CRS Leading Delivery Science and Technology

Newsletter

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What's Inside

Your Membership:

Your Access to the Future of Delivery Science and Technology

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Your membership is your all-access pass to leading research and the delivery science community.

Access: Innovative Research

From the research presented in the journals *Drug Delivery and Translational Research* and the *Journal of Controlled Release*, to the science presented at the CRS Annual Meeting & Exposition, to books and online webcasts, CRS is your source for the best delivery science and technology research.

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The CRS Annual Meeting & Exposition is just the beginning of the great opportunities to connect with delivery scientists. Utilize the online community through the website, find experts through the LATTE database, join a committee, connect on LinkedIn, or join your local chapter, and access one of the most valuable resources – each other.

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Advance your professional skills through volunteering, participating in the mentoring program, and more. CRS offers fellowship programs and recognition through awards. The online career center is one more chance to develop your career in delivery science.

CRS
Leading Delivery Science and Technology

Take advantage of everything your membership has to offer now. Access it all online.

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The CRS Newsletter is the official newsletter of the Controlled Release Society. The newsletter is published six times annually, providing scientific and technical information pertinent to the controlled release community and news about society and chapter activities. Members can receive the newsletter via mail. The newsletter may also be viewed online at controlledreleasesociety.org.

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Visit controlledreleasesociety.org or e-mail crs@scisoc.org on questions about membership, meetings, publications, and services.

Contact dwoodard@scisoc.org for information about exhibiting, advertising or other visibility opportunities.

Yvonne Perrie
Aston University, School of Life and Health Sciences
Aston Triangle, Birmingham, U.K.

What's in a Brand Name? Often One of Your Five a Day

Have you noticed how many companies use a fruit name in their branding, yet have nothing to do with fruit? Here are some obvious, and less obvious, examples we came up with in the lab (and via Twitter) in no particular order:

- Apple—both Apple Records and Apple Macs
- Apricot—this started as a U.K.-based PC company, and their innovations include the first commercial shipment of an all-in-one system with a 3.5-inch floppy drive (ahead of Apple)
- Raspberry Pi Foundation—they provide credit-card sized computers, to support children to learn programming
- Orange and BlackBerry—supplying us mobiles
- LimeWire—a file-sharing company
- SPSS Clementine—a data-mining software tool from IBM
- Papaya Studio—an independent video game company based in California
- Banana Republic, Mango, and Fruit of the Loom—clothing brands
- Persimmon—they build houses in the U.K.
- Pineapple Dance Studios in London
- The Pomegranate Theatre in Chesterfield, U.K.
- Mandarin Oriental hotels
- Mandarin Airlines and Peach Aviation
- Blueberry Therapeutics—a drug discovery and development company based in the U.K.
- Grapefruit Creative, a marketing company in Nottingham, U.K.

One of the major issues most of us are facing is the cut in funding for scientific research. To ensure that the value of investing in science is appreciated, the impact of our research must be openly accessible, and often branding of our research can help. Examples of this include the branding of the Higgs boson as the "God particle". This was apparently first created as a joke by Leon Lederman and Dick Teresi.[1] Love it or hate it, this term has been adopted by the media. Strong branding and exploitation of social media may be things we need to consider more. This should not be left to the "Facebook generation" (I'm not sure this classification is useful; I know a lot of kids, parents, and grandparents who are on Facebook). So perhaps if you have not tried it yet, you could have a look at the Controlled Release Society's LinkedIn group, which Andy Lewis set up and runs for CRS. This already has 4,544 members; with our common interest, not much branding of our science is needed, but it is a great platform to share ideas and help ensure we can communicate as a global community.

Hope to see you in Honolulu,

Yvonne ■

[1]www.businessinsider.com/branding-science-to-save-us-all-2013-3

Kazunori Kataoka
University of Tokyo
Tokyo, Japan

Strategic Planning Is a State of Mind

A Japanese proverb states, "Planning without action is a daydream. Action without planning is a nightmare." Yet, despite the fact that most of us know and understand the importance of planning, many of us dread it.

For some, it is the word "strategic" that creates a seeming burden—the belief that such planning requires omniscience or unique insight. Still others lament that such planning takes place by committee or must pass through layers of approvals, making it a tedious or filtered process that has the potential to create a watered down or less effective result.

It is true that strategic planning is not always an easy task and that it is typically done by consensus. But to me, the process of planning is as important as the plan itself. It is like solving a mathematical equation: the more you do it, the more you train your mind to think mathematically. Similarly, the more strategic planning you do, the more you begin to think strategically.

Sitting down with my CRS colleagues to focus on our association's strengths, values, goals, and opportunities is a time of knowing and relating. It is an opportunity to move into a frame of mind that allows for focusing energies on the needs of our colleagues and members. It is the inner work that must be done in order to manifest the outer work that happens at our meetings and through our publications and events.

To some, the word strategic may sound cold and calculated, yet it is anything but. The CRS strategic plan focuses on fundamental questions familiar to anyone on any journey, be it personal or professional: Who are we? Where are we going? How are we going to get there? Strategic planning is not only a state of mind, it is a work in progress.

The CRS Board is focusing its thoughts and conversations on the key initiatives outlined here. By periodically revisiting the value of our society's contributions and the important role we have to play, we ensure our continued success and vitality. We see the road that is unfolding before us and can take to it with greater clarity and confidence.

My confidence is with you, my colleagues and fellow members. I have no doubt our association will only continue to grow and prosper.

International Development
We will continue and expand our international mission by encouraging worldwide membership and delivering our science and technology to the world. This will be achieved through vibrant chapters, encouraging and facilitating wide geographical spread of members serving on all committees and boards, mounting workshops and satellite meetings worldwide, and aspiring to hold the annual scientific meeting in non-EuroAmerican locations and through a high-quality and informative website featuring innovative webcasts.

Our Science and Technology
Our science and technology will be delivered internationally primarily through our annual science meeting but also through workshops, satellites, books, journals, and webcasts. We will continually seek to identify new products and services. In the coming five years, we will build translational/regulatory offerings and enhance linkages with clinical and industrial users of our science and technology. We will continually scan new fundamental science and ensure we are linked with the foundational sciences.

Governance and Resourcing
We will encourage and develop high-performing committees and boards. This will be achieved through clearly specified charges, defined policy and procedures, appropriate resourcing, and continual recruitment and training of enthusiastic volunteers, enabling rollover of the membership on committees. We will build a strong financial organization through sound planning of activities and careful stewardship of resources.

Membership
We will continually strive to increase our international membership and offer services that achieve high retention. We will recognize outstanding achievements and contributions through appropriately targeted awards.

Marketing and Communication
We will continue to be an open organization through effective communication with the international membership using a variety of strategies. We will build strategies for communication between committees, boards, members, and staff to ensure an open, friendly, and efficient organization. We will continually assess our competition and market our organization to ensure we protect our niche.

Kazunori Kataoka ■

A Scientific Rendezvous with Prof. David Brayden, University College Dublin, Ireland

Vishwas Rai, Ph.D.,[1] and Bozena B. Michniak-Kohn, Ph.D.[2]

Dr. David Brayden is currently an associate professor of drug delivery at the School of Veterinary Medicine at University College Dublin (UCD) and is a fellow of the UCD Conway Institute of Biomolecular and Biomedical Research in Ireland. Dr. Brayden joined UCD as a lecturer in veterinary pharmacology in 2001, was appointed a senior lecturer in 2005, and became an associate professor in 2006. In 2012, he was the first Irish scientist to be made a fellow of the Controlled Release Society. From 2007 to 2008, he also served as a director of research for the School of Agriculture, Food Science and Veterinary Medicine.

Dr. Brayden received his Ph.D. in pharmacology at the University of Cambridge, United Kingdom, in 1989 and was appointed to a postdoctoral research fellowship at Stanford University, U.S.A. In 1991, he joined the pharmacology laboratory of the Irish biotech company Elan Corporation in Dublin as a senior scientist, followed by a project manager position working on several joint-venture drug delivery research collaborations with U.S. biotech companies.

Dr. Brayden is the author of more than 200 research publications and patents. He serves on the editorial advisory boards of *Drug Discovery Today, European Journal of Pharmaceutical Sciences, Advanced Drug Delivery Reviews,* and the *Journal of Veterinary Pharmacology and Therapeutics*. In 2010, he became an associate editor of the new international journal *Therapeutic Delivery*. He was chairman of the United Kingdom–Ireland Local Chapter of the Controlled Release Society (2003–2006), cochair of the veterinary programs at the CRS Annual Meetings (2003–2006), and served on the CRS Board of Scientific Advisors (2006–2009) before being admitted to the CRS College of Fellows in 2012.

Dr. Brayden's major research interests are in oral peptide delivery and specifically in novel formulations of calcitonin. During his tenure at UCD, Dr. Brayden has been a successful Science Foundation Ireland (SFI) principal investigator, completing his PI research grant on the topic of oral delivery of novel muco-adhesive polymeric peptide conjugates in 2009. His current lab group comprises four Ph.D. students, two postdocs, and one technician. Dr. Brayden's research group has been awarded a number of prestigious honors, including the best research paper prize of the *Journal of Veterinary Pharmacology and Therapeutics* (2005) and the American Biographical Society Hippocratic Award for services to medicine (2012).

Apart from maintaining an intensive teaching schedule, Dr. Brayden also serves as director of the Irish Drug Delivery Network Strategic Research Cluster, funded by SFI since 2008. This program links scientists and engineers in partnerships across academia and industry to address crucial research questions, foster the development of new and existing Irish-based technology companies, and grow partnerships with industry that could make an important contribution to Ireland—and its economy. In this role, he leads the cluster team of scientists across four academic centers: the UCD Conway Institute and the schools of pharmacy at Trinity College Dublin, Royal College of Surgeons in Ireland, and University College Cork.

Q *Initially, I would like to ask you some questions about your educational experiences in graduate school. Why did you decide to take another higher academic degree? What made you select the pharmacology program at University of Cambridge?*

A My opportunity at Cambridge arose through a mixture of luck, timing, and my CV being spotted by a potential supervisor. I was actually enrolled in my first year in a postgraduate M.Sc. pharmacology thesis programme at UCD when I saw an advertisement by the University of Cambridge that was sent to Irish universities. They were looking for applicants with first-class honours, so I applied as it had a fantastic reputation in science. In 1985, it was also expected that you would do your Ph.D. abroad, as Ireland was entering a deep economic depression at the time, and there was little research grant money available. Then, a few months later, Prof. Alan Cuthbert, a fellow of the Royal Society (FRS) and head of the Pharmacology Department at Cambridge, wrote to me and said he was interested in my CV, as I had relevant research experience in my M.Sc. project on cystic fibrosis

[1] Chrono Therapeutics Inc., Waltham, MA, U.S.A.
[2] Center for Dermal Research, NJCBM, and Ernest Mario School of Pharmacy, Rutgers–The State University of New Jersey, U.S.A.

(CF). He had separate grant money and, between us, we wrote a successful scholarship grant to the British Council. I then got into Peterhouse College at Cambridge in 1985 and stayed there for four years. I couldn't believe that someone that well known would take that chance on me without ever even having met me! However, I was always going to do a Ph.D., as I enjoyed my undergraduate thesis work, and it was almost expected of that group of 12 honours students at UCD. But to answer your question, Cambridge selects you, not the other way around!

Q *What are your memories (good and bad) of your graduate experience? What was your thesis project, and how did you approach the hypotheses and solve some of the major challenges?*

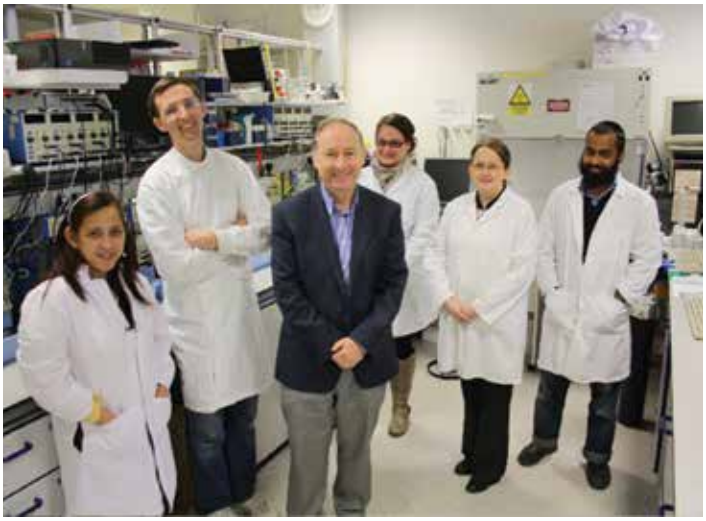
A My project was to see if I could grow sweat glands in culture from CF patients and to see if the gene defect in chloride transport persisted, as this would allow *in vitro* assays to test novel drugs. I eventually learned how to pick out sweat glands from skin and to grow out epithelial cells on plastic and then onto filter supports for transport studies. This was long before you could buy Transwell® filters, and we used to make our own for 10% of the cost. For the first year, I messed up a lot and kept infecting precious cells, some of which came from patients undergoing heart-lung transplants. Alan Cuthbert was a great supervisor, though, and he had me doing other related side projects so I would get well trained and have thesis data coming through all the time. He didn't really like me taking holidays at Christmas to go home, though, as one time when I returned to Cambridge, fungus was crawling out of my cultures, and he ignored me for about a month! Then, I cracked the cell culture piece and the project took off—I recall getting about a year's worth of good data in two months, and I was in the lab in that period at all times of the day and night. The Cambridge pharmacology department and Alan Cuthbert's lab were full of really clever people, and ideas came from all sides in that environment. I would be introduced to scientists who had molecules that could work in my epithelial transport system, and it was up to me to make the collaboration happen. My early papers from that time were in good journals, and one of Alan Cuthbert's strongest points was that he taught his students how to formulate hypotheses, how to prove them, and then how to write properly. Cambridge was one of the happiest times in my life, and all the memories of college life were fantastic. At Peterhouse College, you would often be invited to meet the college's Nobel Prize winners at formal dinners, all part of the experience.

