wide range of possible candidate excipients ; a total of 10 common and novel compounds were co-extruded with PEO. These were PEG6000, cell CMC, "TONE" brand polycaprolactone, solid paraffin, magnesium stearate, polyvinyl(alcohol), arabinogalactan (oligosaccharide derived from the American Western Larch tree), agarose, calcium chloride and sodium chloride, which was added to a number of these as an additional excipient. At the last stage of this study beeswax was also tried, but was combined with PEO via a different empirical methodology to that used for forming the PEO-extruded rods. Owing to the large number of excipients investigated which would have led to a large number of drug/PEO/excipient permutations/trials, it was decided to concentrate on only one drug to test the ability

Table. 2 The primary function of excipients used as 5% or 20% w/w loadings which were co-extruded with PEO-303 rods containing also ~1% (w/w) sodium salicylate. Rods were also co-extruded with 10 % (w/w) sodium chloride unless otherwise stipulated.

Excipient	**Mode of action for slowing PEO-303 gelation in the release medium**	**Co-extrudability with PEO-303**
Agarose (No NaCl added)	Competes with PEO for water to delay PEO gelation	Good
Arabinogalactan (No NaCl added)	ditto	Good
Calcium chloride (No NaCl added)	Competes with PEO for water in similar manner to NaCl but to a greater extent owing to the influence of the divalent Ca2+ ion which results in a more heavily hydrated ion	Good
Carboxymethylcellulose ("cell CMC")	Competes with PEO for water to delay PEO gelation	Good
Lactose	Competes with PEO for water to delay PEO gelation	Extremely poor leading to blocking of the extrusion apparatus
Magnesium stearate	Provides hydrophobic layer to delay gelation of PEO by water	Very poor leading to low quality, non-cohesive rods
Paraffin wax	ditto	Good, though uniformity of mixing of PEO, drug + excipients is problematic
PEG6000	Competes with PEO for water to delay PEO gelation	Good
PVA (polyvinyl alcohol).	ditto	Good
Sodium chloride (not used on its own)	Used as an adjuvant in most excipient-added samples to compete with PEO for water so delaying PEO gelation	Good, although large salt crystal size may not promote the best uniformity of mixing of solid components
TONE polycaprolactone	Temporary encapsulant for PEO rod to delay access of water to PEO	Good

of these substances to delay drug release. Of the drugs trialled and discussed earlier, it was decided to use sodium salicylate because of its rather rapid release rate from the PEO (only) extruded rod as shown in Fig. 5. Hence powder mixes consisting of ~1% by weight of drug, and 5 or 20% by weight of excipient (remainder PEO) were prepared. To provide an additional amount of competition for gelation, it was also decided to include 10% by weight of NaCl in all samples (apart from arabinogalactan, agarose and calcium chloride). The powder mixes were then extruded in the usual manner as described earlier.

Extrusion results involving excipients

Although extruded rods could be successfully prepared from most PEO/Na salicylate/excipient combinations using temperatures of 80-100 ºC in the extruder, a number of combinations exhibited manufacturing issues. In particular, attempts to co-extrude PEO/drug with 20% lactose proved virtually impossible due to the material sticking intractably in the extruder. Only some segments could be obtained, which were insufficient for release testing. Co-extrusion with 20% Mg stearate at 85-90 ºC was also problematic because the material was too "slippery", thereby providing a barrier to extrusion of any rod of substance. Fragile poorly formed and/or filled rods were the result. Lowering the temperature of extrusion led to grainy and brittle rods. Rods containing 20% cell CMC by weight tended to extrude only above 100 ºC and caused some blackening in some parts of the rods produced, which had to be rejected. TONE polycaprolactone, while extruding to produce rods of acceptable quality, was a substance that was difficult to clean out of the barrel of the extruder. Paraffin exhibited issues similar to magnesium stearate. Its slipperiness in the extruder often made it challenging to extrude rods efficiently, especially when present at 20% by weight (which may have been associated with challenges in homogenizing a powder mix containing that high level by weight of paraffin).

The group of samples containing AG or agarose or $CaCl_2$ as excipients without NaCl could also be extruded to produce acceptable quality rods; although for samples containing 20% agarose by weight, blockage of the extruder barrel occurred and the $CaCl_2$-containing mixes led to selective "sieving/separating out" of the $CaCl_2$ granules near the top of powders being introduced into the feed inlet of the extrusion barrel. This raises questions about the uniformity of excipient throughout the extruded rod produced (although the resultant rods were observed to contain speckles of the calcium salt throughout the body of the rod). Given the excipients existed in different physical forms from powders/granules to waxy or oily solid/chunky materials, the issue of how uniform the rods were in composition when extruded from a powder mix needed to be considered.

Results of release experiments.

All extruded rods produced were tested for release with the usual sampling at the nominal 1 h, 2 h, 3 h and 24 h soaking times in 40% EtOH/H_2O at 37ºC. In Fig. 8 and Fig. 9 bar graphs are shown for UV-detected sodium salicylate concentrations measured of all replicates tested for each PEO/Na salicylate/excipient combination at the1 h,2 h, 3 h and 24 h sampling points, with a comparison bar indicating the calculated 100% release concentration (in the 5th column to the right of the columns indicating concentrations at 1 h, 2 h, 3 h and 24 h sampling points from left to right in the bar graph). Data for the excipients used with NaCl included at 10% by weight are shown in Fig. 8, while Fig. 9 shows data for the excipients used without NaCl. For all PEO (only) / sodium salicylate replicates the level of drug detected in the release medium after 24 h of soaking exceeds that of the expected value, assuming total release of all the drug into the 100 mL of release medium.

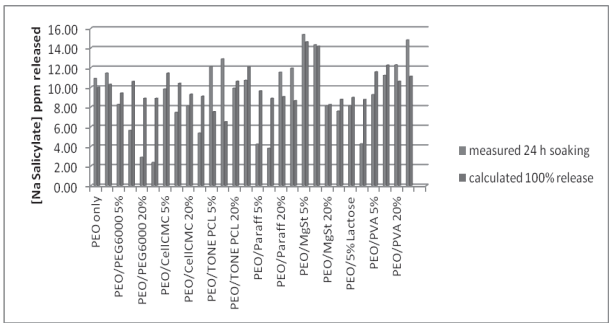


Fig. 8. UV-assayed data for [Na salicylate] released from soaking of extruded rods containing PEO and drug with or without various excipients in 40% EtOH/H_2O solution at 37 ºC for 24 h. Columns should be read left to right for measured 24 h soaking and calculated 100% release for each replicate tested.

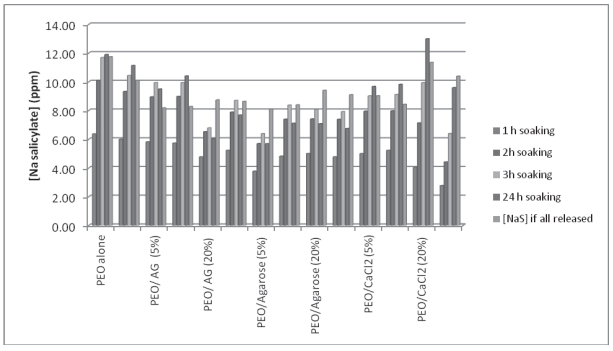


Fig. 9. UV-assayed data for [Na salicylate] released from soaking of extruded rods containing PEO and drug with or without various excipients in 40% EtOH/H_2O solution at 37 ºC for 24 h. These extruded rods did not have 10% (w/w) NaCl incorporated into pre-extruded powder mixes. Columns should be read left to right for measured 1 h, 2 h, 3 h, 24 h released [Na salicylate], and calculated 100% release concentrations for each replicate tested.

These data from Fig. 8 and Fig. 9 for the PEO(alone) replicates reflect the rapid release of drug into the release medium as expected of (gelling) PEO and in line with the previously described release trials. The partial non-agreement with calculated 100% release values may also reflect the fact that extrusion of the drug with PEO into rods could be compositionally non homogeneous, so that "1% by weight of drug in the unextruded powder" may not mean 1% by weight in the extruded rod. However, the level of agreement between the 24 h sampled concentrations and the calculated 100% release concentrations expected from the rods were within 1 ppm for the PEO (only)/drug samples and the behaviour of replicates was consistent. There will also be experimental error in the

calculation of the concentrations from UV assay. The most noticeable effect of the excipients on the disintegration of the PEO rod in the release medium was seen in rods observed at the nominal 1 h sampling point, where most of the sample rods containing excipients appeared visually to disintegrate less relative to PEO(alone)/drug extruded rods. Also, in support of this, the measured values for [Na salicylate] at 1 h sampling were all lower than the corresponding value for the [Na salicylate] released from PEO (alone)/drug extruded rods. This suggests a short-term inhibition process of PEO gelation is occurring. However, when rods with excipients were considered in terms of their release behaviour, especially the rods containing magnesium stearate, PVA, 20% by weight paraffin, and TONE PCL, the actual measured release of sodium salicylate at 24 h in relation to the calculated 100% release of drug expected from the rods ranked the systems as ones of similar effectiveness to or less effective than PEO alone in restricting release of drug. Hence, it was obvious that formulation with these particular excipients did little to stem the release of the drug from the soaked extruded rods, and so were limited in any role they might have had as a physical barrier or as components that interfered with PEO gelation. Indeed the PEO/TONE PCL co-extruded rods were a case in point, because outwardly they gave the deceptive appearance of retaining their rod shape when observed at 1 h, 2 h and 3 h soaking times when, in fact, what had actually happened (as borne out by UV assaying) was that the PEO had leached out of the internal parts of the rod into the medium, leaving the TONE PCL-encapsulating shell intact but empty.

Other PEO/excipient combinations for which data are illustrated in Fig. 8 and Fig. 9 gave potentially interesting results: the rods containing PEO/PEG6000, PEO/ cell CMC, PEO/ paraffin 5%, PEO/lactose 5% and PEO/ agarose (no NaCl) gave measured 24 h sodium salicylate concentrations which were consistently (and for some systems (PEG6000 and 5% paraffin) significantly below the calculated 100% release values expected (for both replicate rod samples tested). Some systems, however, such as the PEO/drug/5% lactose mix did give very different absolute values of measured [Na salicylate] values between the replicates which raises in these samples the spectre of compositional non-uniformity in the extruded rods as discussed above. The consistency of behaviour with respect to lower observed overall 24 h release concentrations than what is expected from calculated 100% release values could, however, also suggest that these particular excipients have indeed had the desired effect of retaining the drug within the PEO gel mass, whether it be through forming a physical barrier to the drug being released or via competing with PEO for water during the gelation process. Possibly, the biggest effect imparted by the excipient is realized in the first hour of soaking, as demonstrated by the visual observations on the delayed disintegration of the rods in the aqueous alcoholic release media relative to the typical, rapid PEO(alone)/drug extruded rod disintegration behaviour.