Q *How was your transition from the United Kingdom to the United States? Did you notice any major differences between the U.S. and U.K. systems? How different was the environment at Stanford University to that at the University of Cambridge?*

A In the space of a week, I went from the formal atmosphere of a 500-year-old dark Cambridge college to the beautiful, bright "new" Stanford campus, where some people went to lectures in shorts and on skates. I took up a post as a postdoctoral researcher in Prof. Jeff Wine's CF lab. As a graduate student at Cambridge, I was part of the college system and all its rules, whereas postdoctoral research at Stanford was all about papers and making breakthroughs. As an environment, again it was an amazing place full of brilliant people. I remember going to a seminar by Lubert Stryer, who had actually written one of the most famous biochemistry textbooks I studied as an undergraduate. Stanford was very exciting, with visits by presidents and writers to the campus on a daily basis.

Q *Would you recommend an experience in the U.S. academic system to young researchers from Europe? What advice would you give to such researchers about the transition?*

A I would. At Cambridge when the U.S. offer came, they told me to take it, as it is important to learn how science research is done in the United States. I suppose that, being from Ireland, my U.S. move was pretty typical of many of that generation, as the economics of Ireland were terrible in 1989 (unfortunately not unlike the current period), but doing a postdoc abroad is a pretty essential part of research training in any case. The question is whether you will return at some point. My aunt and uncle immigrated to California in the 1950s and remained there, but when you are in your mid-20s, you don't really think of these things, as such decisions tend to look after themselves later. The transition was not difficult, and I quickly settled into Jeff Wine's lab, which was very international and accommodating to visitors. I got married earlier in the year during my Ph.D., and having a partner share the experience made the move easier.



Members of the Brayden lab (from left: Dr. Leilani Santos from Melbourne, Australia; Dallin Hubbard, visiting Ph.D. candidate from University of Utah, U.S.A.; Dr. David Brayden; Sevenja Sladek, Ph.D. student from Germany; Dr. Martina Gogarty from Dublin, Ireland; and Tauseef Ahmad, Ph.D. candidate from Delhi, India). Additional members are Ed Walsh (Ph.D. candidate from Dublin), Tanira Aguirre (Ph.D. candidate from Brazil), and Fiona McCartney (Ph.D. candidate from Dublin).

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Interview with Brayden continued from page 5

Q *Please tell us a little about your experience during your postdoctoral research. Was the postdoctoral research related in any way to your graduate research project? How did you manage the transition to being a postdoctoral fellow?*

A When I was writing up my Ph.D. in 1989, I wrote to Jeff Wine at Stanford as, similar to Alan Cuthbert, he was a top man in CF research, and his group were excellent at patch clamping, a technique to look at ion channels in single cells. I wanted to stay in CF research, as there was a lot of unfinished business around the ion channel defect once the gene was discovered in 1989. This was the time when many naively thought that gene therapy with an adenovirus vector would quickly cure CF. In the project, we wrote a quite decent paper about the mechanism of action of a blocker of a chloride exchanger for the *American Journal of Physiology*. One lab experience I remember clearly to this day was actually seeing the important chloride channel responsible for the CF defect popping away under a patch clamp from a cell on the oscilloscope. This was the channel that was eventually correctly assigned as CFTR, as there was a major dispute in the literature over the identification. At Stanford, as a fresh postdoc I was quite junior in a lab full of experienced scientists, but this meant I got great training. Also, Jeff Wine had very different qualities from Alan Cuthbert, so I learned from two of the best mentors and have the highest admiration for both as they had major influences on my career, and I have maintained contact with both ever since. Jeff's own daughter has CF (she is still well today), so it was personal for him, and it motivated the laboratory in a positive way.

Q *You decided to move from academia to industry and then back to academia. Please tell us about your experiences with these two different worlds.*

A In 1990 I went to a CF conference after the gene was cloned and the channel defect was discovered. It was obvious that the molecular biologists were then going to be the key players in CF, so I started thinking about how I could adapt my skills in intestinal epithelial ion transport into other areas. At Stanford, the top drug delivery company, Alza, was close to the campus, so I kept hearing about them and their research, and this set me thinking about leveraging my knowledge from ion transport to drug transport and that the models I had worked on could be adapted for oral drug delivery. Then, in 1991, Elan in Ireland advertised a one-year job in Dublin to set up their *in vitro* pharmacology lab, and I saw an opportunity to return and at least to be able to say that I gave it a shot before emigrating. Elan provided excellent training and facilities, and in the 10 years I actually spent with them, I was given a lot of responsibility in managing joint ventures with U.S. biotechs, again with excellent on-the-job training. They allowed me to build my own group and saw that publishing research would give the technologies a lot of credibility, but it also allowed me to maintain an international research profile. In many ways, I continued as an academic in Elan and had tremendous freedom, certainly in the first few years. The big difference from academia was that the research was all about meeting milestones and deliverables, and it was team-based but highly competitive within the company. In 2001, I was looking for a new challenge, and it emerged precisely from the relationships I had helped build between Elan and the academic community through joint supervision of Ph.D. students, having summer students in the lab, and lecturing at UCD. UCD rather surprisingly suggested that I should apply for a lectureship in veterinary pharmacology at UCD (even though I am not a vet!), and another phase began. Since 2001 I have run my own research lab working on oral drug delivery, teaching pharmacology to vets and scientists, writing grants and papers, and putting through Ph.D. students. Being an academic these days requires entrepreneurial skills, so the training I got in Elan has been of great benefit, as keeping the show on the road can be similar to running a small company. It certainly helped me when I was appointed director of the SFI Irish Drug Delivery Network Cluster, a public-private partnership, in 2007.

Q *You are also involved with companies as an independent consultant. Please share with us any important advice you may have.*

A I enjoy consultancy work, as it gives me access to cutting-edge science and scientists, and I learn as much from the client as the other way around. I would never do it as a day job, however, as the pressure to have clients would be immense and the income unreliable. My advice, if undertaking consultancy, is to be completely trustworthy in relation to confidentiality and declare even perceived conflicts of interest up front. As a consultant working with several companies, you are being placed in a very responsible and sensitive position, and you have to compartmentalise knowledge so as not to compromise any client's know-how and strategy. It is also a given that you provide the service on time and to the highest quality and never promise more than you can deliver or consult in areas outside your competency. Reputations can be lost very quickly, and drug delivery research is a small world.

Q *Tell us some of the highlights of your current research areas.*

A We have just published a paper in *JCR* on how intra-articular injections of nanocomplexes of hyaluronic acid, chitosan, and salmon calcitonin resolved inflammation in a mouse model of inflammatory arthritis.[1] This was the result of a three-year collaboration during which we showed that calcitonin down-regulated an inflammatory mediator, NR4A, and then we reproduced it *in vivo* by formulating it in a nanocomplex. It is one of the most technically difficult pieces of research I was ever involved in, as it required experts in NR4A, the KBxN mouse, and formulation of nanocomplexes, none of which was very familiar to me, so I had to generate the team and glue the pieces together. The importance of the work is primarily the demonstration that the mouse model can be used to screen nanomedicines for inflammatory arthritis. Current research is mainly through a large EU FP7 consortium (TRANS-INT) on oral nanomedicines with 19 partners, including Sanofi and Roche (www.trans-int.eu), where we are providing one of the

oral nanoparticle formulations, are examining uptake in the intestine, and will be loading with selected peptide payloads. We are also working on a nutraceutical project funded by the Irish Department of Agriculture examining how we can make a milk-derived bioactive tripeptide nanoparticle that might lower blood pressure.

Q *Tell us which of your publications you are most proud of and why.*

A My very first paper during my Ph.D. still means a lot to me.[2] I don't know how important it was really, but I do remember what I had to go through to get it published and that every piece of data in it was mine. My supervisor would spend days making sure that every word in the paper was accurate, and I have always tried to do the same for my own Ph.D. student papers. It is rare to get that sense of ownership again as you move on in your career. At Elan, we wrote a paper on microparticle uptake by the intestine that has been cited 135 times.[3] I don't recall that it was particularly special at the time, and maybe many cited it to disagree with it! Other papers from that period that we thought were really important were rarely cited, so you never know! With Per Artursson's group at Uppsala, we wrote a well-cited and controversial paper on the human M-like cell model.[4] This model can be used to examine particle and pathogen uptake *in vitro*, and we still use it profitably in our current research. Of the more recent papers, our *ADDR* one on how sodium caprate was researched from cells to current clinical trials in oral formulations is one that provides a roadmap on how to take such a substance right through to potential market.[5] Finally, for my vet colleagues, we got a best paper award from *JVPT* in 2005 for the discovery that the antiparasitic agent selamectin inhibited P-glycoprotein, and this had clinical relevance.[6]

At the 2012 CRS Annual Meeting, David Brayden was inducted into the CRS College of Fellows. Left to right: Kazunori Kataoka, David Brayden, Theresa Allen, and Martyn Davies.

Q *Please tell us about your teaching courses. What is the teaching focus area, and how do you apply effective teaching practices?*

A On my first day in UCD, an experienced colleague took me aside and told me that I shouldn't be there if I was not interested in teaching, even though I was hired ostensibly to set up a research programme. I completely agree with this and cannot abide a tendency for some universities to hide away their top researchers from teaching duties. I teach undergraduate courses in pharmacology to vet students and courses in drug discovery and development to final-year science students. I also make a big effort in delivering specialist modules to UCD's structured Ph.D. programme. In my first few years in UCD, I attended every course going on to see how to improve my teaching as, although I was a decent enough presenter, that is not the same as learning how to teach students. Staff are expected to develop online teaching portfolios encompassing philosophy and reflection and also to listen to feedback from external examiners and students. There is a focus now on online material, and the IT aspects of teaching are rapidly changing. In fact, I did my first narrated online lecture when I was chairman of the CRS Webcast Committee, about two years before I did any for the university, so again, a good example of how CRS can benefit its volunteers in many ways.

Q *Do you have any advice for young scientists who face many challenges with shrinking finances for grants but also many new opportunities with globalization of research?*

A Strange times indeed with very little certainty on grant funding. A paradox for drug delivery scientists is that the focus of governments on applied translational research actually puts them in a far more fundable position than basic biomedical scientists. This may not be much consolation for grant writers operating in environments where less than 20% success is the norm, so we are all having to accept our share of rejection in grants and to look at referee comments as objectively as possible before getting back on the horse. I'm sure most of the *CRS Newsletter*'s academic readers are busy writing economic and impact statements for their recent research grant applications, so this is a new language and set of requirements for the modern grant writer. Still, drug delivery researchers should be able to adapt to the current trends better than most. They need to think laterally and to collaborate with top scientists from many disciplines to elevate the scientific impact of their applications. In addition, drug delivery researchers have the possibility of generating industry collaborations more easily than other disciplines, and these are also generating favour with funding agencies, who want to promote and provide support for these relationships. Young scientists trained in my own lab have done well in industry or as young lecturers and postdocs in all parts of the world. What they each have in common is the necessary fierce determination and ambition, allied to technical ability.

Interview with Brayden continued on page 8

Interview with Brayden continued from page 7

Q *Your current appointment is at a veterinary school. Tell us a little more about what the environment offers at such a school for those of us who have not had this experience.*

A The UCD vet school is the only one in Ireland and is over 100 years old. It produces 120–130 vets a year in its American and European Veterinary Medical Association accredited degree programme. The staff are a mix of clinicians and preclinical lecturers like me, and the school's research ranges from the study of small and large animal diseases, zoonoses, and parasitology to more basic research in animal physiology. The school has a training hospital for students to treat companion animals and horses and a farm for large animal research in the country. The hospital has had unusual cases from the zoo (arriving by police escort), including a much-loved tiger. The vets get the same kind of training as medical doctors, and one of their boasts is that they can treat more than one species! It's possible to get animal tissue for drug delivery work in addition to rodents, so it's an interesting place to do research.