Soaking of PEO/excipient/sodium salicylate powder mixes in 40% ethanol/water for 48 h

In order to determine the uniformity of the PEO/sodium salicylate and PEO/sodium salicylate/excipient powder mixes prior to extrusion, three systems were investigated with two replicate samples per system prepared. The systems chosen were: PEO alone with drug, PEO/NaCl (10% by weight)/cellulose CMC/ (20% by weight) and PEO/ NaCl (10% by weight)/paraffin (5% by weight). NaCl is a hard crystalline solid, Cellulose CMC is a powder, while paraffin is a chunky/waxy/oily solid; hence, these materials represented the spectrum of physical dispersion types of excipient that were mixed with PEO in the previous experiments described in this study. The powder mixes prepared were made up identically to those made in previous release experiments except that 0.1-0.6 g of each of the mixed powder systems was pre-weighed into the release pottles used (in duplicate) without extrusion into rods. 100 mL of release medium was then added to these powdered samples and the pottles sealed. To ensure full dissolution and, because soaking was conducted at ambient temperatures, the powders were allowed to remain in the release medium for 48 h as opposed to the customary 24 h for the rods. Furthermore, they were kept in the dark to prevent any spurious light-mediated decomposition of the sodium salicylate over this prolonged soaking time. After this period of time the solutions were all observed to be reasonably clear though viscous with some settling of gel on the bottom. They were shaken prior to taking samples for the single UV analysis. The results are shown for all replicates tested as a bar graph in Fig. 10.

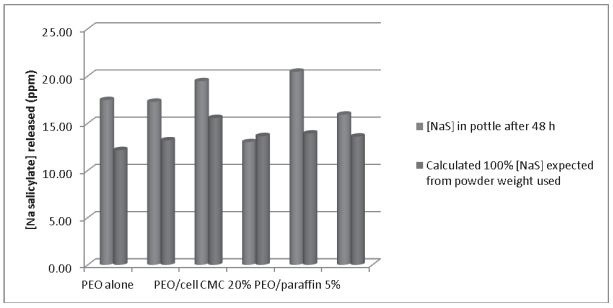


Fig.10. Bar graphs showing the concentration of sodium salicylate released from powder mixes of PEO with sodium salicylate (~1% w/w), cell CMC and paraffin (with each sample also containing 10% (w/w) NaCl) that had been soaked for 48 h in 40% EtOH/H_2O at ambient temperature in the dark. [NaS] = concentration of sodium salicylate. Data are shown for both replicates per system studied. The left hand column in each group is the UV-assayed concentrations and the right hand column is the calculated 100% release concentration expected from the weight of powder sampled in 100 mL of release media.

With the exception of one rod replicate sample (PEO/cell CMC), the pottles gave higher [sodium salicylate] values than expected from the calculated 100% release concentrations for the rods used. Dilution errors would not feature in this data as no samples were withdrawn until the end of the soaking period where they were assayed by a single UV analysis. As a consequence, no solvent was replaced during the 48 h soaking period. Some of the results in Fig. 10 contradict the extruded rod results in Fig. 8 and Fig. 9, where lower concentrations than the calcu-

lated 100% release concentrations for the rods used were observed for 24 h release (e.g., PEO/NaCl/paraffin 5% by weight, see Fig. 8). There could be several interpretations of these results. One is that the powder mixes, especially those containing chunky/ waxy excipients like NaCl and paraffin, exhibit compositional homogeneity issues when a small subset of sample (i.e., 0.1-0.6 g as in this experiment) is taken from a larger prepared powder mix. The other interpretation, or more appropriately caveat, is that it may not be wise to compare results for release of drugs from powdered soaked samples as opposed to extruded rods from the same powders because the act of extruding the mix into a rod is aiding in mixing the excipients, sodium salicylate and PEO intimately, so that beneficial effects like provision of a physical barrier or competing with PEO for water are brought into effect, thereby stemming release of drug into the release medium as intended.

Experiments involving release from PEO/drug extruded rods that had been precoated with physical barrier coatings prior to immersion in the 40% EtOH/H_2O release media

The mixed results from the PEO/drug/excipient co-extruded rod studies as discussed above led to consideration of research trials where physical barriers were instead placed on the PEO/drug extruded rods as an alternative strategy to delay release of drug from the gelating rods. By placing a physical barrier via a total or partial encapsulation of the rod itself, it was reasoned that controlled release of the drug might be realized through a slow breakdown or erosion of the barrier film.

In general this was trialled using 1% by weight of metoprolol succinate as the drug with the same release sampling protocol as was used in the previously described studies. Barrier coating systems using SPAN80 and HGDS (applied by dipping rods in molten mixtures of these components followed by rapid cooling) that involved comparison of release of drug from rods which were fully coated, coated with one end of rod exposed, coated with both ends of rod exposed and uncoated rods were prepared and tested. In short, no results from such a system were obtained because the barrier coating completely disintegrated and clouded the release medium, so rendering UV analysis impossible. Another barrier coating (which cannot be mentioned for commercial reasons) was also trialled and applied by dipping in molten mixtures of the barrier coating. This, though not clouding the medium, was found to provide a very weak barrier to the disintegration of the rods through PEO gelation. Parts of the coating were observed to have curled at the end of the soaking period, so providing little protection to the underlying PEO rod. Hence, the "rod coating" approach was not taken any further.

"PEO/beeswax composites"

The research experiences and lack of success associated with controlling release of drug from PEO/drug/excipient co-extruded rods with or without barrier coatings prompted a change in research strategy with respect to achieving a significant (i.e. beyond 1 h of soaking) inhibition of release of drugs in matrices containing PEO.

The change in strategy involved not preparing the extruded rods but instead creating discs of co-melted PEO and beeswax. This work, which was initially done at the end of this study as a brief but successful experiment, showed a significant delay in the release of drug. It was further developed in a summer research project by BSc Tech student Ho Ying Yuen in 2010, who displayed the research as a poster presentation at a Waikato Sustainable Bioeconomy Student Poster conference held at the University of Waikato in May 2010 where she was awarded one of the three poster prizes offered in the competition decided by industrially-based judges. Commercial interest was sparked in this after the conference. As a result, research and development of this system, albeit in a different direction to its original use as a drug delivery agent, are now proceeding with promising applications. Some of the disclosable results of the further study of this system were presented at the recent NZIC conference in Hamilton in November 2011.[12]

In conclusion, this empirical study has demonstrated the practical issues of using PEO in extruded rod systems for drug delivery. Fast gelation of the PEO in aqueous solutions can lead to rapid release of drugs; and, apart from the well known strategies used by earlier workers in this field, simple strategies involving co-extruded excipients and physical barrier coatings as used in this study, may only have limited impact for delaying release. Further work concentrating on the success of the comelted PEO/ beeswax system as a delivery matrix is continuing. Some of the disclosable aspects of this technology will be the subject of a separate publication in the future.

Acknowledgements

MRM is grateful to the University of Waikato for the provision of sabbatical research leave during which this study was carried out. The authors acknowledge Interag and DEC Manufacturing Ltd, Te Rapa, Hamilton for the loan of their benchtop extrusion device during the period of this study as well as for the provision of facilities and consumables to undertake this research. We also acknowledge Douglas Pharmaceuticals in West Auckland for an earlier gift of drugs that were used in this research.

References

1. Rothen-Weinhold, A.; Gurny,R.; Dahn, M. *Pharm. Sci. Technol. Today*, **2000**, *3(7)*, 222.
2. Dhawan, S.; Dhawan, K.; Varma, M.; Sinha,V.R. *Pharm. Tech.*, **2005**, September, 82.
3. Pinto, J.F.; Wunder, K.F.; Okoloekwe, A. *AAPS PharmSci,* **2004**, *6(2)*, Article 15 (*http://www.aapspharmsci.org*).
4. Repka, M.A.; Prodduturi,S.; Stodghill, S.P. *Drug Dev. Ind. Pharm*., **2003**, *29*, 757.
5. Crowley, M.M; Zhang, F.; Koleng, J.J.; McGinty, J.W. *Biomaterials,* **2002**, *23*, 4241.
6. Read, M.D.; Coppens, K.A.; Hall, M.J.; Koblinski, B.D.; Larsen, P.S.; Shrestha, U. *Ann. Tech. Conf. - Society of Plastics Engineers*, **2010**, 1203.
7. Coppens, K.; Hall, M.; Larsen, P.; Shrestha,U. ; Read, M. *Ann. Tech. Conf. - Society of Plastics Engineers*, **2006**, 1402.
8. Perissutti, B.; Newton,J.M.; Podczeck, F.; Rubessa,F. *E. Pharm. Biopharm.*, **2002**, *53*, 125.
9. Gruet, P.; Maincent, P.; Berthelot, X.; Kaltsatos, V. *Adv. Drug Del. Rev.*, **2001**, *50*, 245.

10. Pugliese, Peter T. (Milmark Research, Inc., USA). U.S. **(1977)**, 5 pp. US Patent 4049830 19770920. Application: US 75-629222 19751106. Priority: US 73-366159 19730601; US 74-523333 19741113.
11. Berry, E.A.; Hillerton, J.E. *J. Dairy Sci*., **2002**, *85(1)*, 112.
12. Thomas, K.; Mucalo, M.; Thorburn, Q.; Oakley, A. "On the Development of novel matrices for delivering beneficial compounds in vivo in agricultural industry", *NZIC 2011 Conference, oral presentation, Industrial and Materials Chemistry Symposium*, University of Waikato, November, 2011.
13. *B. Pharmacop.*, London, 2012.
14. Gardyne, S.J.; Mucalo, M.R.; Rathbone, M.J. *Results in Pharma Sci.* , **2011**, *1(1),* 80-87.
15. Emami, S.H. *Polyethylene Oxide Hydrogels, Synthesis and Characterisation*, VDM Verlag Dr. Muller Aktiengesellschaft &Co. KG, 2008.
16. Hulsmann, S.; Backensfeld; T., Keitel, S.; Bodmeier, R. *Eur. J. Pharm. Biopharm*., **2000**, *49*, 237-242.
17. Hoare, T.R.; Kohane, D.S. *Polymer*, **2008**, *49*, 1993.
18. Pifferi, G.; Restani, P. *Il Farmaco*, **2003**, *58*(*8*), 541.

Grants and awards

2012 Prime Minister's Science Prizes now open

The Prime Minister's Science Prizes recognise the impact of science on New Zealanders' lives. They are an opportunity for the people of New Zealand to celebrate the contribution of our current scientists and to encourage those of the future. Each year five prizes are awarded, with prize money totalling $1 million.

Closing dates for these are all 24 July 2012.

Prime Minister's Science Prize

Is in recognition of a transformative science discovery or achievement which has led to an economic, health, social and/or environmental impact on New Zealand, or internationally. Areas include physical, chemical, biological, social and technological sciences, mathematics and engineering. The prize is $500,000.

Prime Minister's MacDiarmid Emerging Scientist Prize

Is for an outstanding emerging scientist undertaking research in New Zealand for a PhD, or graduates within 5 years of having completed their PhD. To be eligible the entrant must have been awarded their PhD from 1st January 2007, or later. The prize is $200,000.

Prime Minister's Science Teacher Prize

This Prize will be given in recognition of an outstanding teacher of Science. This prize is worth $150,000, with the recipient receiving $50,000 and the recipient's school receiving $100,000.

Prime Minister's Science Media Communication Prize

This Prize will be given to a practising scientist who is an effective communicator and will provide them with an opportunity to further develop their knowledge and capability in science media communication. The prize is $100,000 to the recipient

Prime Minister's Future Scientist Prize

This Prize is for a secondary school student for their achievements in carrying out a practical and innovative research or technology project. It is a Scholarship of $50,000 to support the recipient's tertiary education.

See: www.pmscienceprizes.org.nz for more information

Rutherford Foundation Trust Postdoctoral Fellowships

These fellowships will enable recipients to undertake full-time research programmes within New Zealand in areas of science, technology, engineering or mathematics at an eligible research institution.

They are offered for two years and each year the fellow receives a stipend of $65,000. In addition, a GST-inclusive fund is paid each year of NZ$26,000 to support direct and indirect research costs of which up to NZ$5,000 can be used to support conference travel. Closing date 1 August 2012.

See: www.royalsociety.org.nz/programmes/funds/rutherford-foundation/funding-opportunities/post-docs/

The Freemasons Roskill Foundation Postdoctoral Fellowship

This will enable recipients to undertake a full-time research programme within New Zealand or the United Kingdom on topics concerned with ameliorating the ageing process.

This Fellowship is concerned with advancing knowledge in areas that are related to ageing with an emphasis on understanding the biology of the ageing process and/or the discovery of potential new therapeutic targets; however, the focus remains broad-based and also supports ageing-related research in more applied or basic areas.

See: www.royalsociety.org.nz/programmes/funds/rutherford-foundation/funding-opportunities/freemasons/

Rutherford Discovery Fellowships

These prestigious Fellowships will support the recipients for a five-year term and provide funding up to $160,000 a year (excl. GST). With this scheme, the New Zealand Government is supporting the development of future research leaders, and assisting with the retention and repatriation of New Zealand's talented early- to mid-career researchers.

Early- to mid-career researchers are researchers who have been conferred with their doctoral degree between three and eight years prior to the year in which the Fellowship is awarded. Applicants must be either New Zealand citizens or applicants who have continuously resided in New Zealand for at least three months prior to their application and hold, or are deemed to hold, a New Zealand resident visa.

A web-based on-line system will be used for applications. Prospective applicants must first contact their research office coordinator to obtain login details for the Proposals On-Line web-based portal.

Applications close on 27 June 2012.

For further information see: www.royalsociety.org.nz/programmes/funds/rutherford-discovery/

Article

Novel polyoxometalates: is antimony the new molybdenum?

Brian K Nicholson[1] and Christopher J Clark[2]

[1]Chemistry Department, University of Waikato, Hamilton, New Zealand
(email: *b.nicholson@waikato.ac.nz*)

[2]Bioengineering Technologies, Plant and Food Research Centre, Hamilton, New Zealand
(email: *Chris.Clark@plantandfood.co.nz*)

Key words: Polyoxometalates; Antimony; ESI mass spectrometry

Polyoxometalates based on Mo, W or V have been known for a long time and present a diverse range of structures, with the $[XMo_{12}O_{40}]^{n-}$ Keggin ions (X = P, Si ,…) perhaps the best known.[1] They are still subject to intense research with >4000 papers published in the past five years.

Following on from our study[2] of aryl arsonic acids $RAsO_3H_2$, which are straightforward molecular species based on four-coordinate As(V), we became interested in the corresponding antimony compounds. Although aryl stibonic acids of nominal formula $RSbO_3H_2$ have been known for over 100 years,[3] their composition has remained uncertain, as they form only amorphous solids, have complicated titration behaviour and only limited solubility. The presumption has been that they are polymeric, based on 5- or 6-coordinate Sb with Sb-O-Sb linkages, though direct evidence is sparse.[4] Recently, it has been shown by Beckman that if very bulky R groups are used, then relatively simple dimers such as $(2,6\text{-}Mes_2C_6H_3Sb_2O_2(OH)_4$ (Mes=mesityl) can be isolated, but these represent a special case.[5]

Using electrospray ionisation mass spectrometry (ESI-MS), we were able to show conclusively that $RSbO_3H_2$ acids (R = *p*-tolyl, *p*-ClC_6H_4, *p*-$O_2NC_6H_4$), rather than being ill-defined polymers, existed mainly as discrete aggregates of overall formula $[H_{12}(RSb)_{12}O_{30}]$, see Fig. 1.[6] There was some evidence for other nuclearities (Sb_{14}, Sb_{16}, etc.) but these were invariably minor.

While the ESI-MS results indicated the formulae, no structural conclusions could be drawn, and attempts to grow single crystals for X-ray analysis have been singularly unsuccessful.

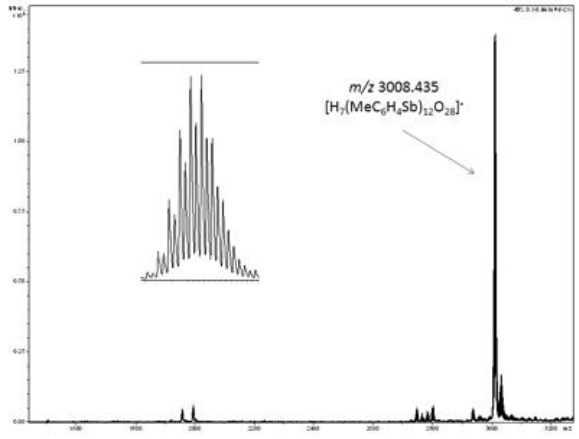


Fig. 1. The negative-ion ESI mass spectrum of *p*-tolyl stibonic acid in MeCN showing the specificity of the aggregation to give $[H_8(MeC_6H_4Sb)_{12}O_{28}]$. The inset shows the characteristic isotope envelope arising mainly from the twelve Sb atoms (I = ½).

It was noted from the mass spectral results that, unless special precautions were taken, there was a strong tendency for the acids to entrain Na^+ carried over from the syntheses, and even carefully purified samples developed ions containing Na^+ by adventitious leaching from glassware.[6,7] We therefore embarked on a systematic survey of the acid salts formed with a variety of metal cations in the hope of providing crystalline samples for X-ray diffraction. The only prior report in this area came from Winpenny's group, who had shown that a number of complex polyhedra based on antimony could be prepared using solvothermal methods.[8] Their studies, along with ours and some parallel ones from Baskar's group,[9,10] have now established an expanding range of novel polyoxostibonate structures, some of which have direct parallels with polyoxomolybdates and some of which are unique.

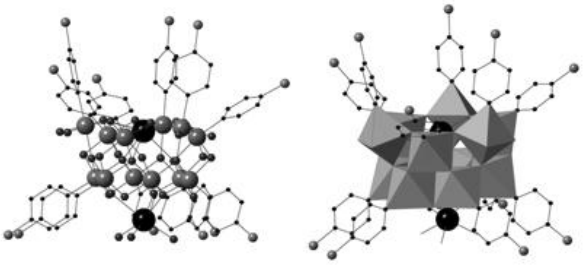


Fig. 2. The structure of $[K_2H_{10}(p\text{-}ClC_6H_4Sb)_{12}O_{30}]$ as stick-and-ball and in polyhedral representations.

With medium-sized cations Na^+ or K^+ the characteristic structures are as shown in Fig. 2.[6,11] They consist of a hexagonal antiprism of six-coordinate Sb atoms with a planar lower layer and a puckered upper one. The framework is completed by thirty oxygen atoms, comprising six triply-bridging, eighteen doubly bridging and six terminal ones. There are two main cation sites. One is 10-coordinate, lying within the hexagonal channel, attached to nine framework O atoms, with an H_2O coordinated in the final position. This encapsulated cation is very firmly attached within the cavity, which serves as an inorganic equivalent of a crown ether.

A second cation site is six-coordinate, lying below the channel entrance, connected to three framework O atoms and three H_2O molecules. This position is more promiscuous and can be occupied by Rb^+ or Ba^{2+} as well as by Na^+ or K^+.[12] Additional cations may be involved in less well-defined sites depending on the crystallisation conditions, either loosely attached to the main core or as fully solvated cations in the crystal lattice. The differing numbers of cations and their charges is compensated for by differing degrees of protonation of the cluster. These hex-

agonal antiprismatic species have a precedent in one of the components in a complex structure.[8]

With the larger cations, Ba^{2+} or Rb^{+}, a more open structure forms, with an Sb_{14} framework, generating a bowl that cradles the cation in an eleven-coordinate site.[13, 14] The overall formula is $[MH_{10}(RSb)_{14}O_{34}]^{x-}$ (M= Ba^{2+} x = 0; M = Rb^{+} x =1) and the six-coordinate antimony atoms are linked to six triply-bridging O atoms, twenty four doubly-bridging O atoms and four terminal OH groups (Fig. 3). This geometry is unique to polyoxostibonates.[13]

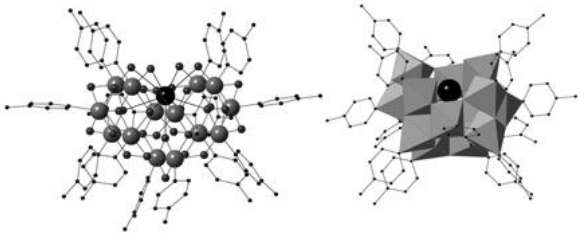


Fig. 3. The structure of bowl-shaped $[BaH_{10}(p\text{-}MeC_6H_4Sb)_{12}O_{34}]$.

Sb_{16} examples been established which have a geometry that can be generated from our Sb_{14} examples by removing the cation and capping the open face with two extra edge-shared $\{RSbO_6\}$ octahedra.[8, 10] In contrast, with the smaller cation Li^{+} a complex was isolated with a more condensed core and overall formula $Li_4[LiH_3(RSb)_{12}O_{28}]$.[13] One of the Li^{+} ions is fully encapsulated within the cluster core in a tetrahedral site, and the overall geometry corresponds to the rare γ isomer of the Keggin ion $[XMo_{12}O_{40}]^{n-}$, Fig. 4.[15] The remaining Li^{+} cations are attached to external faces of the polyoxmetalate.