Q *Please tell us about your favorite activities and hobbies when you are not involved with research and your other duties.*

A I do a lot of hill walking with family and friends in County Wicklow, known as the garden of Ireland, which is 10 km from where we live. I read a lot and am in a book club that meets in one of Dublin's oldest pubs. I played competitive amateur league tennis until this year, when my lower back told me to stop punishing it and to give it a break. I also play the violin and was trained to grade 8 standard in my teens, so the odd bit of practice keeps me sane, especially if one of my graduate students is driving me up the walls. Other than that, I am a keen sports fan, going to many Leinster and Ireland rugby games and going through the regular torture of watching Liverpool FC on television.

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More Educational Opportunities from CRS

These CRS workshops will take place at the 2013 AAPS Annual Meeting & Exposition
November 10–14, 2013
San Antonio, Texas, U.S.A.

Introduction to Microencapsulation Technologies Workshop

Knowledge of multiple encapsulation technologies and how they are applied is valuable information for developing new products or solving existing problems. It is important, at a minimum, to have a basic understanding of all commonly available processes and their applications. This workshop provides an introduction to common micro- and nanoencapsulation processes and their various applications. The workshop is structured to 1) introduce common encapsulation techniques, 2) review common materials, and 3) provide an overview of the wide range of applications for controlled release products.

Workshop Organizers
James Oxley, Southwest Research Institute, U.S.A.
Irwin Jacobs, Particle Dynamics International, LLC, U.S.A.

Mitigating Risks for Patients When Developing Oral Controlled Release Dosage Forms Workshop

The focus will be to understand the possible risks to patients and approaches to manage them when developing oral extended-release (ER) dosage forms. The discussion will relate to the design, development and manufacture of commonly used ER systems. Industry leaders and subject matter experts will provide scientific basis to the material science, formulation, and process attributes that will help to mitigate risks, under the umbrella of quality by design (QbD). The overall goals of such approaches are to improve quality, reduce costs, but maintain patient safety and treatment.

Workshop Organizers
Ali Rajabi-Siahboomi, Colorcon, U.S.A.
Mansoor Khan, CDER, USFDA, U.S.A.

Register online at www.aaps.org. Information about these workshops is also available on the CRS website at **controlledreleasesociety.org**.

Welcome New CRS Members

Aly Abdelbary
Rachit Agarwal
Yurika Agato
Lucas Ahrens
Afsana Akhter
Norah Albekairi
Beatrice Albertini
Have Alija
Martin Alm
Oday Sajjad Alsawad
Isil Altintas
Helene Andersson
Hidenori Ando
Santosh Aryal
Jesper Bahnsen
Timothy Barnes
Colin Barrow
Rory Bell
Eric Benjamin
Susanne Beyer
Gaurav Bhatia
Pranav Bhujbal
Marie Boegh
Katarina Bolko
Garland Bonner
Brooks Boyd
Akshay Buch
Stephen Buckley
Mechthild Burmester
Bing Cai
Jing Cao
Maxx Capece
Sheiliza Carmali
Edmund Carvalho
Dalia Castro-Vidal
Antonio Cervadoro
Jorge Cervantes
Ling-Yun Chang
Chen Chen
Kuan Chen
Xishan Chen
Jasper Chiu
Hana Cho
Hyun-Jong Cho
Soonki Cho
Duhyung Choi
Sung Yoon Choi
Yeonho Choi
Young Chan Choi
Young T. Choi
Rina Chokshi
Mahavir Chougule
David Chu
Amanda Clark
Jason Coleman
Dustin L. Cooper
Daniel J. Corbett
Gerald Cummings
Miriam Dadparvar
Nicolas Darville
Rajesh Dave
Aine De Baroid
Paolo Decuzzi
Yuko Deharu
Ditixa Desai
Giustino Di Pretoro
Matthew Dickerson
Duc Do
Bhuvana Doddapaneni
Takayuki Doen
Hisato Doi
Yannan Dou
Christina Draheim
Christine Dufes
Craig L. Duvall
Elizabeth Enlow
Ha Na Eom
Zhongjian Fang
Shady Farah
Stefan Fischer
Ana Luiza Forte
Susan O. Freers
Li-Tse Fu
Takaaki Funatsu
Yong Gan
Sofie Gardebjer
Xuemei Ge
Dean Glettig
Morvarid Goharzadeh
Philippe Gorria
Akinori Goto
Matthew Greene
Alexis Guillot
Thilak Gunatillake
Shiyan Guo
Simerdeep Singh Gupta
Na-Kyung Han
Mariko Harada-Shiba
Mai Hazekawa
Maho Hirabe
Yasuhiro Hiraishi
Cheol Am Hong
Matej Horvat
Nazir Hossen
Huangpin Hsieh
Chieh-Shen Hu
Jun Hu
Xiao Hu
Zhenhua Hu
Yu-Fen Huang
Ho-Wah Hui
Sangmin Hyun
Diana Ickowicz
Narimoto Ishizuka
Shoko Itakura
Ashwinkumar Jain
Rohit Jain
Maziyar Jalaal
Yejin Jang
Chen Jiang
Xinguo Jiang
David Johnson
Tomoko Kanei
Chen-Yu Kao
Shyam B. Karki
Pankaj Ranjan Karn
Roger Kaspar
Eriko Kawamura
Riku Kawasaki
Filis Kazazi Hyseni
Jaehong Key
Lars Kilaas
Chun-Ho Kim
Dong-Hyun Kim
Dongkyu Kim
Eun Ji Kim
Eunjoo Kim
Eunmi Kim
Hong Kee Kim
Hyun-Chul Kim
Jin-Qyu Kim
Jong Oh Kim
Keun-Sik Kim
Ki Hyun Kim
Sang Yoon Kim
Su-Hyeon Kim
Marten Klukkert
Kevin Koziatek
Katja Kristan
Emily Krogstad
Vijay Kulkarni
Hagar I. Labouta
Frederic Lallemand
Scott Lamb
William Lambert
Hwankyu Lee
Slgirim Lee
Jongbin Lee
Kyuho Lee
Phillip K. Lee
Jardin Leleux
Fransisca Leonard
Ellen Q. Li
Xiang Li
Yuanpei Li
Jiahorng Liaw
Junyeul Lim
Sung Mook Lim
Tzuyin Lin
Dongzhou Liu
Jian Liu
Shan Liu
Tse Ying Liu
Tzu-Yu Liu
Xiang Liu
Korbinian Loebmann
Darryl F. Love
Yi Luo
Priscilla Luz
Guanghui Ma
Xinrui Ma
Elena Macchi
Hiroo Maeda
Kazuya Maeda
Yoshiya Maegawa
Yutaro Maekawa
Rahul Manek
Paolo Marizza
Yasunori Matsukami
Yoko Matsumoto
Yu Matsumoto
Minami Matsuura
Takuya Matsuyama
Sabine May
Patricia Mazureki Campos
Brian Mcmillan
Kehley Miller
Yelloji-Rao Mirajkar
Ankit Mittal
Noriko Miyamoto
Jingxin Mo
Guadalupe Moctezuma
Nancy Monteiro-Riviere
Wesam Waleed Mustafa
Kaisa Naelapaa
Shotaro Nagase
Takashi Nakamura
Hayley Nehoff
Kazuhiro Nishida
Anna Novikova
Luis Novo
Akiko Ogino
Nuri Oh
Ayaka Okamoto
Brandon Orawiec
Asuman Yekta Ozer
Murali Monohar Pandey
Han Jung Park
Hansoo Park
Min-Ho Park
Rameshwar Patil
Ashish Pattekar
Linda Persson
Stephanie Phan
Brenda Pinto
Alexey Popov
Vibha Puri
Dongmei Qiang
Renuka Ramanathan
Ranadheer Ravula
Signe Ridderberg
Jim E. Riviere
Ina Rosenberger
Kenneth Rubow
Eduardo Ruiz-Hernandez
Erik Rytting
Kenichi Sakai
Neda Samadi
Sampada S. Sawant
Mathieu Schmitt
Carl Schoellhammer
Daniel Schweizer
Bo-Bae Seo
Jeong-Min Seo
Ken Seufert
Suhaili Shamsi
Sanjeev Sharma
Shoucang Shen
Julie Shi
Pu Shi
Sanjun Shi
Yang Shi
Atsuo Shigeno
Ho-Chul Shin
Jeong-Hyun Shin
Teppei Shirakura
Parshuram G. Shukla
Masaharu Somiya
Youngju Son
In-Ho Song
Yun-Mei Song
Tycho Speaker
Sven Staufenbiel
Soren Steffensen
Rachel Stephenson
Bernd Sterner
Zhiguo Su
Erina Suemitsu
Jung Soo Suk
Wei-Jhe Syu
Yoshimasa Takafuji
Rafael Teruiti Takamoto
Atsushi Tamura
Songwei Tan
Hiroki Tanaka
Jie Tang
Mary Tang
Sung-Ling Tang
Kristian Tangso
Sebastien Taurin
Anthony K. Taylor
Rakesh Tekade
Peter Thomsen
Zhigana Tian
Naama Ester Toledano
Masami Ukawa
Andrew Urquhart
Iris Van Der Heijden
Alex Van Herk
Takehiko Wada
Rike Wallbrecher
Colin Walsh
Chi-Hwa Wang
Hui Wang
Jianxin Wang
Qiming Wang
Qing-Qing Wang
Dallas Warren
Jorrit Water
Carl A. Webster
Wei Wei
Xin Wei
William Wild
Caixing Wu
Chuan-bin Wu
Fei Wu
Jiang Wu
Lieyi Wu
LinPing Wu
Tian Wu
Robert Wulff
Hongnan Xia
Xiaofei Xiang
Dan Xu
Guofeng Xu
Jinke Xu
Yingying Xu
Mayo Yamashita
Liu Yang
Zongning Yin
Sujin Yoon
Hwa In Yoon
Miyako Yoshida
Susanne Youngren
Hongjiang Yuan
Joseph A. Zeleznik
Jin Zhang
Jinping Zhang
Xinxin Zhang
Yu Zhang
Jianhua Zhu
Yu Zhu

Emerging Challenges for Global Delivery

July 21–24, 2013 • Hawaii Convention Center • Honolulu, Hawaii, U.S.A.

One of the Most Expansive Programs in Recent Years

Chair Mark Saltzman, Yale University, U.S.A., and his fellow Annual Meeting Program Planning Committee members have spent months examining, reviewing, organizing, and diligently combing the landscape of delivery science to put together a meeting that lives up to CRS's reputation as the premier source for scientific information in the controlled release delivery field. "Science forms the core of the meeting," said Saltzman. "That's what we focused on first and foremost. We want to bring thought-provoking, cutting-edge research to the forefront."

The number of approved abstracts (close to 800), along with an impressive list of invited speakers and scientific sessions covering some of the most important and emerging issues in delivery science, reflects the committee's focus and efforts. "Organizing this year's program was truly a team event," said Saltzman. "It's gratifying when you see it all come together—especially with the level of response we've had this year."

2013 Annual Meeting Program Planning Committee

Chair
Mark Saltzman, Yale University, U.S.A.

Deputy Chair
Ick Chan Kwon, KIST, Korea

Members
Marcel Bally, British Columbia Cancer Research Centre, Canada
Marcus Brewster, Johnson & Johnson, Belgium
Sarah Eccleston, Aptuit Ltd., United Kingdom
Chuck Frey, Coating Place Inc., U.S.A.
Justin Hanes, Johns Hopkins University, U.S.A.
Hideyoshi Harashima, Hokkaido University, Japan
Nicole Papen-Botterhuis, TNO, The Netherlands
Joshua Reineke, Wayne State University, U.S.A.
Christian Seiler, Merck Sharp & Dohme, United Kingdom

Who's Coming?

The abstract submission authors, invited speakers, and exhibitors provide a good indication of the organizations that will be represented at the 40th Annual Meeting & Exposition of CRS. The list will be updated periodically as registrations are received. To see the most up-to-date list, go to controlledreleasesociety.org and look under 2013 Annual Meeting/Overview.

An Impressive List of Invited Speakers

Saltzman's team also focused on another core feature of the annual meeting: providing opportunities for attendees to connect with some of the leading minds in the controlled release field. "The annual meeting should be a place where you can obtain information and insight you wouldn't get anywhere else," said Saltzman. With that in mind, the program planning team put together a plenary program offering a firsthand look at some of the most important emerging research along with a unique opportunity to gain insight into the commercial side of discovery and innovation.

Plenary speaker Kenzo Takada, chairman and founder of Evec, Inc., and professor emeritus at Hokkaido University, Japan, will speak on "Human B-Lymphocytes as a Source of High-Affinity, Really Fully Human Antibodies." Takada has studied molecular mechanisms of oncogenesis by Epstein-Barr virus for 40 years. He is the author of over 150 peer-reviewed publications and received the Minister of State for Science and Technology Policy Award and the Hokkaido Science and Technology Award, and he was the director of the Institute for Genetic Medicine, Hokkaido University, from 2002 to 2006. Evec is one of the most successful bio venture companies, having its head office in Sapporo, Japan. It was established in 2003 as a spin-off from Hokkaido University. Evec has a unique technology to produce high-affinity native antibodies from human lymphocytes using Epstein-Barr virus. The method first induces the proliferation of B-lymphocytes from human blood using Epstein-Barr virus and then isolates those producing the antibodies of interest. Licensing agreements have been concluded with Boehringer Ingelheim Pharmaceuticals (Germany) and Astellas Pharma (Japan) for two types of antibodies in 2008 and 2011, respectively.