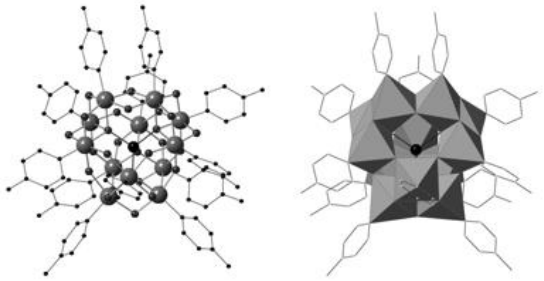


Fig. 4. Two representations of the structure of $[LiH_3(p\text{-}MeC_6H_4Sb)_{12}O_{28}]^{4-}$.

Other isomers of Keggin ions (δ and ε) are formed[8,16] when transition metals ions Mn^{2+}, Co^{2+} or Zn^{2+} are incorporated, giving $[M(RSb)_{12}O_{28}]^{6-}$ species which have the transition metal in the centre and the main group metal Sb as the framework atoms (Fig. 5); hence, these have been dubbed 'inverse Keggin ions'.[8] The overall charge is compensated for by other cations coordinated to the external surface of the cluster via framework O atoms.

So far then, we and others have established an intriguing family of polyoxostibonates with geometries based on four different Sb_{12}, one Sb_{14} and one Sb_{16} core polyhedra (Fig. 6). There is mass spectral evidence for other core nuclearities but these have so far defied isolation.

It is noteworthy that we have found that these compounds

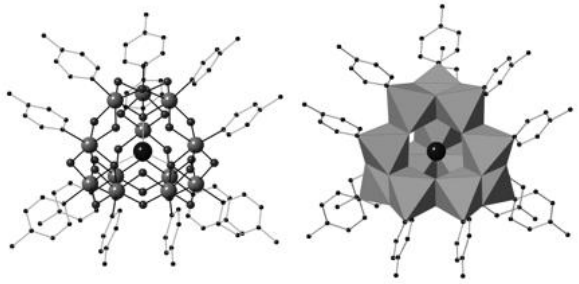


Fig. 5. The structure of the $[Co(MeC_6H_4Sb)_{12}O_{28}]^{6-}$ ion, corresponding to the tetrahedral ε-isomer of the "reverse-Keggin ion" type.

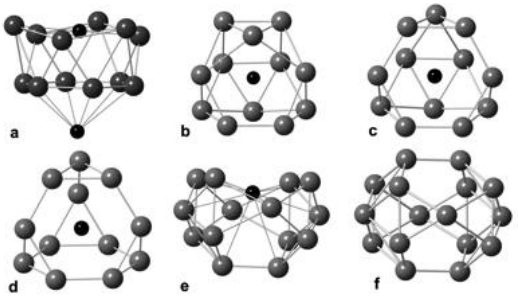


Fig. 6. The range of polyhedral so far known for polyoxostibonates; (a) hexagonal antiprism with cations Na^{+} or K^{+}; (b)-(d) the γ, δ and ε isomers of the reverse-Keggin ions found for the Li^{+}, Co^{2+} and Zn^{2+} examples; (e) the bowl shaped Ba^{2+} complex and (f) the empty Sb_{16} cluster.

form readily under ambient conditions; the more stringent solvothermal conditions used earlier are unnecessary.[8] Another point of contrast is that the polyoxostibonates are formed from alkaline solutions, whereas traditional Mo or W species are generated under acidic conditions. The polyhedra that are generated appear to be templated by different sized cations but at this stage syntheses are serendipitous, based on trial and error rather than any systematic approach. Future work will undoubtedly provide extra novel examples of polyoxostibonates, and should further determine the importance of cation size, the effects of changing the steric properties of the R group, and the relevance of pH and other parameters on producing particular species. The physical properties of these new materials are so far completely unexplored, so potential uses are yet to be established; we note polyoxomolybdates have many applications as catalysts, as analytical reagents, as sensors and as biologically active compounds, so their antimony analogues may be equally versatile.

Acknowledgements.

We thank Cody Wright for synthesis of the aryl stibonic acids and for mass spectral studies as part of his MSc studies, and we are very grateful to Tania Groutso (University of Auckland), Shane Telfer and Geoff Jameson (Massey University) for assistance with the X-ray crystallography, which is far from routine because of the high levels of solvation and ready loss of crystallinity.

References

1. Pope, M. T. *Heteropoly and Isopoly Oxometalates*, Springer-Verlag, Berlin, **1983**; Long, D. L.; Burkholder, E.; Cronin, L. *Chem. Soc.*

Rev. **2007**, *36*, 105-121.

2. Lloyd, N. C.; Morgan, H. W.; Nicholson, B. K.; Ronimus, R. S. *J. Organometal. Chem.* **2008**, *693*, 2443-2450.
3. Hasenbäumer, J. *Ber. Dtsch. Chem. Ges.* **1898**, *31*, 2910-2914.
4. Doak, G. O. *J. Am. Chem. Soc.*, **1946**, *68*, 1991-1995.
5. Beckman, J.; Finke, P.; Hesse, M.; Wettig, B. *Angew. Chem. Int, Ed*. **2008**, *47*, 9982-9984.
6. Clark, C. J.; Nicholson, B. K.; Wright, C. E. *Chem. Comm*. **2009**, 923-925.
7. Wright, C. E. MSc Thesis, University of Waikato, 2010.
8. Baskar, V; Shanmugan, M.; Helliwell, M.; Teat, S. J.; Winpenny, R. E. P. *J. Am. Chem. Soc.* **2007**, *129*, 3042-3043.
9. Prabhu, M. S. R.; Jami, A. K.; Baskar, V. *Organometallics* **2009**, *28*, 3953-56.
10. Jami, A. K.; Prabhu, S. R.; Baskar, V. *Organometallics* **2010**, *29*, 1137-1143.
11. Nicholson, B. K.; Clark, C. J.; Wright, C. E.; Groutso, T. *Organometallics* **2010**, *29*, 6518-6526.
12. Clark, C. J.; Nicholson, B. K. *unpublished*.
13. Nicholson, B. K.; Clark, C. J.; Wright, C. E.; Telfer, S. G.; Groutso, T. *Organometallics* **2011**, *30*, 6612-6616.
14. Nicholson, B. K.; Clark, C. J.; Jameson, G. B.; Telfer, S. G.; Groutso, T. *unpublished*.
15. Zhang, F. Q.; Guan, W.; Zhang, Y. T.; Xu, M. T.; Li, J.; Su, Z. M. *Inorg. Chem*. **2010**, *49*, 5472-5481.
16. Nicholson, B. K.; Clark, C. J.; Telfer, S. G.; Groutso, T. *Dalton Trans*. **2012**, *submitted*.

Conferences

4th Penang International Conference for Young Chemists

30 January – 1 February 2013, City Bayview Hotel, Penang, Malaysia

The theme of this conference is "Chemistry: Empowering Science Beyond Boundaries". It aims at sharing knowledge, interaction and networking among local and international researchers and encouraging cross-linking between various fields of chemistry.

The conference consists of oral and poster presentation in the following fields of chemistry: analytical, environmental, industrial, inorganic, materials, natural product, organic, physical, polymers.

Closing date for registration and abstract submission: 30th November 2012

Website: web.usm.my/icyc/

The XIII International Congress of Toxicology 2013

30 June – 4 July 2013, Seoul, Republic of Korea, Asia

This congress will offer you many opportunities to exchange advanced knowledge on toxicology. This year's congress will be comprised of keynote lectures given by world-renowned scholars, in addition to symposiums, workshops, debates, as well as oral and poster sessions. Topics include toxicology, medicinal chemistry, pharmaceutical chemistry, drug delivery and food chemistry.

Deadline for abstract submission: January 31st 2013

See website: www.ict2013seoul.org/

14th European Symposium on Organic Reactivity (ESOR 2013)

1 - 6 September 2013, Prague, Czech Republic, Europe

The ESOR Symposia are dedicated to fundamental research in organic chemistry and related areas, emphasizing the understanding of reactions (e.g., mechanisms, energetics) as well as the structures of compounds and materials. Experimental as well as theoretical contributions are welcomed with a particular preference for multidisciplinary approaches.

The programme will include plenary and invited lectures, oral presentations, poster presentations, and an exhibition. We wish to cover all important areas of physical-organic chemistry and its interactions with other sciences, e.g., mechanistic studies as a driving force in modern synthesis, physical-organic chemistry of complex systems, new experimental and theoretical methods in organic chemistry.

See: www.uochb.cz/web/structure/1073.html

OBITUARY

Sir Paul Callaghan 1947 – 2012

Scientist with an inspiring curiosity

Barely a month before his death an obviously illness-wracked Sir Paul Callaghan stood in front of an audience to talk about Zealandia. He didn't need to be there – ecologist Charles Daugherty had offered to step in. He was so ill he warned the crowd he might tire and need to sit. Or he might have to hand over to Professor Daugherty if he couldn't make it through. But he just couldn't waste the opportunity to promote a pet project.

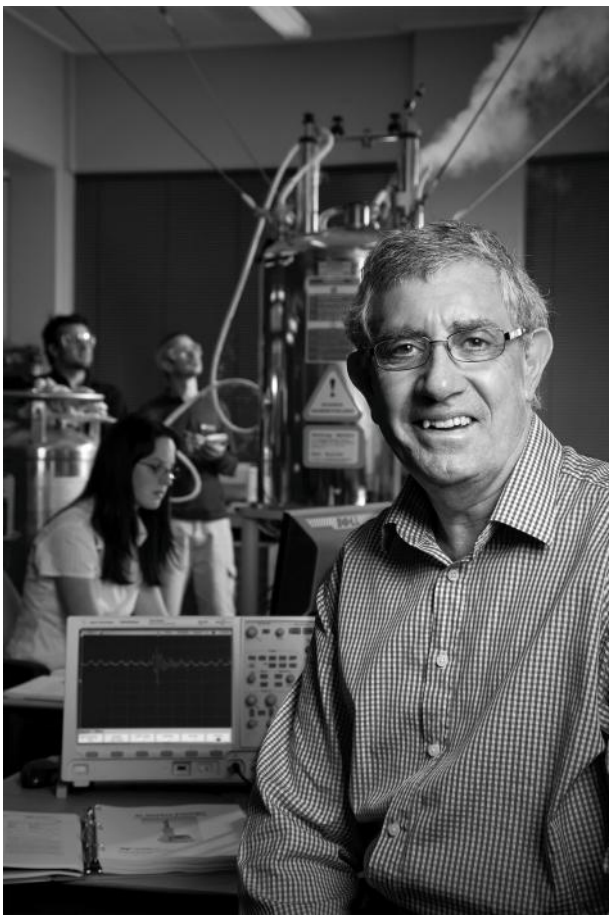
The effort cost him dearly – he landed in hospital two days later, where he remained for a month before being allowed home to die last week. It's a measure of the man that, despite the consequences of that talk, he told *The Dominion Post* he'd do it all again.