Josh Wolfe's plenary lecture, "Hype and Hope: A View from a Venture Capitalist," provides a venture capital investor perspective on commercializing scientific breakthroughs, raising capital, recruiting talent, and building a high-growth high-tech venture. He dispels myths and shares insider views on the high-stakes, risky, and competitive world of venture investing. How can you secure nondilutive funding? What are the key terms to seek or be wary of when negotiating a deal? What are the new and emerging trends VCs are pursuing, and where are they shunning opportunities? Wolfe, who is founding partner and managing director, Lux Capital, U.S.A., is a columnist with *Forbes*, editor of the *Forbes/Wolfe Emerging Tech Report*, and host of a show on the Forbes Video Network. He has been an invited guest to the White House and Capitol Hill to advise on nanotechnology and emerging technologies; a lecturer at MIT, Harvard, Yale, Cornell, Columbia, and NYU; and a frequent guest on CNBC and CNN. Mr. Wolfe graduated from Cornell University with a B.S. in economics and finance.

Plenary speaker Paula T. Hammond, David H. Koch Professor of Engineering, Department of Chemical Engineering and Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology, U.S.A., will speak on "Electrostatic Nanolayer Delivery Platforms: From Macro- to Nanopharmacies." Hammond is a member of MIT's Koch Institute for Integrative Cancer Research, the MIT Energy Initiative, and a founding member of the MIT Institute for Soldier Nanotechnology, a multimillion-dollar Army-funded university-affiliated research center launched in 2002 that is now in its second phase of funding. Prof. Hammond was awarded the NSF Career Award, the EPA Early Career Award, and the DuPont Young Faculty Award. In April 2010, Hammond was named Scientist of the Year at the Harvard Foundation's Albert Einstein Science Conference. She was featured in 2011 as one of the Top 100 Materials Scientists by Thomson Reuters, based on citation and overall impact, and she has published over 200 papers in refereed journals.

The latest information on bioactives, consumer and diversified products, and preclinical sciences and animal health are the focus of this year's 20 scientific sessions and five mini-symposia.

Expand Your Knowledge with a Premeeting Educational Workshop

Controlled Release Dosage Forms and Product Development Strategy for Expected New Regulatory Trends

Cosponsored by Ashland Specialty Ingredients
Chairs: *Ubrani Venkataram and Yanning Lin, Food & Drug Administration, U.S.A.*

Oral Delivery of Bioactives Using Lipid-Based Drug Delivery Systems

Cosponsored by Avanti Polar Lipids, Inc.
Chairs: *Anette Müllertz, University of Copenhagen, Denmark, and Sarah Hook, University of Otago, New Zealand*

Using *In Vitro–In Vivo* Correlation (IVIVC) to Meet Challenges in Global Delivery

Cosponsored by SOTAX Corporation
Chair: *Vivian Gray, V. A. Gray Consulting, Inc., U.S.A.*

You may register for a workshop only and not attend the CRS Annual Meeting. Advance registration is required. If you have already registered for the meeting, contact Sue Casey (scasey@scisoc.org) to add a workshop to your registration. Limited number of reduced-rate student/postdoc tickets available. See the CRS website for complete details.

Sponsor a Workshop – Learn how your organization can receive recognition by sponsoring one of these workshops. Contact Debby Woodard at dwoodard@scisoc.org.

40th Annual Meeting & Exposition of the Controlled Release Society

July 21–24, 2013
Hawaii Convention Center
Honolulu, Hawaii, U.S.A.

CRS Leading Delivery Science and Technology

controlledreleasesociety.org/meeting

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Hawaiian Location Offers Unique Advantages

As the crossroads of the Pacific, Hawaii is positioned as a center of commerce with global appeal. The emerging markets of China, India, and other Pacific Rim countries offer huge potential for those in the delivery field, from pharmaceuticals to consumer and diversified products. A growing number (nearly 25%) of the CRS membership comes from Asia and the Pacific Rim, and this area is already served by seven CRS chapters.

Honolulu is also surprisingly affordable. According to OmniTrack Group, Inc., studies show that San Diego, New York, San Francisco, New Orleans, and Philadelphia all have higher daily per diem costs than Honolulu, including airfare and hotel costs. CRS has also negotiated discounted hotel rates for CRS annual meeting attendees at the Hilton Hawaiian Village.

Nestled on 22 acres, the Hilton Hawaiian Village grounds include lush tropical gardens, waterfalls, exotic wildlife, five swimming pools, and the Duke Kahanamoku Lagoon, perfect for kayaking and stand-up paddle surfing.

Rainbow Lanai, courtesy of the Hilton Hawaiian Village.

Scientific Sessions Invited Speakers

Challenges Around Brain Delivery: Sampling Site Issues and Interspecies Extrapolations
Margareta Hammarlund-Udenaes, Uppsala University, Sweden

Drug Delivery for Developing Countries/Global Challenges
Kim Woodrow, University of Washington, U.S.A.

Drug Targeting, Pharmacokinetics, and Biodistribution: Differences Between Species
Jim Klostegaard, University of Texas, U.S.A.

Emerging Technologies
Dan Luo, Cornell University, U.S.A.

Food, Nutraceuticals, and Personalized Diet
Martin Kussmann, Nestlé Institute of Health Sciences SA, Switzerland

Imaging and Characterization Techniques for Drug Delivery: Systems and Targeted Drug Delivery
Karsten Mäder, Martin-Luther University Halle-Wittenberg, Germany

Micro- and Nanoparticle Design
David Weitz, Harvard University, U.S.A.

Modern Agriculture and Aquaculture
David Powell, ProFishent Inc., U.S.A.

Personal and Home Care
Jiten Dihora, Procter & Gamble, U.S.A.

Oral CR – Pharmaceutical Formulations, Technologies, and Development Strategies
Peter Timmins, Bristol-Myers Squibb, United Kingdom

Oral CR – Predictive Tools (*In Vitro/In Vivo/In Silico*)
Sandra Klein, UNI Greifswald, Germany

Parenteral Sustained Release Drug Delivery
Steven Schwendeman, University of Michigan, U.S.A.

Peptide and Protein Delivery
Tarek Fahmy, Yale University, U.S.A.

Processing Technology/Manufacturability
Beth Hill, Johnson & Johnson, U.S.A.

Regional Delivery: Challenges in Ocular Delivery and Pulmonary Delivery
Samir Patel, Clearside Biomedical, U.S.A.

Rising Suns in Asia
Yukio Nagasaki, University of Tsukuba, Japan

RNAi and DNA Delivery
Chae-Ok Yun, Hanyang University, Korea

Smart Building and Construction Materials and Coatings
Henk Jonkers, Delft University of Technology, The Netherlands

Solubilization Technology: A Key Enabler for the Delivery of Poorly Soluble Drugs
Ravi Shanker, Pfizer, U.S.A.

Topical/Transdermal Drug Delivery
Rainer Müller, Freie University Berlin, Germany

Networking: A Key Part of Every Annual Meeting

With such an expansive program and attractive venue, the anticipated attendance at this year's meeting means greater opportunities to connect and network. Personal interaction forms an important part of the program and includes both social events and opportunities for discussion and debate.

"The CRS annual meeting is international and diverse, with more than 1,300 attendees representing some 300 companies, 225 universities, and 40-plus countries typically in attendance."

Roundtable Discussions

Roundtable discussions are in-depth interactive sessions with a panel of experts who share their findings and opinions. This year's roundtables include:

Ocular Drug Delivery

Novel Biomaterials for Ocular Drug Delivery
Cochairs: Ruiwen Shi, Allergan Inc., U.S.A., and Clive Wilson, University of Strathclyde, United Kingdom

Invited Speakers

Bulk-Scale, DNA-Based Hydrogels for Drug Development and Delivery
Dan Luo, Cornell University, U.S.A.

Rational Design for Bio/Pharma Materials for Drug Delivery: Past, Present, and Future
Andrew Urquhart, University of Strathclyde, United Kingdom

Oral Drug Delivery

Multiparticulate Oral Drug Delivery Systems for Fixed Dose Combinations
Cosponsored by Colorcon
Cochairs: Ali Rajabi-Siahboomi, Colorcon Inc., U.S.A., and Sarah Eccleston, Aptuit Ltd., United Kingdom

Invited Speakers

Designing and Utilizing Multiparticulates for Fixed Dose Combination Dosage Forms
Brett Caldwell, Bend Research, U.S.A.

Multiparticulates in Developing Novel Fixed Dose Combination Products
Michael Valazza, Catalent, U.S.A.

Nanomedicine

Challenges Associated with Commercialization of Nanomedicines
Cochairs: Christine Allen, University of Toronto, Canada, and Marcel Bally, British Columbia Cancer Research Centre, Canada
Speakers to be named.

CRS Connect

Sponsored by Aptalis Pharmaceutical Technologies

The CRS Annual Meeting mobile app makes networking among attendees more convenient than ever. Within the app is CRS Connect, which enables fellow attendees to easily search for one another by name, company, or specific area of interest. The tool also includes messaging and appointment request features and can be used on mobile devices and tablets or accessed with a laptop computer through the desktop URL. Specific instructions for using CRS Connect can be found on the CRS website.

Young Scientist Events

Cosponsored by Diurnal Limited, Microtek, and Upsher-Smith Labs

Early career professionals and students have several avenues for networking and skill-building during the meeting. A full-day workshop scheduled for Saturday, July 20, titled "Fundamentals of Controlled Release Drug Delivery: Physiochemical and Biological Aspects" will focus on the fundamentals of the design and performance of innovative controlled release drug delivery systems.

Effective communication is the theme for a half-day workshop that will be held on Sunday, July 21. The workshop is a continuation of the Professional and Self Development workshop series showcased during past annual meetings and will focus on developing interpersonal relationships, improving listening and negotiating skills, resolving conflict, and strengthening assertiveness. Intercultural communications will also be covered.

The Get Up! Get Educated! sessions begin Monday and Tuesday mornings at 7:00 a.m. These hour-long sessions focus on specific topics that are designed especially for young scientists. The topics for this year's meeting are "Nanomedicines for Drug Delivery Across Epithelial Barriers: Intestines, Skin, and Lungs" and "Quality by Design: Systematic Development of Pharmaceutical Products."

The roundtable discussion, "Commercializing Ideas from Academia: Past Lessons and Current Challenges," will feature a discussion on the challenges of developing a business model while competing with the pharmaceutical industry. The panel will feature successful entrepreneurs who will share their experiences and challenges in commercializing ideas from academia.

The always popular Young Scientist Networking Event offers an opportunity to meet with other young scientists and those young at heart at a venue unique to the culture of the host city. This year's event will take place at Jimmy Buffett's at the Beachcomber Restaurant and Honolulu Surfing Museum. CRS

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plenary speakers Paula Hammond and Josh Wolfe, along with several members of the CRS Board, will also be in attendance. This is always a sell-out event, so those interested in attending are encouraged to purchase their tickets early.

Preclinical Sciences & Animal Health Get-Together

Cosponsored by Merial

The CRS Preclinical Sciences & Animal Health (PSAH) Division was launched at last year's CRS Annual Meeting and is designed to serve scientists involved in the development and regulation of drugs and biologics intended for veterinary use as well as those working in preclinical drug development. The division has been very active this past year, providing its members with the most up-to-date information on the study of therapeutics in animals, whether from the standpoint of drug development for a certain species or from the perspective of the use of various species to support the development of drugs for human use. PSAH Division members and those with an interest in this area are invited to attend the Preclinical Sciences & Animal Health Get-Together, featuring a presentation on the beagle dog as a preclinical species, including historical use of the beagle as a research species, potential pitfalls, and future directions. After the presentation, the event will conclude with valuable face-to-face networking time for those in attendance.

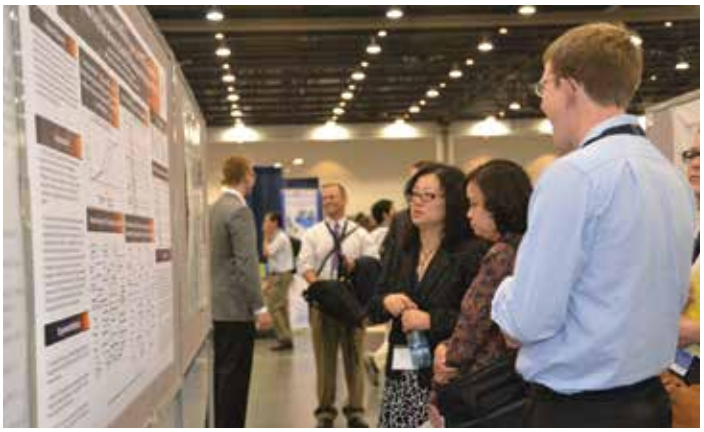
Consumer & Diversified Products Division Luncheon

Cosponsored by Coating Place, Fleet Laboratories, and Ronald T. Dodge Company

The Consumer & Diversified Products Division (C&DP) focuses on encapsulation and controlled release research for food, nutraceuticals, personal care, cosmetics, home care, agriculture, textiles, and coatings. Members of the C&DP Division or those who have an interest in this area can meet and network at a special buffet luncheon that will be held at the Hawaii Convention Center. There will also be a C&DP Division business meeting on Wednesday, and anyone who is interested is invited to attend.