World class scientist, leader, passionate advocate for a better, more prosperous New Zealand, Sir Paul's contribution is difficult to quantify or classify. Sir Paul's accolades and achievements are too numerous to list here but include the Rutherford Prize, the Sir Peter Blake medal for leadership, Principal Companion of the New Zealand Order of Merit. In 2010, he won the international Gadiünther Laukien prize for his ground-breaking work using radio waves to detect the motion of molecules.

During the past year, as 2011 New Zealander of the Year he toured the country packing out lecture theatres and town halls promoting his vision for New Zealand, gaining traction for his dual message of fostering a niche high-tech economy that will lift New Zealand out of the economic doldrums, and looking after the natural environment that gives New Zealand its point of difference, its ability to attract star talent despite lower pay. But it is for science that Sir Paul will be most widely remembered.

His curiosity and penchant for experimentation started early. Brought up on a quarter acre section in Wanganui, Sir Paul hardly had the illustrious beginning his later achievements might suggest. His father, Ernest, a draper and mother, Mavis, had less than a year of secondary school education between them. He went to Wanganui Tech – not the posh Collegiate across town – and spent his time blowing up rocks with Molotov cocktails.The 200-metre nearby tunnel made a fabulous echo chamber. He made his first crystal set radio at primary school, and was excited to pick up two stations. He was exuberant and troublesome and caned more than the average teen. Fortunately Wanganui was a forgiving place and, despite frequent cornerings by police and traffic cops, he talked his way out of any serious trouble.

Those early scientific experiments segued into Sir Paul studying maths and physics at Victoria University, funding his study with a part-time job at the Imlay freezing works. He excelled, winning a scholarship to study low temperature physics at Oxford University.



Having worked with some of the best brains, and best facilities, in the science world, Sir Paul returned to New Zealand in 1974 to lecture at a tiny fledgling physics department in sleepy Palmerston North, where he worked for 27 years, eventually heading up the department. Here Sir Paul defined both his career and his pragmatic approach to science.

There was no physics equipment, but the chemistry department had just bought a nuclear magnetic resonance (NMR) spectrometer. Rather than being the impetuous child that demands to work on their scientific field whatever, Sir Paul looked at his skills and what was available, and began research using the NMR spectrometer.

PhD student Andrew Coy, who has worked with Sir Paul for 25 years and now runs Magritek – the NMR company Sir Paul co-founded – remembers an inspiring teacher with an extraordinary capacity for work. "He was just always so energising and passionate about what he did. When I was doing my PhD we'd be sitting there doing some experiments getting all excited and suddenly it would be 3am. I would drag myself back into the lab in the morning and Paul had already been in there and started the next experiment and was excited about the results of the next one."

It was an age of practical pioneers. Few students did their doctorates in New Zealand and research funds and knowledge were scarce. If the equipment didn't fit the purpose, you made your own.

That adaptability set up Sir Paul for one of his most significant scientific contributions, using NMR to measure brine content in Antarctic sea ice, helping scientists better understand the global climate structure. A complex and unique system, the sea ice was beyond the capabilities of existing measuring tools. So Sir Paul designed and built new hardware specifically for the purpose. He first visited Antarctica in 1994, but returned again and again to refine his experiments.

In 2001, Sir Paul moved to Wellington and Victoria University and spearheaded the campaign to launch a centre of research excellence. They won funding and set up the MacDiarmid Institute, with Sir Paul as its inaugural director.

Present director Professor Kathryn McGrath, who collaborated with Sir Paul for 12 years, says it is impossible to divorce Sir Paul's scientific achievements from his impact on fellow scientists. "He got his energy from other people, he sparked off other people all the time. There's nothing more exciting than if you think something is really cool and then someone that you respect starts to also say it is really cool. Once he became involved with something and was invigorated by it he was a bit of a machine really."

Before Sir Paul was diagnosed with bowel cancer in 2008, colleagues knew something was seriously wrong. They assumed he had worked himself into the ground. The joke around the office was that, while Sir Paul was having chemotherapy, he worked for the first time at the rate of a normal person.

But he also had a life. When he wasn't in the lab, Sir Paul was usually out walking, or spending time with wife Miang. At international conferences he would take the opportunity to climb some nearby mountain. And he'd go out for drinks with colleagues always the young ones. Leave the old fogies to themselves.

For all his contribution to fundamental science, one of Sir Paul's proudest achievements was setting up a company to commercialise his NMR technology. Magritek was born in 2004, with two staff and enough cash to see them through six months. It makes and sells portable NMR measuring devices using a scaled down version of the science used in magnetic resonance imaging (MRI) scans. Eight years on, the company has expanded its range, employs 23 staff and sells to international oil companies and pharmaceutical companies.

In later years, Sir Paul earned a reputation as a science communicator, fronting a show with Kim Hill on Radio New Zealand and giving talks around the country. Inspired by the example of Nobel Prize winner Alan MacDiarmid, Sir Paul was desperate to convince New Zealanders that science could be interesting and comprehensible. In 2009, he wrote *Wool to Weta*, about his vision for transforming New Zealand's culture and economy.

He obviously loved talking – Professor Daugherty knew after ten minutes of that Zealandia talk that Sir Paul would make it through to the end. "You could see him gaining strength. I've heard him speak on many occasions on a whole range of topics and it used to really annoy me that he never gave a bad one. Evolutionary biologists like me always get frustrated when physicists start telling us about evolution. But he always had something interesting to say."

Professor Daugherty first worked with Sir Paul when he was asked, after being diagnosed with cancer, to review the Allan Wilson centre, with which Professor Daugherty was involved. "Working on that I saw how perceptive he was, and how committed to helping others. He had nothing to gain by doing this, he just thought it was the right thing to do."

Scientist to the end, Sir Paul took advantage of a break between chemotherapy treatments to experiment with controversial vitamin C treatment. When it didn't work, he courageously made public his experience to debunk the treatment.

Sir Paul's reach was extraordinary and he will be mourned around the world. In Sir Paul's last week, Professor McGrath dreamed that the research centre he founded was leaking from every orifice. "I took that as a metaphor, in part that he was such a force in all aspects. He loved teaching, he loved fundamental science, he loved to communicate, he loved to support people. There is not going to be a person like him for a while. There will be other people that have his characteristics, but I may not know them. He makes you want to be better. Everybody needs that I think."

Professor Sir Paul Terence Callaghan, scientist; b Whanganui, 19 August 1947; m Susan Audrey Roberts (dis), m Miang Lim; 1s 1d; d Wellington, March 24, aged 64.

Nikki MacDonald
***The Dominion Post*, Wellington**

*Reprinted with permission of *The Dominion Post*. Sources: Dominion Post library; Professor Charles Daugherty; Professor Kathryn McGrath; Andrew Coy; Interviews with Sir Paul Callaghan

OBITUARY

Alan Arthur Turner 1934 – 2012

Alan Turner loved chemistry. From a very early age he wanted to be a chemist wearing a white laboratory coat. At the age of 18, he left school to join Shell New Zealand as a laboratory technician. There, his talent as a chemist was recognized and he was encouraged to go to university. He gained his Chemistry degree in 1958 from part-time study at Victoria College, where he met his future wife, Iivi Alet, who was completing her MSc degree; they were married in the early 60s.

Upon graduation, Alan went back to Shell full-time, was recognised as a careful and methodical chemist, and was quickly given major responsibilities that included the development of the first NZ-based grease making plant, then under construction. He spent many months at grease plants in the UK learning the black art of making grease, returning in 1962 to develop the new operation at Seaview. In 1963, he moved to Auckland as a Technical Sales Adviser and then to Christchurch in the same role. He was promoted to Industrial Markets Manager in the Head Office and, in the late 1960s, became Technical Manager responsible for all product development, quality control and customer service activities with a staff of *ca.* 25. He was a strict but fair boss.

While Technical Manager, the oil shocks of the early 1970s hit and the price of oil increased from $US3 to $US12 a barrel almost overnight! This price increase contributed substantially to a worsening of NZs terms of trade; weekend petrol sales were banned and carless days introduced on 30 July 1979. Much of Alan's energy as Technical Manager was then directed towards the development of alternative transport fuels, initially compressed natural gas (CNG) and then LPG. For the latter a new car was purchased, converted to LPG, and test driven by Alan throughout the North Island for a year to prove the performance of LPG in petrol engines. Later, the trial was extended to a taxi fleet in Wellington and eventually to general use by the public. With the advent of Maui gas, the use of methanol as a transport fuel was Alan's next challenge. He organised a large international symposium in Auckland involving world experts that led to an industry unit in New Zealand to evaluate methanol/petrol blends in our vehicle fleet.

In 1978, the Government established the Liquid Fuels Trust Board (LFTB) to evaluate alternative automotive fuels for NZ and, because of his expertise, Alan was soon seconded to it. He much enjoyed this challenge involving, as it did, investigations as varied as Southland lignite coal and the European butter mountain as possible fuel sources. Alan's secondment to the LFTB ended in 1990 and he retired from Shell at the same time.

Throughout his career with Shell and the LFTB both Alan and Iivi were actively involved with the Institute's Wellington Branch. They both served on the committee over many years taking on various roles and were regular attendees at monthly meetings. After such meetings Alan would often claim, with a twinkle in his eye, that he didn't understand the point of the lecture, but when he asked a question it was clear that he had understood much more than he let on.

In 1989, Alan was asked to help NZIC at the National level. The Institute had, for many years, been run by Ted Harvey (the Hon. Gen. Sec.) and Denis Hogan (the Registrar). Both gentlemen retired at about the same time and the Institute needed to find someone who could not only take over their role but bring the office functions of the Institute up to date. Alan accepted this, set up an office in IPENZ offices in Molesworth Street, and for the next eight years he was both Honorary General Secretary and Executive Officer of the Institute. This was effectively a half-time position, which Alan undertook on an honorary basis. He transformed the way in which the Institute conducted its business and he ran the operation like clockwork.