CRS President's Banquet

A high point of the annual meeting, this year's CRS President's Banquet will showcase the global breadth of the Controlled Release Society. CRS local chapters will highlight recent groundbreaking achievements in delivery science taking place within their geographical areas, spanning the world from the United Kingdom to China to New Zealand. The event will be held at the Hilton Hawaiian Village and will feature a dinner reflective of the Hawaiian Islands' cuisine and culture. Outgoing CRS President Kazunori Kataoka will close the evening with a brief presentation reflecting on his year serving as the society's president.



Close to 800 abstracts have been accepted for this year's annual meeting, one of the largest numbers in recent years.

Mini-Symposia Invited Speakers

Breakthrough Technologies in Drug Delivery Systems from Asia

Cosponsored by Japan Society of Drug Delivery System

Kwangmeyung Kim, KIST, Korea
Hirofumi Takeuchi, Gifu Pharmaceutical University, Japan
Zhiyuan Zhong, Soochow University, China

Drug Combination Products
Charlie Boone, University of Toronto, Canada
Lawrence Mayer, Celator Pharmaceuticals Corporation, Canada
Liangfang Zhang, University of California, San Diego

Energy: Problems Within the Industry That Controlled Delivery Can Solve
Anne Dalager Dyrli, RESMAN, Norway
Jo Darkwa, University of Nottingham Ningbo, China
James Oxley, Southwest Research Institute, U.S.A.

Hybrid Groups: Bridging the Gap Between Industry and Academia
Karimah Es Sabar, Center for Drug Research and Development, Canada
Patrick Griffin, The Scripps Research Institute, U.S.A.
Bert Klebl, The Lead Discovery Center at Max Planck, Germany

Nanoparticles and Cancer
Michelle Bradbury, Memorial Sloan Kettering Cancer Center, U.S.A.
Jordan Green, Johns Hopkins University, U.S.A.
Yuanpei Li, University of California–Davis, U.S.A.

Sourcing Products and Discovering New Innovations

Every CRS annual meeting offers the opportunity to connect with companies that are partners and pioneers in delivery science. CRS Innovation Sunday is a day packed with sessions that feature the latest products and technologies. Technology Forums hosted by individual companies focus on in-depth facets of products and services that support research and development in delivery science. At the Soapbox Sessions, industry presenters "get up on their soapbox" to give a quick glimpse of some of the most innovative technologies and products in development today. These sessions are a great way to get an insider's look at emerging products.

Also part of CRS Innovation Sunday, this year's Industry Roundtable, titled "Global Perspectives on Emerging and Established Delivery Markets," will include a panel of business development and R&D executives from Asia, Europe, and North America, who will provide insight into the latest trends, challenges, and needs in delivery science. The day's events conclude with the Exposition Grand Opening and Welcome Reception.

Soapbox Sessions

Acuitas Therapeutics
Bend Research Inc.
BioModics Aps
Bioneer: Farma Faculty of Health Sciences, Denmark
Cabot Corporation
Ceridia Pty. Limited
GrayBug
Losan Pharma (in collaboration with Henkel Corporation)
Paraytec Ltd.
Particle Dynamics International
PNST LLC dba Tranzerm Solutions
Polymer Therapeutics, LLC
RESMAN AS
Serina Therapeutics, Inc.
Surface Measurement Systems
Theraly Pharmaceuticals
TNO

Technology Forum Presentations

Capsugel
Catalent
CIMA Labs
Colorcon & Dow Food & Pharma Solutions
Hovione
Medimetrics Personalized Drug Delivery, Inc.
MedinCell SA
Mott Corporation
Purac Biomaterials & OctoPlus
SOTAX Corporation

Registration Is Open!

controlledreleasesociety.org/meeting

Honoring CRS Leaders Past, Present, and Future

Tram Dang

"The Sung Wan Kim Postdoctoral Fellowship has given me the wonderful opportunity to freely explore different aspects of a new field of study."

You're Invited

Join us Monday, July 22, in Honolulu, Hawaii, prior to the CRS Annual Meeting Plenary Session to hear Sung Wan Kim Postdoctoral Fellowship 2012 awardee Tram Dang discuss her postdoctoral appointment in the laboratory of Prof. Ali Khademhosseini at the Brigham and Women's Hospital and the Harvard Medical School. Tram Dang's work at MIT led to this postdoctoral fellowship in which she is involved in research at the interface of engineering and immunology.

The Sung Wan Kim Postdoctoral Fellowship Award honors Prof. Kim for his CRS leadership and pioneering research in delivery science.

Give It Forward

You can help support excellence in delivery science through your support of the CRS Foundation. Donations can be made online at controlledreleasesociety.org/about/foundation

In 2007 CRS established the CRS Foundation, a 501(c)(3) educational endowment, to honor individuals who have made notable contributions to the society and its technologies and to support the scientific training of its future leadership.

CRS FOUNDATION

Exposition Grand Opening & Welcome Reception

The Exposition Hall is the place for the business of delivery science and profitable collaboration. It is also the central hub for poster viewing, program breaks, prizes, and refreshments. The exposition kicks off on the evening of CRS Innovation Sunday, July 21, and continues through July 23. Come to the Exposition Hall for discovery, solutions, and opportunities!

NEW! Stop by the Asia Pacific Pavilion to meet first-time exhibiting companies from the Asia Pacific region.

2013 CRS Exhibiting Companies

3M Drug Delivery Systems
Advanced Polymer Materials Inc.
Agilent Technologies
Akina, Inc.: PolySciTech Division
Asahi Kasei America
Avanti Polar Lipids
BASF
Bend Research Inc.
BioPharm Solutions, Inc.
Catalent
CIMA Labs
Colorcon Inc.
Corden Pharma Switzerland
CoSci Med-Tech Co., Ltd.
Covaris
Dissolution Technologies
Drug Delivery Partnerships Conference
Drug Development & Delivery
DURECT Corp./Lactel Absorbable Polymers
Elsevier
EMD Millipore
Evonik Degussa Corporation Pharma Polymers
Freund-Vector Corp.
Glatt Air Techniques, Inc.
Halozyme Therapeutics
Hovione
Lipoid LLC
Medimetrics
MedinCell
The Methodist Hospital Research Institute/Methodist Academy
Michelson Prize & Grants
NanoSight
Nisso America Inc./Nippon Soda Co., Ltd.
NOF Corporation
Northern Lipids Inc.
Novozymes Biopharma
OctoPlus, a subsidiary of Dr. Reddy's Laboratories Ltd.
ONdrugDelivery
Partnership Opportunities in Drug Delivery – PODD
Patheon
Pharmaceutical Technology
PharmaCircle
Polymun Scientific GmbH
PolyPeptide Group
Purac Biomaterials
QPharma AB
Saint-Gobain Performance Plastics
Scintipharma Inc.
Sekisui Medical Co., Ltd.
Simulations Plus, Inc.
Sirius Analytical Inc.
SkyePharma
SOTAX Corporation
Southwest Research Institute
Springer
Surface Measurement Systems
Technology Catalysts International Corporation
Texture Technologies Corp.
Vision Processing Technologies, Inc.
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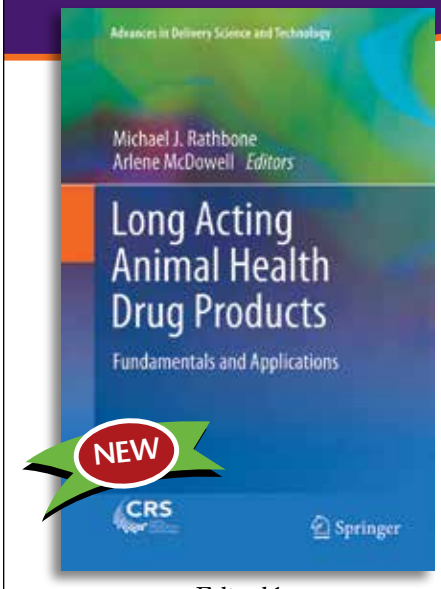

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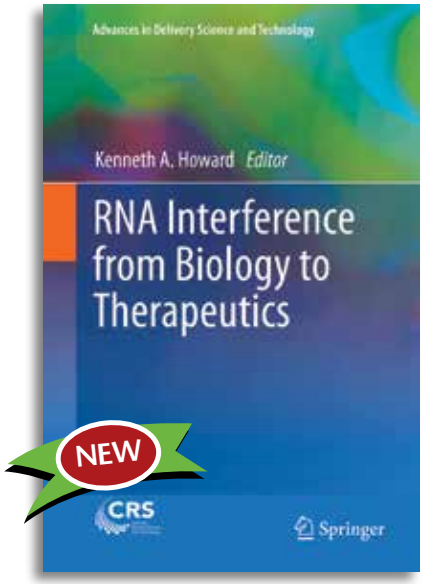

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The Effect of Nanoconstruct Physicochemical Characteristics on Biological Activity

Hayley Nehoff, Sebastien Taurin, and Khaled Greish
Pharmacology and Toxicology Department, University of Otago, Dunedin, New Zealand

Introduction

It has been almost 30 years since Maeda and colleagues first described the enhanced permeability and retention (EPR) effect. The promise of the EPR effect for nanomedicine was great. However, currently only 11 nanoconstructs have reached the market, with a large number of nanoconstructs failing in clinical trials.

It is our view that understanding of the relationship between nanoconstruct physicochemical characteristics and biological behavior is necessary for the progress of nanomedicine toward the clinic. In this study, we used a micelle-delivery platform based on poly(styrene co-maleic acid) (SMA) to encapsulate the chemotherapeutic agent doxorubicin. SMA has been widely investigated in drug delivery, with proven biocompatibility and biodegradability.[1,2] In addition, the SMA-based delivery system allowed the formation of stable micelles with a predetermined loading and controlled release rate.

With this consideration, SMA-doxorubicin micelles with different loading and release profiles were synthesized and characterized to examine the effect of these variables on their activity against prostate and breast cancer cell lines.

Methods

SMA micelles were prepared as schematized in Figure 1.

Dynamic light scattering was used to measure size and charge. Release rate was measured using a 1,000 Da cutoff membrane over 72 hr at 37°C. The proportion of doxorubicin released was determined using UV absorbance at 478 nm and represented as a percentage of the stock concentration.

Cytotoxicity was evaluated using the prostate cancer cell lines DU145 and PC3 and breast cancer cell lines MCF-7 and MDA-MB-231. The cytotoxicity was measured after 72 hr treatment using the sulforhodamine B assay. Expression of endocytic proteins was measured by Western blot analysis. Cells were seeded in six-well plates and grown to 80% confluency. Protein was extracted and separated on a 10% SDS-PAGE gel and analyzed by Western blot with primary antibodies.

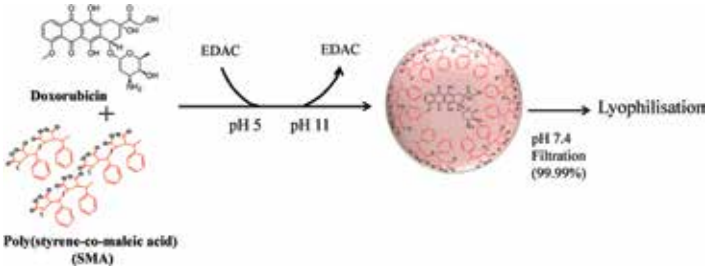

Figure 1. *Schematic representation of the SMA-doxorubicin synthesis. SMA, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide) (EDAC), and doxorubicin were added to the solution at pH 5. After stabilization, pH was increased to 11 to allow micelle formation. Micellar suspension was adjusted to pH 7.4, filtered, and lyophilized.*

Results and Discussion

We generated three SMA micelles with doxorubicin loadings of 4.4, 14.5, and 28.4% (Table 1). The sizes of the micelles were conducive to the exploitation of the EPR effect, as particles above 7 nm will escape glomerular filtration in the kidney.[3] The charges of the micelles were nearly neutral (Table 1). Lower loading of the micelle resulted in increased solubility. An inverse relationship was observed between the loading of a micelle and the release rate, with lower loading resulting in a higher release (Table 1).

Table 1. Physicochemical characteristics of the doxorubicin micelles.