One of Alan's duties was to liaise with the myriad of national chemical societies and he developed a real interest in what those societies were doing for chemical education in secondary schools. As a result of this liaison, a Canadian quiz, *Chem 13*, was introduced to NZ schools with Alan as administrator. The Australians were next off the block and Alan was appointed coordinator for what became the Australian National Chemistry Quiz. This quiz still provides a major focus for secondary school students on the relevance of chemistry in an exciting and stimulat-

ing way. Last year this quiz had more than 117,000 entries, from 1,467 schools and 15 countries. Alan and Iivi coordinated the ANCQ quiz from their Brooklyn home for 20 years - Alan believed passionately in the value of this type of activity.

At the end of Alan's term as Executive Officer he returned to the Branch Committee serving as Treasurer and providing advice to the younger chemists on the committee. He was always supportive; Brian Halton, the recently retired editor of this journal, tells me that he would frequently receive phone calls from Alan saying how much he had enjoyed a particular article in the latest issue, and if he had any criticism to make it was always very gentle.

Apart had wide interests beyond chemistry: he loved his wine and kept an excellent cellar. He and Iivi were founding members of the Magnum Society, Wellington's leading wine appreciation society and they were founding shareholders in the Te Kairanga winery in Martinborough. He also loved music, cricket and good company. His wife Iivi was born in Estonia and Alan and his family were prominent members of the small, but close-knit, NZ Estonian community, hosting many of its functions in their home. He and Iivi made several trips to Estonia after the break-up of the Soviet Union and made contact with her relatives there. On the day of his funeral, the Estonian flag was flown at half-mast over the consulate in Wellington.

Alan Turner died from cancer on April 17 and is survived by his mother, his wife, two daughters, and four grandchildren.

David Weatherburn [with thanks to Roscoe Turner (no relation) for details of Alan's career]

Chem News

Talented New Zealand science students to visit CERN and then attend the London International Youth Science Forum and CERN

The London International Youth Science Forum (LIYSF) is a yearly event which enables talented young students to participate in an international science event and meet other young scientists from around the world.

Six senior secondary school students from New Zealand have been chosen by the Royal Society from over 300 applications to attend the LIYSF. They are:

- Andy Chen, Macleans College, Howick, Auckland
- Robert Shin, Macleans College, Howick, Auckland
- Gabriella Templer, ACG Parnell College, Auckland
- Rachel Love,Takapuna Grammar School, Auckland
- In Sung Hwang, Massey High School, Auckland
- Rachael Wiltshire, Samuel Marsden Collegiate, Wellington

These students were chosen because of their high academic achievements and their interest in science. The Talented School Students Travel award, which is funded by the Ministry of Science and Innovation and administered by the Royal Society will cover 80% of the cost of the trip.

They will initially be travelling to CERN to take part in the CERN discovery programme, which is also part of the LIYSF. Here they will be able to look behind the scenes at one of the worlds largest scientific research centres which houses over 2500 scientists researching particle physics.

They will then travel to London to attend LIYSF which is a two-week residential event held at Imperial College London and in 2012 this runs from 16-30th August. The programme includes lectures, seminars and site visits to industrial research centres, laboratories and universities.

Sir Roy Anderson (Professor of Infectious Disease Epidemiology, Imperial College) will present the opening address on the theme 'The Human Planet' while the closing lecture, will be given by Prof. Trevor Jones CBE who is the Director General of the Association of the British Pharmaceutical Industry.

There will also be a number of seminars, lecture demonstrations and visits to London, Oxford and Cambridge scientific research establishments.

For more information see: *www.liysf.org.uk*

Four New Zealand Students chosen for 2012 International Chemistry Olympiad

The International Chemistry Olympiad (IChO) will be held in Washington from July 21-30th 2012 and four students have been chosen to represent New Zealand. They are:

- Andy Chen, Macleans College
- Robert (Min Sup) Shin, Macleans College
- Matthew Lie, Westlake Boys High School
- Henry (Pak-Hang,) Yuen, Auckland Grammar School

This is an annual competition for the world's most talented chemistry students at the secondary school level. Nations around the world send a team of four students, who are tested on their chemistry knowledge and skills in a five-hour laboratory practical and five-hour written theoretical examination.

For more details on this year's event see: *www.icho2012.org*

First compulsory licence in India serves as wake up call to global pharmaceutical firms

Tim Stirrup and Katherine Hebditch

Baldwins Intellectual Property, PO Box 5999, Wellesley St, Auckland
(email: tim.stirrup@baldwins.com or katherine.hebditch@baldwins.com)

In the first judgement of its kind, the Indian Patent Office has granted a compulsory licence to generic drug manufacturer Natco Pharma Limited to manufacture and sell Bayer Corporation's patented cancer treatment Nexavar. The judgement could have ramifications for how global pharmaceutical firms do business in India and other countries.

Bayer's drug Nexavar contains a patented bi-aryl urea which inhibits enzyme targets in the MAP kinase pathway. Since protein kinases are often overactive in cancerous tissue, the inhibitor was found to be useful in the treatment of advanced stage liver and kidney cancer. A patent was granted in a number of countries with the grant in India coming in early 2008. Although the drug does not cure the cancers outright, it does extend the life of a patient with kidney cancer by an average of four to five years, and with liver cancer by an average of six to eight months.

As discussed in our July 2010 Patent Prose Article, *Compulsory Licensing in a Nutshell*, every major patent system in the world has provisions for the government or court to intervene and grant a competitor the right to use or manufacture a patented invention if certain conditions are met. However, use of these provisions by governments to grant compulsory licences has been rare. In these rare instances, the governments have generally relied on a provision in the WTO's TRIPS Agreement which allows the grant of compulsory licences in cases of "extreme urgency" or "national emergency".

Indian patent law also allows for a compulsory licence to be granted by the Patent Office if certain other criteria are met. Firstly, a reasonable request for a voluntary licence must have been refused by the patentee. Natco Pharma had previously asked Bayer to grant them a licence to sell the drug, but Bayer had refused; therefore, this criterion was met. In addition, further criteria stipulate that a compulsory licence may be granted if the patentee has not:

(a) satisfied the reasonable requirements of the public with respect to the patented invention; or

(b) made the invention available to the public at a reasonably affordable price; or

(c) worked the invention in the territory of India.

Only one of criteria (a) to (c) needs to be met for a compulsory licence to be granted.

The Commissioner of the Indian Patent Office found that the first criterion had been met as Bayer had only made their drug available to about 2% of patients with kidney/liver cancer at the appropriate stage for treatment. In their defence, Bayer argued that the alleged infringement of their patent rights by another generic drug manufacturer had limited their sales. The Commissioner did not accept this argument, based mainly on the fact that Bayer is currently suing the other generic manufacturer for alleged patent infringement in an attempt to stop such sales of the drug. Therefore the reasonable requirements of the Indian public had not been met.

The second criterion requires the patentee to make the invention available to the public at a *reasonably affordable price*. There was debate about how this price should be calculated. Natco Pharma argued that a government worker would have to work for three and a half years to be able to purchase a month's course of the medicine at the standard dose (approximately $NZ6,600), and that this was not reasonably affordable. Bayer argued that the price of the drug is justified as it not only encompasses the considerable research and development costs to bring Nexavar to market, but must also fund a drug pipeline that includes many failed drug targets that do not make it to market. Bayer pointed out that since 2007, they have brought only two new molecular entities and one new combination product to the market; this for a cumulative research and development spend of 8 billion Euros.

The subjective nature of such a debate makes it hard to draw any firm conclusions on how a reasonably affordable price should be calculated. Bayer pointed out that if the equation is purely one in which the cost of production by a generic manufacturer is compared to the patentee's price, the generic will always win out. The Commissioner considered that despite Bayer's arguments, the primary reason that the drug was only used by 2% of the eligible patients was due to it not being reasonably affordable to them therefore the second criterion was also met.

The third criterion requires that the invention be worked in India by at least three years from the date of grant. This is a general requirement for any patented invention in India and a statement must be filed with the Patent Office each year stating how the invention has been worked. Critically, the Commissioner interpreted the term "work" to mean more than simply importing the invention and also requires manufacturing of the invention in India. Despite having manufacturing facilities for drugs in India, Bayer had not manufactured Nexavar, therefore, the Commissioner adjudged the third criterion for grant of a compulsory licence to be satisfied.

The judgement as it relates to the "working" requirement is likely to be a serious bone of contention for many patentees. It means that a competitor may potentially be granted a compulsory licence solely due to the fact that

the patentee does not manufacture their invention in India. This has ramifications for a huge number of international patent owners and raises serious questions about how far the Indian Patent Office can go in stipulating how a patentee conducts their business. In addition, it brings home the importance of a patentee actually commercialising a patented invention in India rather than relying on the patent to block competitors.

Having decided that a compulsory licence was to be granted, the Commissioner also decided the terms of the licence. A 6% royalty margin on Natco's sales of the drug is to be paid to Bayer. Additional terms include a) that the price of one month's treatment should not exceed 8,880 rupees (NZD$210), b) Bayer will provide no legal, regulatory, medical, technical, manufacturing, sales, marketing or any other support of any kind to Natco, and c) that Natco shall provide the patented drug to at least 600 needy and deserving patients per year free of charge.

Bayer have appealed the judgement. Therefore, it is unclear whether this could be the start of many such licences or if the judgement will be overturned. In the wake of the judgement no doubt other pharmaceutical companies in similar positions will be carefully reviewing their business and pricing strategies. In addition, they would be wise to treat any request for a licence from a local generic manufacturer as a sign that further action may be in the offing.

The judgement and its subsequent appeal will be carefully watched by other countries that are a base for thriving generics manufacturing businesses, such as Brazil and China. The outcome may pave the way for these countries to follow suit when faced with similar circumstances. While the immediate impact of the judgement on Bayer is likely to be small, the potential for future judgements in the same vein relating to different products and markets will set alarm bells ringing throughout the global pharmaceutical industry.

If you have any queries regarding intellectual property related matters (including patents, trademarks, copyright or licensing), please contact: *tim.stirrup@baldwins.com or katherine.hebditch@baldwins.com*

Patent Proze
Baldwins Intellectual Property
PO Box 5999
Wellesley Street
Auckland

Katherine Hebditch and Tim Stirrup of Baldwins Intellectual Property in Auckland specialise in chemistry and biotechnology patents. Katherine obtained her PhD in organic chemistry from the University of Manchester in the UK in 2004. She is currently working towards registration as a patent attorney. Tim obtained his PhD in molecular biology from the University of Southampton in the UK in 2007. He is also working towards registration as a patent attorney.

Dates of Note

On 21 July 2000, an international collaboration of scientists at the US Department of Energy's Fermi National Accelerator Laboratory announced the first direct evidence for the subatomic particle called the tau neutrino, the third kind of neutrino known to particle physicists. *Gustav* ***Hertz***, the German quantum physicist who shared (with James Franck) the 1925 Nobel Prize for Physics for confirming that energy can be absorbed by an atom only in definite amounts, was born on 22 July 1887, 125 years ago. On the same day in 1922, *Jokichi* ***Takamine*** died. He was the Japanese-American biochemist and industrialist who isolated the hormone adrenalin (now called epinephrine) in 1901. On 23 July 1937, 75 years ago, the isolation of pituitary hormone was announced by Yale University. *Rosalind Elsie* ***Franklin***, the English physical chemist and X-ray crystallographer, was born on 25 July 1900, the day in 1997 when it was announced that human stem cells had been cultured in a laboratory using tissue taken from aborted human embryos. *Conrad Arnold* ***Elvehjem***, the American biochemist who identified that nicotinic acid was a vitamin, died on 27 July 1962. *Karl Raimund* ***Popper***, the noted Austrian-British philosopher of science, was born on 28 July, 1902. *Archer* ***Martin***, the English biochemist who shared (with R.L.M. Synge) the 1952 Nobel Prize for Chemistry for the development of paper partition chromatography, died on 28 July, ten years ago, the day in 1977 that the 799-mile trans-Alaska oil pipeline began full operation. On 29 July 1927, the first iron lung (electric respirator) was installed (at Bellevue Hospital in New York) for the post-war polio epidemic. *Jean Antoine Claude* ***Chaptal***, the French chemist who authored the first book on industrial chemistry and coined the name *nitrogen,* died on 30 July 1832.

Sir *Joseph Henry* ***Gilbert***, the English chemist who as co-director of the Rothamsted Experimental Station for over 50 years established a premier reputation for research at the first organized agricultural experimental station in the world, was born on 1 August 1817. *Richard* ***Kuhn***, the Austrian biochemist awarded the 1938 Nobel Prize for Chemistry for his work on carotenoids and vitamins, died that day in 1967. *Alexander Graham* ***Bell*** died on 2 August 1922. *Richard* ***Willstätter***, the German chemist whose study of the structure of chlorophyll and other plant pigments won him the 1915 Nobel Prize for Chemistry, was born on 13 August 1872 and died on 3 August 1942. *Heinrich Otto* ***Wieland***, the German chemist and winner of the 1927 Nobel Prize for his work on steroid chemistry, died 55 years ago on 5 August 1957. *Paul A. M.* ***Dirac***, the English theoretical physicist known for his work in quantum mechanics and for his theory of the spinning electron, was born on 8 August 1902, the day *Viktor* ***Meyer*** died in 1897 and the day in 1802 that *Germain Henri* ***Hess***, the founder of thermochemistry was born. *Ralph Walter Graystone* ***Wyckoff***, the American scientist and pioneer in the application of X-ray methods to determine crystal structures, was born on 9 August 1897. *Arne Wilhelm Kaurin* ***Tiselius*** was the Swedish biochemist who won the Nobel Prize for Chemistry in 1948 for his work on electrophoresis; he was born on 10 August 1902, the day five years earlier, in 1897, that *Felix* ***Hoffmann*** successfully prepared chemically pure and stable acetylsalicylic acid. *Erwin* ***Schrödinger*** was born on 12 August 1887, 125 years ago.

Eduard ***Buchner***, of 'funnel' fame, died on 13 August 1917. *Johan* ***Gadolin***, the Finnish chemist who discovered the element yttrium in 1794, died on 15 August 1852. *Irving* ***Langmuir***, the American physical chemist whose study of molecular films on solid and liquid surfaces created the field of colloid research, died on 16 August 1957. On 19 August 1947, the first full synthesis of vitamin A was reported by Dutch chemists, *Jozef Ferdinand* ***Arens*** and *David Adriaan van* ***Dorp***. *Adolf von* ***Baeyer***, who synthesized and formulated the structure of indigo, and gained the 1905 Nobel Prize for Chemistry, died on 20 August 1917. Sir *John Cowdery* ***Kendrew***, the English biochemist who determined the structure of myoglobin and shared the 1962 Nobel Prize for Chemistry (with Perutz), died on 23 August, 15 years ago. On 23 August 1617, the first one-way streets were established in London. *Michael* ***Faraday*** died on 25 August 1867. *Cyril Stanley* ***Smith***, the British-American metallurgist who determined the properties and technology of plutonium and uranium, died on 25 August, 60 years ago. *Georg* ***Wittig***, the German chemist whose organophosphorus studies led to the 1979 Nobel Prize for Chemistry (with H.C. Brown), died on 26 August, 25 years ago. On 28 August 1837, (175 years ago) pharmacists *John* ***Lea*** and *William* ***Perrins*** began the manufacture of Worcester Sauce. *Edward Mills* ***Purcell***, the American co-discoverer of NMR and winner of the 1952 Nobel Prize for Physics (with F. Bloch), was born on 30 August, 100 years ago, the same day in 1852 that *Jacobus Henricus* ***van't Hoff*** was born. This is also the day *Charles-Bernard* ***Desormes***, the French chemist who made determined the exact composition of CO and CS_2, died 150 years ago in 1862. Sir *George* ***Porter*** died 10 years ago on 30 August, while *Friedrich Adolf* ***Paneth***, the Austrian chemist who devised methods to isolate and measure as little as 10^{-10} cm^3 of helium slowly released by traces of radioactive elements in rocks, was born on the same day 125 years ago.

Francis William ***Aston***, the British physicist who won the Nobel Prize for Chemistry in 1922 for his development of the mass spectrograph, was born on 1 September 1877, while *Frederick* ***Soddy***, the English chemist and physicist who received the Nobel Prize for Chemistry in 1921 for investigating radioactive substances, was born the next day of the same year, 2 September 1877. This day in 1752 was the last day of the Julian calendar in Great Britain, Ireland and the British colonies, including those on the east coast of America. Eleven days were skipped to adopt the Gregorian calendar, designed to realign the calendar with equinoxes. Hence the following day was 14 September 1752. *Max* ***Bodenstein***, a noted German chemist, died on 3 September 1942. Sir *Frederick Augustus* ***Abel***, the English chemist and military explosives specialist who invented cordite in 1889 with the chemist Sir James Dewar, died on 6 September 1902. Sir *John* ***Cornforth***, totally deaf from the age of 16 years, was the Australian-born British chem-

ist who shared the 1975 Nobel Prize for Chemistry (with Vladimir Prelog) for his work on the stereochemistry of enzyme-catalyzed reactions; he was born on 7 September 1917. *David* ***Packard***, the American entrepreneur and electrical engineer who co-founded the Hewlett-Packard Co., was born 100 years ago – also on 7 September. *Hans Georg* ***Dehmelt*** was the German-born American physicist who shared the 1989 Nobel Prize for Physics (with Wolfgang Paul and Norman Ramsey) for the development of the ion trap technique; he was born on 9 September 1922. *Carl Gustaf* ***Mosander***, the Swedish chemist and mineralogist whose work revealed the existence of numerous rare-earth elements and who discovered lanthanum (La), was born on 10 September 1797. *Irène* ***Joliot-Curie***, the French physical chemist and wife of Frédéric, who shared the 1935 Nobel Prize for their discovery of artificially produced radioactive elements, was born on 12 September 1897.

Leopold Stephen ***Ruzicka***, the noted Croatian-Swiss chemist, was born on 13 September 1887. This same day in 1922 saw the world's highest shade temperature of 58 °C recorded at the African village of Al Aziziyah, about 40 km south of Tripoli in Libya. *Pavel Nikolayevich* ***Yablochkov*** was the Russian electrical engineer who invented an improved arc lamp, the Yablochkov candle in 1876; he was born on 14 September 1847, 165 years ago. The lamp was relatively inexpensive and used in public buildings and to light streets for several decades prior to the advent of incandescent lighting. *Neil* ***Bartlett***, the English-American chemist who formed the first noble gas compound, $XePtF_6$, was born on 15 September 1932. The Montreal protocol on substances that deplete the ozone layer was signed 25 years ago, on 16 September 1987. *Torunn* ***Garin*** was the Norwegian chemical engineer who helped develop aspartame sweetener as a sugar substitute while working for General Foods; she was born on 19 September, 65 years ago (and died on 26 April 2002). Sir *James* ***Dewar***, of low-temperature phenomena fame, was born on 20 September 1842. Sir *George* ***Stapledon***, the British agriculturalist and pioneer who developed grassland science, was born on 22 September 1882, while *Wilbur Olin* ***Atwater***, the American who developed agricultural chemistry, died the same day in 1907. *Friedrich* ***Wohler***, the German chemist most recognised for his synthesis of urea from ammonia, but who also isolated beryllium, yttrium and crystalline silicon, died on 23 September 1882. Sir *Barnes Neville* ***Wallis***, famed for his 9000-lb bouncing dambuster bombs, was born on 26 September 1887, 125 years ago. This is the day in 1917 that *Harrison Scott* ***Brown***, the American geochemist known for his role in isolating plutonium for its use in the first atomic bombs and for studies regarding meteorites and the Earth's origin, was born. *Antoine Jérôme* ***Balard***, the French chemist who discovered bromine in 1826, was born on 30 September 1802, the day 80 years later that *Hans Wilhelm* ***Geiger***, the German physicist who introduced the Geiger counter, was born.

On 1 October 1957, the drug thalidomide was first marketed (in West Germany). Sir *William* ***Ramsey***, the noted Scottish chemist who discovered the inert gases neon, krypton and xenon, and co-discovered argon, radon, calcium and barium, was born on 2 October 1852. This date is important in the history of chemistry as i) Baron *Alexander R(obertus)* ***Todd*** (of Trumpington), the British biochemist whose research on the structure and synthesis of nucleotides, nucleosides and nucleotide coenzymes gained him the 1957 Nobel Prize for Chemistry, was born then in 1907; ii) ten years later *Christian René* ***de Duve***, the Belgian cytologist and biochemist who discovered lysosomes and peroxisomes, was born; while iii) *Svante* ***Arrhenius*** died on this same day in 1927. On 3 October, 60 years ago, *Hurricane*, the first British atomic bomb, was tested at Monte Bello, Australia. The 65th anniversary of Max Planck's death is 4 October; he is the father of the quantum theory. *Rodney* ***Porter***, the British biochemist who (with G.M. Edelman) was awarded the 1972 Nobel Prize in Physiology or Medicine for discoveries concerning the chemical structure of antibodies, was born on 8 October 1917. *Emil* ***Fischer***, the noted German chemist awarded the Nobel Prize for Chemistry 110 years ago this year (1902) in recognition of his investigations of the sugar and purine groups of substances, was born on 9 October 1852. Sir *Cyril Norman* ***Hinshelwood***, the English physical chemist who worked on reaction rates and reaction mechanisms, particularly that of the combination of hydrogen and oxygen to form water and who shared the 1956 Nobel Prize for Chemistry with Nikolay Semyonov, died on 9 October 1967.