Loading	Size (nm)	Charge (mV)	Solubility (mg/mL)	72 hr Release Rate (%)
4.4%	10.68	–0.054	112.5	43.3
14.5%	12.40	–0.064	43.4	19.8
28.4%	14.59	–0.055	14.3	8.0

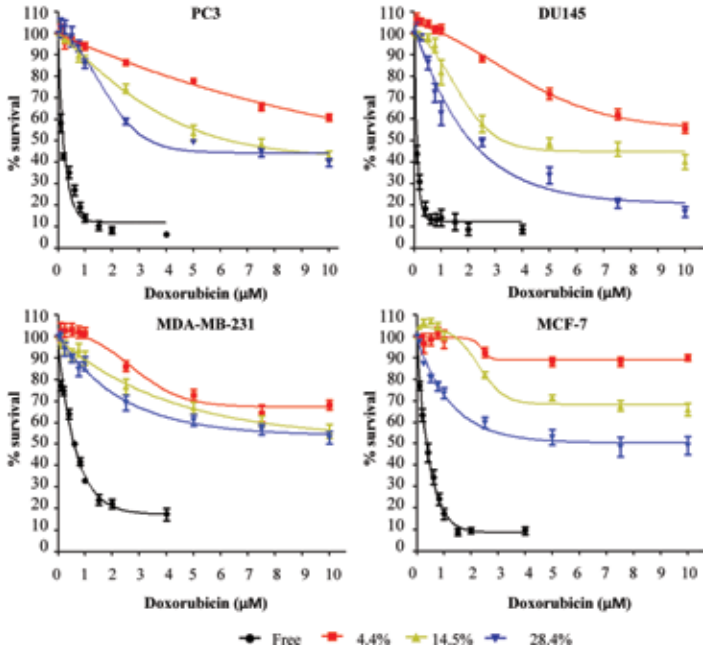

Figure 2. *Survival of a variety of cell lines following 72 hr treatment.*

Relative to free doxorubicin, the toxicity of micellar doxorubicin was reduced in all cell lines (Figure 2). Free doxorubicin enters the cell via diffusion, whereas micellar doxorubicin must be endocytosed. Distinct patterns of cytotoxicity were observed in all four cell lines in relation to micellar drug loading. MDA-MB-231 cells showed negligible dependence of cytotoxicity on the loading of the micelles. MCF-7 and DU145 cells showed a clear delineation between the cytotoxicity observed with different loadings.

The discrepancy in cytotoxicity observed between the different cell lines can be linked to differences in endocytic processes.

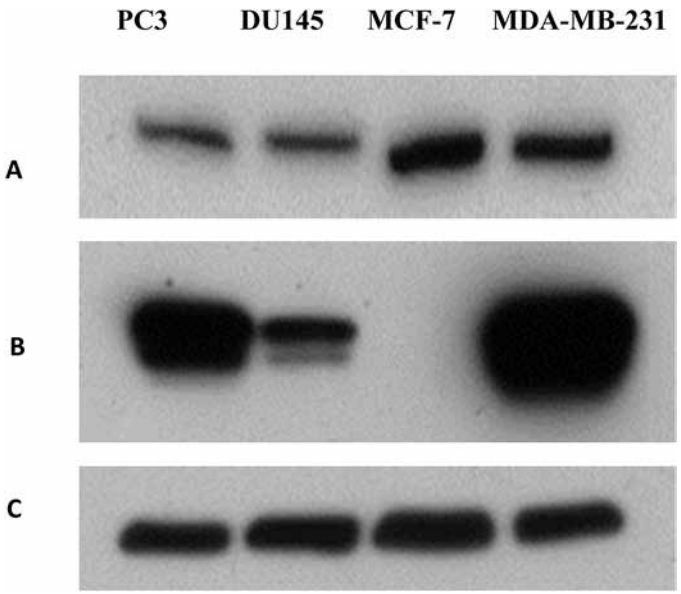

Figure 3. *Western blot analysis of clathrin (A), caveolin-1 (B), and β-tubulin (C) in PC3, DU145, MCF-7, and MDA-MB-231 cells.*

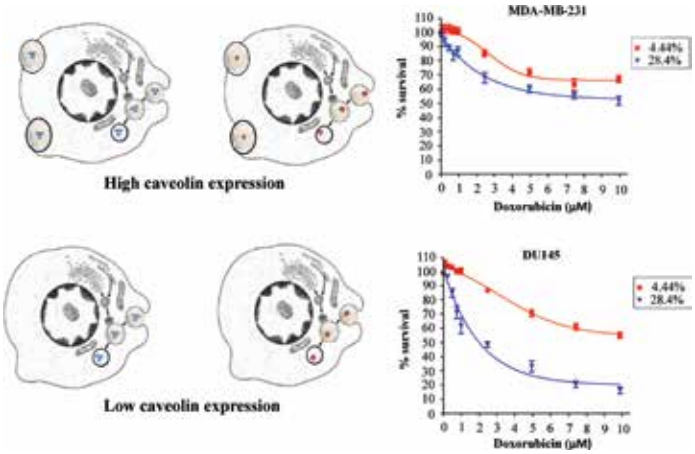

Figure 4. *Schematic representation of our hypothesis regarding the correlation between the level of cellular caveolin-1 expression and the differential cytotoxicity induced by micelles with different loadings. High caveolin expressing cells efficiently internalize all loadings (top panel), whereas low caveolin limits the internalization, accounting for the significant difference in cytotoxicity (lower panel).*

There are two major endocytic pathways mediated by either clathrin or caveolin-1. The relative expression of caveolin-1 and clathrin were determined by Western blot analysis. Clathrin expression was found to be slightly higher in breast cancer cell lines than in prostate cancer cell lines, but that did not justify the difference in cytotoxicity observed between the cell lines. A significant difference in caveolin-1 expression was observed across all cell lines (Figure 3).

The observation of the correlation between cytotoxicity patterns and caveolin-1 expression in the cell lines led to the conclusion outlined in Figure 4. Briefly, a high level of caveolin-1 expression, as seen in MDA-MB-231 cells, can result in a high uptake of micelles with equivalent cytotoxicity regardless of micelle loading owing to no endocytic limitation of micellar uptake. In DU145 cells, with low levels of caveolin-1 expression, the uptake of micelles was low, and so the total amount of doxorubicin inside the cells was dependent on the loading of the micelle. In MCF-7 cells, with undetectable levels of caveolin-1 expression, the uptake of the micelle was likely to be a consequence of non-caveolin-dependent uptake, and so the amount of doxorubicin within the micelle became important for the amount of doxorubicin that entered the cell.

The total cytotoxicity achieved was dependent upon the cells' sensitivity to doxorubicin itself. MDA-MB-231 cells were relatively insensitive to free doxorubicin (Figure 2). For this reason, the micellar doxorubicin was relatively ineffective, despite high uptake. MCF-7 and DU145 cells were highly sensitive to free doxorubicin; thus, despite low total uptake of doxorubicin, the amount of induced cytotoxicity was relatively high.

Conclusion

In this study, we showed the relationship between the loading of micelles and their biological activity. The degree of caveolin-1 expression varied in different tumor cell lines and was shown to influence nanoconstruct internalization and activity. Careful understanding of cell-specific interaction with nanomaterials is crucial for achieving a satisfactory biological outcome of nanoconstructs and can improve their potential for clinical application.

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A Systematic Investigation of D-Mannitol Functionality in the Development of Age-Appropriate Formulations

Ali Al-khattawi, Hamad Alyami, and Afzal R. Mohammed
Aston Pharmacy School, United Kingdom

Introduction

Advances in the field of oral solid dosage forms have seen the introduction of technologies specifically aimed for drug delivery of candidates to children and elderly individuals.[1] The main hurdle being faced with these target patient populations is the difficulty of swallowing solid bulky dosage forms. This obstacle has led to the development of orally disintegrating tablets (ODTs) and recently to the influx of various methodologies to manufacture them, including the cost-effective direct compression method. The principal criteria for a successful ODT are good mechanical strength to allow easy handling of the dosage form and fast disintegration in the buccal cavity. Previously, we assessed the criteria for optimum product functionality of ODTs, and it was clear that a strategic choice of excipient played a significant role in the successful formulation of the compressed tablets.[2] The current study aims to investigate the key properties of the most commonly used ODT excipient, D-mannitol, alongside micro/nano analysis of the structure of its powder and compressed tablets. The fundamental knowledge of the excipient's physicochemical and mechanical properties would enable "derisking" the formulation and optimisation of patient-centred dosage forms, whereby the utilised excipients are selected based on the generated evidence-based framework.

Preliminary powder flow characterization of D-mannitol (particle size distribution 37–50 μm) was carried out using a static angle of repose test. This was followed by assessment of the mechanical properties of ODTs by measuring the hardness of compacts of D-mannitol (99.5%, w/w) with 0.5% (w/w) magnesium stearate made at 10–40 KN compression force. The examinations of microstructure and topography of D-mannitol particles and crystals were carried out using scanning electron microscopy (SEM) and atomic force microscopy (AFM), respectively. The SEM analysis involved assessing the microstructure of neat powder (uncompressed) and after compression at 20 KN. Tapping mode AFM was utilised to uncover the surface features of the excipient to assess their influence on tableting performance. An *in vitro* disintegration test was performed based on the USP monograph specifications[3] for ODTs and compared against changes in tablet porosity.

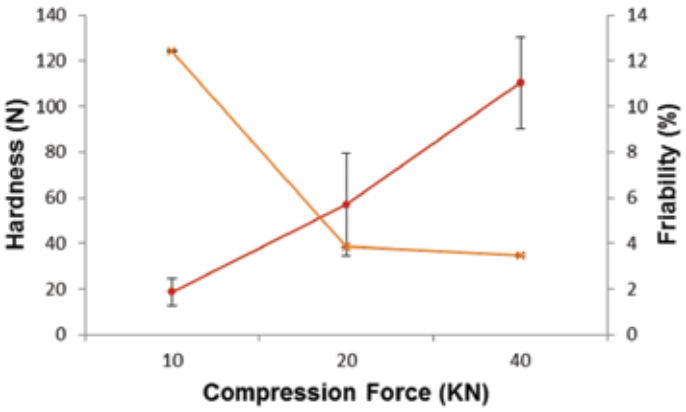

Figure 1. *The hardness (red line) and friability (orange line) profiles of compressed ODTs of D-mannitol (99.5%, w/w) and magnesium stearate (0.5%, w/w) as a lubricant.*

Results and Discussion

Powder characterization of D-mannitol was performed to ensure that the powder form of the excipient flowed well during the processing and tableting stages. The results of angle of repose testing showed that D-mannitol flowed fairly well during the tableting process (35.9 ± 0.38°) despite its small particle size of 37–50 μm. Successively, the results of tableting showed an improvement in the hardness of D-mannitol tablets upon increasing the compression force (from 18.66 ± 3.51 to 110.33 ± 14.74 N). However, the friability of D-mannitol tablets was beyond the 1% levels specified by different pharmacopoeias (Figure 1). It is well known that upon increasing tablet hardness, a concomitant reduction in friability usually occurs.[4] However, the results indicated that D-mannitol tablets were friable, which required investigation into the problem's origin because of the implication it has on handling of formed tablets and on the delivery of the right dose to the patient. D-mannitol was reported to undergo fragmentation in research carried out by Burger *et al.*[5]

In this work, the origin of the fragmentation and brittleness of D-mannitol was explored using SEM and AFM. Electron microscopy was utilised to study the effect of particle morphology of D-mannitol in the neat powder and the resulting compacts. SEM of D-mannitol powder showed an elongated particle morphology (37–53 μm), whereas that of compacted tablets showed the loss of the D-mannitol morphology, that is, loss of the primary particle structure owing to fragmentation (Figure 2A and B). This observation was consistent with prior literature on D-mannitol brittleness.[1,5]

AFM analysis was carried out to understand the fragmentation pattern of D-mannitol and to optimise final product properties based on evidence from mechanistic studies. The investigation of micron and submicron features of D-mannitol crystal showed the presence of multiple crystallites on the surface of the excipient. These fragile objects protruded from and sat upon the surface. They were loosely bound to the D-mannitol particle, as could be seen from both height and amplitude images (Figure 2C and D) generated from the AFM tapping

mode analysis on the surface of the excipient. The weakly bound crystallites were implicated in the high friability (>1%) of D-mannitol ODTs, as they could shift on the surface of the excipient during compression, resulting in dusting on the tablet.

The other important factor contributing to the successful formulation of orally disintegrating tablets is the fast disintegration of these tablets in the oral cavity. The results of disintegration showed good agreement with internal porosity changes upon compression (Figure 3). ODT disintegration time was increasing (36 ± 6 to 250 ± 19 sec) owing to greater densification of particles and reduction in interparticle spaces observed from linear decrease in porosity (from 0.48 ± 0.03 to 0.31 ± 0.06).