Michael James Steuart ***Dewar***, the Scottish organic chemist born in India to Scottish parents in the Civil Service there, and an early master of molecular orbital theory who wrote *The Electronic Theory of Organic Chemistry* (1949) – the first book applying molecular orbital theory to organic chemistry, died on 10 October 15 years ago. On 11 October 1957, the Jodrell Bank radio telescope, then the world's largest radio telescope designed by Sir Bernard Lovell, began operating. *Ascanio* ***Sobrero***, the Italian chemist who discovered the explosive compound nitroglycerin (1847) by adding glycerine slowly to mixture of nitric and sulfuric acids, was born on 12 October 200 years ago. *Nicolas-Théodore* ***de Saussure***, the Swiss chemist and plant physiologist whose quantitative experiments on the influence of water, air, and nutrients on plants laid the foundation for phytochemistry, was born on 14 October 1767, the day 65 years ago that in 1947, *Chuck* ***Yeager***, a WW II fighter pilot, became the first human to fly faster than the speed of sound. *Gustav Robert* ***Kirchhoff***, the German physicist who (with Bunsen) established the theory of spectrum analysis, died on 17 October 1887, 125 years ago. Sir *Ernest* ***Rutherford*** (Baron Rutherford of Nelson) died on 19 October 1937, 75 years ago. Sir *Christopher* ***Wren*** was born on 20 October 1632. On this same day in 1832 *Edward* ***Turner*** wrote a preface to the fourth edition of his textbook, *Elements of Chemistry*, in which he explained his use of symbols to represent reactants and products in a chemical reaction of cyanogen; they solved the difficulty of giving a clear and concise description of. the phenomena in ordinary language. His was the first use of chemical symbols in a British chemistry textbook.

Brian Halton

School of Chemical & Physical Sciences
Victoria University of Wellington

International Union of Pure and Applied Chemistry - Press Release

Element 114 is Named Flerovium and Element 116 is Named Livermorium

IUPAC has officially approved the name flerovium, with symbol Fl, for the element of atomic number 114 and the name livermorium, with symbol Lv, for the element of atomic number 116. Priority for the discovery of these elements was assigned, in accordance with the agreed criteria, to the collaboration between the Joint Institute for Nuclear Research (Dubna, Russia) and the Lawrence Livermore National Laboratory (Livermore, California, USA). The collaborating team has proposed the names flerovium and livermorium which have now been formally approved by IUPAC.

For the element with atomic number 114 the discoverers proposed the name flerovium and the symbol Fl. This proposal lies within tradition and will honor the Flerov Laboratory of Nuclear Reactions where superheavy elements are synthesised. Georgiy N. Flerov (1913 – 1990) was a renowned physicist, author of the discovery of the spontaneous fission of uranium (1940, with Konstantin A. Petrzhak), pioneer in heavy-ion physics, and founder in the Joint Institute for Nuclear Research the Laboratory of Nuclear Reactions (1957). It is an especially appropriate choice because, since 1991 this laboratory in which the element was synthesized, has borne his name. Professor G.N. Flerov is known also for his fundamental work in various fields of physics that resulted in the discovery of new phenomena in properties and interactions of the atomic nuclei; these have played a key role in the establishment and development of many areas of further research.

For the element with atomic number 116 the name proposed is livermorium with the symbol Lv. This is again in line with tradition and honours the Lawrence Livermore National Laboratory (1952). A group of researchers of this Laboratory with the heavy element research group of the Flerov Laboratory of Nuclear Reactions took part in the work carried out in Dubna on the synthesis of superheavy elements including element 116. Over the years scientists at Livermore have been involved in many areas of nuclear science: the investigation of fission properties of the heaviest elements, including the discovery of bimodal fission, and the study of prompt gamma-rays emitted from fission fragments following fission, the investigation of isomers and isomeric levels in many nuclei and the investigation of the chemical properties of the heaviest elements.

The Recommendations will be published in the July issue of the IUPAC journal *Pure and Applied Chemistry* which is available online at *Pure Appl. Chem.*, 2012, Vol. 84, No. 7 (doi: 10.1351/PAC-REC-11-12-03). Priority of claims to the discovery of the elements of atomic numbers 114 and 116 was determined by a Joint Working Party of independent experts drawn from the International Union of Pure and Applied Chemistry (IUPAC) and the International Union of Pure and Applied Physics (IUPAP). The group's report was published in July 2011, *Pure and Appl. Chem.*, 2011, Vol. 83, No. 7, pp 1485-1498 (doi: 10.1351/PAC-REP-10-05-01). A new Joint Working Party, appointed by the Presidents of IUPAC and IUPAP has begun work to assign priority for the discovery of elements 113, 115, 117, 118 and heavier elements, for which claims may be submitted.

IUPAC was formed in 1919 by chemists from industry and academia. For more than 90 years, the Union has succeeded in fostering worldwide communications in the chemical sciences and in uniting academic, industrial and public sector chemistry in a common language. IUPAC is recognized as the world authority on chemical nomenclature, terminology, standardized methods for measurement, atomic weights and many other critically evaluated data. More information about IUPAC and its activities is available at www.iupac.org.

For questions, contact Dr. Terrence Renner, Executive Director, at secretariat@iupac.org.

IUPAC Periodic Table of the Elements

1																	18
1 **H** hydrogen [1.007; 1.009]	2											13	14	15	16	17	2 **He** helium 4.003
3 **Li** lithium [6.938; 6.997]	4 **Be** beryllium 9.012											5 **B** boron [10.80; 10.83]	6 **C** carbon [12.00; 12.02]	7 **N** nitrogen [14.00; 14.01]	8 **O** oxygen [15.99; 16.00]	9 **F** fluorine 19.00	10 **Ne** neon 20.18
11 **Na** sodium 22.99	12 **Mg** magnesium 24.31	3	4	5	6	7	8	9	10	11	12	13 **Al** aluminium 26.98	14 **Si** silicon [28.08; 28.09]	15 **P** phosphorus 30.97	16 **S** sulfur [32.05; 32.08]	17 **Cl** chlorine [35.44; 35.46]	18 **Ar** argon 39.95
19 **K** potassium 39.10	20 **Ca** calcium 40.08	21 **Sc** scandium 44.96	22 **Ti** titanium 47.87	23 **V** vanadium 50.94	24 **Cr** chromium 52.00	25 **Mn** manganese 54.94	26 **Fe** iron 55.85	27 **Co** cobalt 58.93	28 **Ni** nickel 58.69	29 **Cu** copper 63.55	30 **Zn** zinc 65.38(2)	31 **Ga** gallium 69.72	32 **Ge** germanium 72.63	33 **As** arsenic 74.92	34 **Se** selenium 78.96(3)	35 **Br** bromine 79.90	36 **Kr** krypton 83.80
37 **Rb** rubidium 85.47	38 **Sr** strontium 87.62	39 **Y** yttrium 88.91	40 **Zr** zirconium 91.22	41 **Nb** niobium 92.91	42 **Mo** molybdenum 95.96(2)	43 **Tc** technetium	44 **Ru** ruthenium 101.1	45 **Rh** rhodium 102.9	46 **Pd** palladium 106.4	47 **Ag** silver 107.9	48 **Cd** cadmium 112.4	49 **In** indium 114.8	50 **Sn** tin 118.7	51 **Sb** antimony 121.8	52 **Te** tellurium 127.6	53 **I** iodine 126.9	54 **Xe** xenon 131.3
55 **Cs** caesium 132.9	56 **Ba** barium 137.3	57-71 lanthanoids	72 **Hf** hafnium 178.5	73 **Ta** tantalum 180.9	74 **W** tungsten 183.8	75 **Re** rhenium 186.2	76 **Os** osmium 190.2	77 **Ir** iridium 192.2	78 **Pt** platinum 195.1	79 **Au** gold 197.0	80 **Hg** mercury 200.6	81 **Tl** thallium [204.3; 204.4]	82 **Pb** lead 207.2	83 **Bi** bismuth 209.0	84 **Po** polonium	85 **At** astatine	86 **Rn** radon
87 **Fr** francium	88 **Ra** radium	89-103 actinoids	104 **Rf** rutherfordium	105 **Db** dubnium	106 **Sg** seaborgium	107 **Bh** bohrium	108 **Hs** hassium	109 **Mt** meitnerium	110 **Ds** darmstadtium	111 **Rg** roentgenium	112 **Cn** copernicium		114 **Fl** flerovium		116 **Lv** livermorium		

Key: atomic number **Symbol** name standard atomic weight

57 **La** lanthanum 138.9	58 **Ce** cerium 140.1	59 **Pr** praseodymium 140.9	60 **Nd** neodymium 144.2	61 **Pm** promethium	62 **Sm** samarium 150.4	63 **Eu** europium 152.0	64 **Gd** gadolinium 157.3	65 **Tb** terbium 158.9	66 **Dy** dysprosium 162.5	67 **Ho** holmium 164.9	68 **Er** erbium 167.3	69 **Tm** thulium 168.9	70 **Yb** ytterbium 173.1	71 **Lu** lutetium 175.0
89 **Ac** actinium	90 **Th** thorium 232.0	91 **Pa** protactinium 231.0	92 **U** uranium 238.0	93 **Np** neptunium	94 **Pu** plutonium	95 **Am** americium	96 **Cm** curium	97 **Bk** berkelium	98 **Cf** californium	99 **Es** einsteinium	100 **Fm** fermium	101 **Md** mendelevium	102 **No** nobelium	103 **Lr** lawrencium

Notes

- IUPAC 2009 Standard atomic weights abridged to four significant digits (Table 4 published in *Pure Appl. Chem.* 83, 359-396 (2011); doi:10.1351/PAC-REP-10-09-14). The uncertainty in the last digit of the standard atomic weight value is listed in parentheses following the value. In the absence of parentheses, the uncertainty is one in that last digit. An interval in square brackets provides the lower and upper bounds of the standard atomic weight for that element. No values are listed for elements which lack isotopes with a characteristic isotopic abundance in natural terrestrial samples. See PAC for more details.

- "Aluminum" and "cesium" are commonly used alternative spellings for "aluminium" and "caesium."

- Claims for the discovery of all the remaining elements in the last row of the Table, namely elements with atomic numbers 113, 115, 117 and 118, and for which no assignments have yet been made, are being considered by a IUPAC and IUPAP Joint Working Party.

For updates to this table, see iupac.org/reports/periodic_table/. This version is dated 1 June 2012.

INTERNATIONAL UNION OF PURE AND APPLIED CHEMISTRY