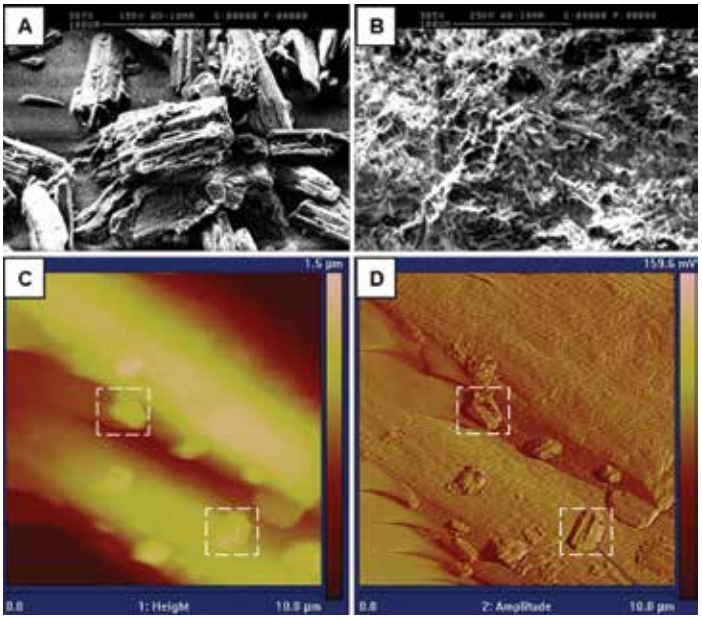

Figure 2. *Micro and nanostructure of D-mannitol. (A) SEM of D-mannitol powder. (B) SEM of a compacted specimen (dissected tablet) of D-mannitol made at 20 KN. (C and D) AFM height and amplitude images, respectively, showing the micron and submicron topography of D-mannitol particles (dashed squares highlight the loose surface crystallites).*

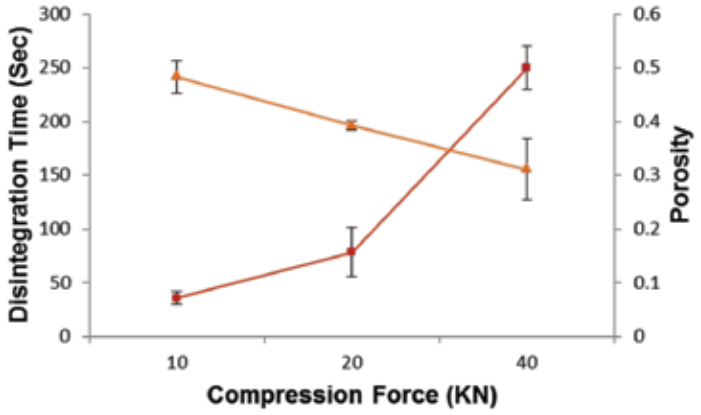

Figure 3. *The disintegration time (red line) and porosity (orange line) profiles of compressed ODTs of D-mannitol (99.5%, w/w) and magnesium stearate (0.5%, w/w).*

Conclusion

D-mannitol showed high friability levels and brittleness when compressed into tablets because of its weak crystal structure and surface fragmentation. As a result, the development of compressed ODTs and other patient-friendly solid dosage forms (such as chewable and effervescent tablets) that utilise D-mannitol could be achieved via topographical or morphological modification of the excipient. Coprocessing and particle engineering are currently being explored as potential routes to achieve tailored properties. In this respect, D-mannitol powder flow properties indicated that processing of the excipient was feasible because of its fair flow behaviour.

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In Vitro Characterization of Liposomal Encapsulated Doxorubicin Using CryoTEM

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Introduction

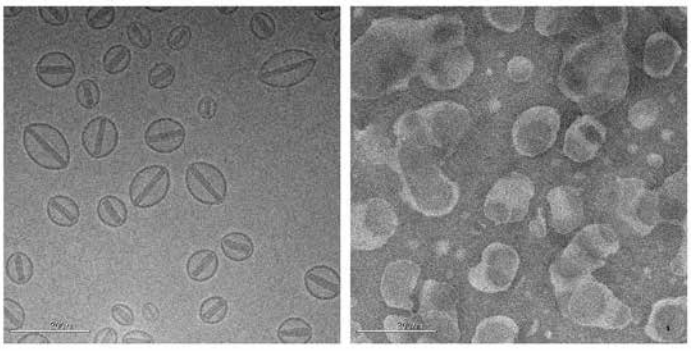
Generic liposomal drug delivery systems must show bioequivalence to the reference-listed drug. The U.S. Food and Drug Administration (FDA) provides recommendations for demonstrating such equivalence for alternative doxorubicin hydrochloride products.[1] *In vitro* characterization recommendations include size distribution, state of encapsulated drug, liposome volume, morphology, and lamellarity. The reference-listed drug is composed of oval-shaped unilamellar liposomes of 80–90 nm approximate mean size, having doxorubicin present mostly inside liposomes as fibrous-bundle precipitate with interfiber spacing of 2.7 nm.[2]

Cryo transmission electron microscopy (cryoTEM) characterization of liposomal encapsulated doxorubicin is presented here. CryoTEM provides direct visualization of liposome assembly, quantitative measurements of various size metrics and physical properties, and definitive characterization of drug encapsulation.

Experimental Approach

Two common specimen preparation methods exist for examination in a transmission electron microscope: negative stain and vitrification.

In negative stain preparations, sample is typically applied to a carbon film substrate supported by an electron microscopy grid, heavy metal salt solution is applied to the sample, the liquid layer is reduced to a thin film, and the sample is allowed to dry.



(A) (B)

Figure 1. *Liposomal encapsulated doxorubicin observed using vitrification (A) and negative stain (B) to preserve the specimen in the TEM. Note that contrast is reversed in the vitrified images relative to the negative stain images. Scale bar is 200 nm.*

Liposome adsorption to the substrate can result in deformation, interaction with heavy metal salts can alter the chemical environment, and the dehydration step can obscure or destroy native particle morphology (Figure 1B).

Using cryoTEM, sample is typically applied to a holey carbon film substrate supported by an electron microscopy grid, reduced to a thin film, and rapidly plunged into a cryogen. Liposomes prepared this way (Figure 1A) are observed in their natural hydrated state, allowing straightforward and unbiased interpretation of physical characteristics. Thus, cryoTEM is the method of choice for characterization of liposomal formulations.

Liposome morphology and assembly are directly determined from images of the vitrified sample (Figure 1A), thereby addressing FDA recommendations for proving drug equivalence. Size distributions can be measured by tracing boundaries of a population of particles using manual and automated methods (Figure 2). Particle contours are used to generate a variety of size metrics, including area equivalent diameter (AED, diameter of a circle of equivalent area), circularity, and an estimate of liposome-encapsulated volume. Liposome lamellarity, fraction of loaded liposomes, and fraction of unencapsulated doxorubicin can be quantified by scoring and counting particles in cryoTEM images.

Three-dimensional (3D) morphology of the sample can be understood by reconstructing a 3D volume from a series of 2D images tilted over a range of angles. The set of tilted images can be mathematically combined to construct a 3D volume. The 3D volume can be examined from different angles (Figure 3), and individual slices in different orientations can provide a more complete understanding of particle morphology.

Methods

Undiluted liposome-encapsulated doxorubicin (3 µL) provided by FormuMax Scientific, Inc., was applied to a holey carbon film–covered 400-mesh copper grid, blotted away with filter paper, and immediately vitrified by rapid plunging into liquid ethane. Grids were stored under liquid nitrogen and transferred to the electron microscope using a cryostage that maintained grid temperatures below –170°C.

Microscopy was performed using a 120 keV FEI Tecnai T12 electron microscope equipped with an FEI Eagle 4K × 4K charge-coupled device (CCD) camera. Images were acquired using Leginon.[3] After identifying potentially suitable areas for

imaging at lower magnifications of 560× and 6,500×, high magnification images of 21,000× (0.50 nm/pixel) and 52,000× (0.21 nm/pixel) were acquired.

Tilted images were acquired at 21,000× magnification from –58° to +58° in 2° increments, using a ≈3–7 $e^-/Å^2$ dose per image at each increment for a total dose of 450 $e^-/Å^2$. Tilted images were aligned and used to reconstruct a 3D volume using IMOD.[4] The volume was rendered and visualized using the Chimera software package.[5]

For the sizing analysis, 21,000× magnification images were prescreened for quality and randomly ordered. Contours were manually traced around each particle in the field of view; particles were only sized if the particle boundaries were clearly defined and the particles were not in contact with the carbon film. A variety of size metrics were then computed from these contours.

Results and Discussion

General Characteristics and Morphology

The sample was composed primarily of oval-shaped unilamellar liposomes (Figure 4) that encapsulated a particle consistent with doxorubicin. Doxorubicin particles exhibit a crystalline structure characterized by a regular spacing of approximately 2.5 nm (Figure 4, yellow inset). Liposome bilayers appeared uniform and approximately 7 nm in width (Figure 4, blue inset).

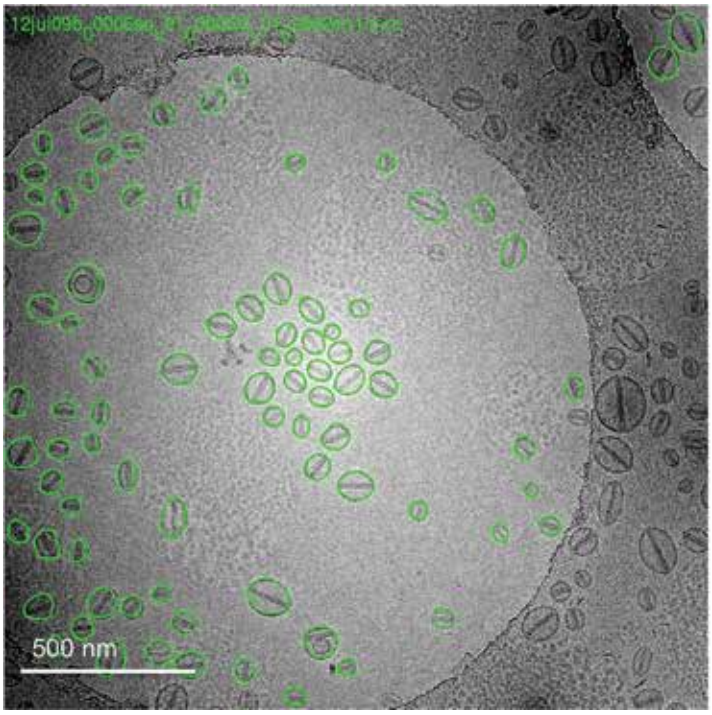
Reconstructed volumes resulting from the tomography study (Figure 3) confirmed that liposomes were intact, generally spherical or elliptical, and that doxorubicin was completely contained within the liposome. Doxorubicin particles were generally positioned across the center of elliptical liposomes. Occasionally observed dense round particles positioned at the center of liposomes (blue arrow, Figure 3) were confirmed to be cylindrical doxorubicin crystals observed end-on. Infrequently observed disk-shaped particles that appeared as rod-shaped (orange arrow, Figure 4) or faint round (green arrow, Figure 4) particles in the projection views were confirmed to be the same object viewed from different directions in the tomograms (yellow arrows, Figure 3).

Quantitative Sizing

Size distribution metrics were computed from traced contours (Figure 2). Metrics included AED (based on using the area of the enclosed perimeter and extrapolating to a spherical liposome), circularity (spherical contours have circularity of 1; square contours have circularity of 0.76), minimum and maximum Feret diameters (the longest and shortest distances across the contours), and enclosed volume (based on AED and compensating for lipid bilayer thickness). Metrics calculated for 311 particles are listed in Table 1.

Table 1. Sizing study results.

Parameter	Mean	Standard Deviation
Number of particles analyzed	311	0
Area equivalent diameter (nm)	72	17
Maximum Feret diameter (nm)	81	19
Minimum Feret diameter (nm)	65	16
Circularity	0.95	0.02
Volume (nm^3)	100,000	90,000



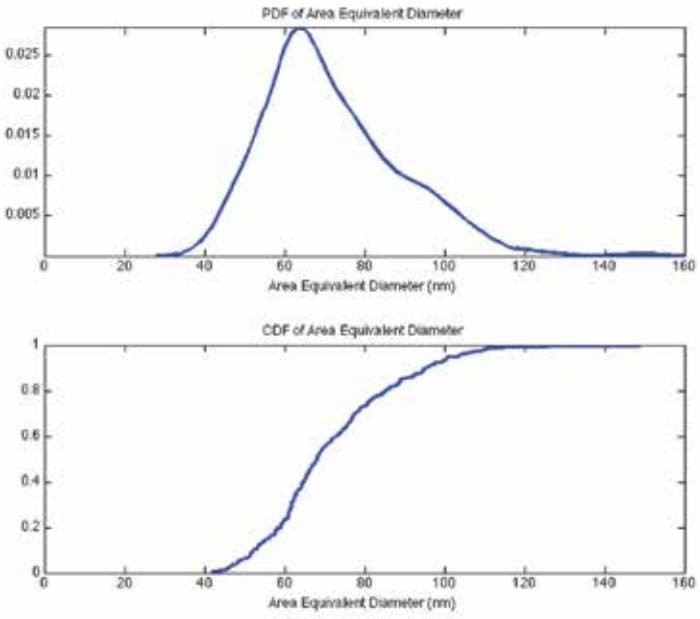


Figure 2. *Contours are manually traced (left) for a set of liposomes to generate size distribution metrics, including the area equivalent diameter. N = 311 for this sizing study. Scale bar is 500 nm.*

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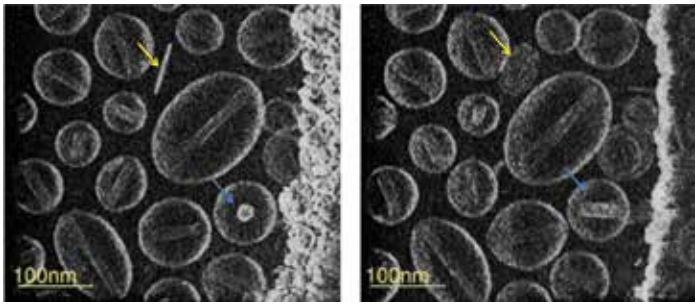

Figure 3. *Rendered reconstructed 3D volume of the sample computed using electron tomography. Contrast has been reversed as compared to the images of vitrified samples. Left and right images show a view of the volume at two different angles. The cylindrical rod of doxorubicin appears as a dense round particle, depending on the angle of view (blue arrows); similarly, disk-shaped particles can appear as rod-shaped or faint round particles (yellow arrows). Scale bar is 100 nm. To view an animated video of the tomogram, visit www.youtube.com/watch?v=zu--EipZ7Yo.*

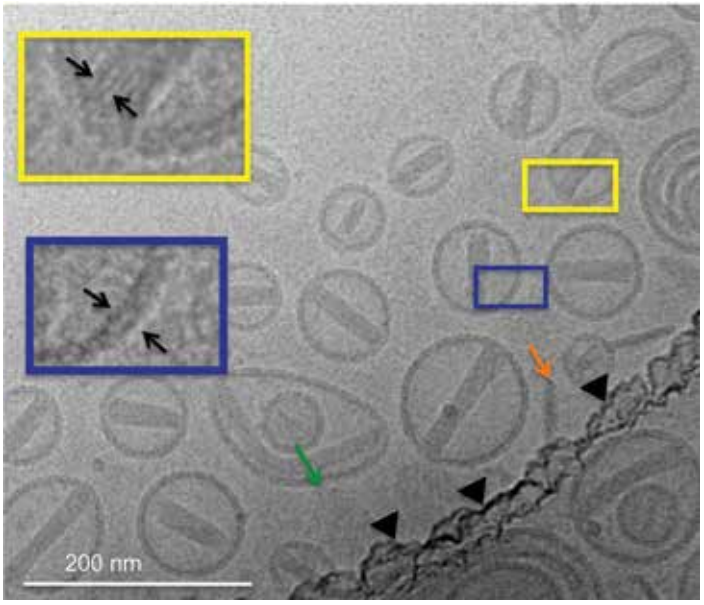

Figure 4. *TEM image of liposomal encapsulated doxorubicin preserved using vitrification, acquired at 52,000× magnification. A layer of particles is observed in their native buffer suspended over a holey carbon substrate. The edge of the carbon hole is indicated by the black arrowheads. Insets are areas of the image at a larger scale; yellow inset shows the ordered packing of the doxorubicin (lines are 2.5 nm apart); blue inset shows the liposome bilayer (of width 7 nm). Infrequently observed disk-shaped objects in the sample appear as rod-shaped (orange arrow) or as faint round particles (green arrow), depending on the angle of view. Scale bar is 200 nm.*

Fraction Counting

Of 471 liposomes analyzed, 98% were loaded with doxorubicin, 2% were empty; 97% were unilamellar; and 2% appeared to contain more than one particle. No instances of unencapsulated doxorubicin were observed.

Conclusion

CryoTEM allows direct visualization and direct determination of morphology and assembly of individual particles. Size distributions can be calculated by tracing the boundaries of a population of particles. Statistics for other characteristics, including liposome lamellarity and percentage of loaded liposomes, can be calculated directly by computing the fraction of particles in various identified categories. The three-dimensional morphology of the sample can be determined by reconstructing a 3D volume from 2D images using electron tomographic methods.[4,5] These methods offer a direct means of providing many of the characterization data recommended by the FDA[1] for establishing bioequivalence of liposomal encapsulated doxorubicin hydrochloride.

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Articles and Websites of Interest in Animal Models of Diseases, Cross-Species Comparisons, and "One Health"

Professor David Brayden[1] and Dr. Terry Bowersock[2]

1. Zebrafish have been highlighted in this column before. A review of the breadth of zebrafish animal models was highlighted in the April 2013 edition of *The Scientist*.[1] The growing interest in zebrafish as a model to study pathogenesis of numerous cancers was highlighted—they also provide the opportunity for novel high-throughput drug screens not available in mice, a system that is unique to this species, avoids the need for transgenics (in mice), and cuts years off drug development timelines. Whereas mice have provided insights into basic mechanisms underlying human malignancy, is it possible that the zebrafish model could provide a major leap forward in rapid progression of genetic and chemical screens?

2. A pig model of cystic fibrosis has been identified that calls into question the role of Na^+ hyperabsorption and depletion of pericellular airway liquid in the pathology of cystic fibrosis.[2] Newborn pigs lacking the cystic fibrosis conductance regulator (CFTR–/– pigs) developed lung disease similar to human cystic fibrosis shortly after birth. However, this occurred without alterations in Na^+ transport or liquid absorption, thereby implicating a defect in anion transport as a key primary factor in cystic fibrosis, since this was sufficient to prime the animals for bacterial colonization of the lungs. In a follow-up review and discussion, three experts on cystic fibrosis commented on the pros and cons of this new model.[3] One reviewer was impressed that this model suggests that bacterial infection can occur in the presence of hydrated mucus membranes, thereby refuting the dogma that the infection is a sequel to dehydrated mucus and suggesting that immune defect may be responsible for bacterial colonization of the cystic fibrosis lungs. Another reviewer suggested that this new model will now have to explain why cystic fibrosis patients are uniquely susceptible to *Pseudomonas aeruginosa* infections and that ion transport drug therapy may need to be reevaluated. A third reviewer suggested that this new model provides a focus on the importance of anion conductance in cystic fibrosis airway disease, especially on development of new therapies directed toward CFTR-dependent anion conductance.

3. Rat brains are more like human brains than previously thought. Jared Smith and Kevin Alloway at Penn State Center for Neural Engineering found that there is a parallel between the motor cortices of rats and humans that has significant relevance to studies of the human brain.[4] They focused on the motor cortex that supports the sensorimotor activity of the rat whiskers and found it to be similar in function to the cortex that supports processing visual stimulation in humans. By tracing the neuronal conductivity in the rat cortex relative to whisker movements, they were able to better understand how the neuronal circuits function and are involved in more complex motor control. Specifically, they found that there were different sensory input regions that were distinct from regions that issued motor commands to the whiskers by using microstimulation techniques. This work opens up avenues to study very complex neural processes in rodents that are more similar to human processes than previously thought.

4. Vaccination of large intestine or vaginal mucosa is effective but largely impractical for control of infections that are initiated at these sites.[5] Oral vaccination would be ideal, but the concern is that the vaccines would be destroyed or activated to stimulate the immune response in the upper intestine and not translate to immunity at these sites. Qing Zhu and coworkers designed a large intestine–targeted oral delivery of microparticles based on pH for release. This induced colorectal immunity in mice and protected them against rectal and vaginal viral challenges. Vaccine targeted to the small intestine, on the other hand, provided no rectal or vaginal immunity. This study may represent a new strategy for induction of rectal and vaginal mucosa.

[1] University College Dublin, Ireland.
[2] Zoetis, LLC (formerly Pfizer Animal Health), U.S.A.

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CRS@AbbVie

Martin Bultmann, President, CRS Germany Local Chapter

AbbVie was the host and sponsor for the annual meeting of the Germany Local Chapter of the Controlled Release Society (CRS-de) on March 21 and 22, 2013.

In drug therapy, the formulation is often of crucial importance. The field of controlled release, for example, focuses on the active substance being released over a prolonged period of time so as to facilitate applicability for the patient. CRS-de has set its sights on supporting junior scientists in this area. This mainly occurs through providing an informative platform as well as by offering scientific lectures and practical workshops.

As AbbVie is also committed to ensuring top-notch training for young researchers, the company also supports CRS-de's work. Therefore, AbbVie hosted the society's annual meeting in March. Around 100 participants from academia and industry visited the Ludwigshafen site for two days. On the first day, graduate and Ph.D. students had the opportunity to practice their soft skills in various workshops with professional trainers:

- Rhetoric and successful presentation
- Working in an international team
- Working in matrix organizations
- Managing conflicts
- Design of experiments (DoE)
- Lean Six Sigma principles (process optimization and efficiency gains)
- Facility tours
- Quality risk management (QRM) and Quality by Design (QbD) principles
- Academia meets industry

The selection of workshops offered was the outcome of a survey conducted by the Germany Local Chapter in 2012: students and teaching staff from academia as well as industry representatives were asked about courses and skillset trainings offered or deemed necessary from all three perspectives. This "voice of the customer" survey resulted in the selection of the abovementioned workshop topics.

Oral presentation in the AbbVie lecture hall.

The Design of Experiments workshop, which later included a practical exercise with catapults built on the fly to assess input factors, outputs, and quantitative effects and to build a working model.

On the second day, two exciting scientific lectures and 10 oral presentations were held by Ph.D. students. A large poster session with 45 contributions rounded out the meeting, which ended by presenting awards of 250 EUR each to the best presenters of two posters and one oral presentation.

Furthermore, Prof. Dr. Dagmar Fischer was honored for her long-term dedication and participation in the CRS-de board. Dr. Martin Bultmann was elected new CRS-de president, and Dr. Regina Scherließ was elected vice president.

Lutz Asmus, senior scientist at AbbVie, summed up: "It was a great opportunity for students to gain new insights into current academic developments and to directly communicate with university-based researchers." The feedback from the participants was also positive throughout: "I now know more about the way of thinking in the industry as well as the skills that really matter besides fundamental science," said one Ph.D. student. The workshops, which were "an excellent choice and absolutely matching my needs for additional skills," and the informal atmosphere during the meeting were also highly praised. "I particularly profited from talking to young employees about their introduction into working life," one student reported. The icing on the cake for the young scientists was being able to gain tips on how to compile their CVs and job applications. This service was offered by AbbVie Talent Acquisition and turned out to be very popular.

The success of this informative and interactive two-day event is an important contribution to scientific progress and development of our future scientists. The CRS-de board gratefully acknowledges the 20,000 EUR sponsorship by AbbVie, which enabled the huge variety of workshops and this outstanding meeting. ■

Drug Delivery Australia 2012: Sixth Annual Meeting of the Australian Chapter of the Controlled Release Society, November 26–27, 2012

Ben Boyd, President, CRS Australian Local Chapter

The annual meeting of the CRS Australian Local Chapter was rebranded as Drug Delivery Australia starting in 2012 to better identify with scientists conducting drug delivery research from the engineering, materials science, biology, and clinical fields. DDA2012 was held at the Monash Institute of Pharmaceutical Sciences in Melbourne immediately prior to the Globalization of Pharmaceutics Education Network (GPEN) conference at the same venue. Both of these strategic decisions paid off, with over 160 delegates attending from 14 different countries—by far the highest ever attendance for an Australian Local Chapter meeting.

The meeting was the first time that parallel sessions were needed to accommodate the large number of excellent speakers. Themed sessions titled "Lipid-Based Drug Delivery," "Advanced Tools for Characterization in Drug Delivery," "Advanced or Just Retarded—Enhancing and Reducing Drug Uptake," "Macromolecular and Vaccine Drug Delivery," and "Drug Delivery to the CNS," among others, were available. There was something on offer for everyone.

The temporal proximity to GPEN enabled a significant number of international delegates to attend both conferences and enabled an extremely strong showing of invited speakers for the DDA meeting. These included plenary lectures from Val Stella (University of Kansas, U.S.A.) and Peter Swaan (University of Maryland, U.S.A.), as well as a very strong array of invited international speakers including Anette Müllertz (University of Copenhagen, Denmark), Gerrit Borchard (University of Geneva, Switzerland), Marcus Brewster (Johnson & Johnson, Belgium), Steven Schwendeman (University of Michigan, U.S.A.), David Grainger (University of Utah, U.S.A.), Arto Urtti (University of Helsinki, Finland), and Claus-Michael Lehr (Saarland University, Germany).

The top 10 student poster presenters at DDA2012.

Delegates listen intently to one of the many podium presentations during the conference.

The conference also offered a great opportunity to showcase Australian research in drug delivery with invited talks from Frank Caruso (University of Melbourne), Tom Davis (University of New South Wales), Istvan Toth (University of Queensland), Chris Porter and Joseph Nicolazzo (Monash University), Fabio Sonvico (University of Technology Sydney), and Wojciech Chrzanowski (University of Sydney).

Complementing the excellent invited presentations were contributed talks across the different themed sessions and an excellent poster session comprising over 90 poster presentations across all areas of drug delivery. The posters were all excellent quality, and the (mostly) student presenters should all be congratulated on the presentation of their work. The poster sessions at past chapter meetings have always been popular, in part owing to two prizes of $1,000 subsidy to attend the next CRS Annual Meeting. At DDA2012 it was for the CRS meeting in Hawaii, so you can imagine the fierce competition! The best 10 student poster presentations were selected for a short posters-on-the-podium session, where each student had three minutes to convey their research before the best two were selected for the travel bursaries. The two winners were judged and declared: Orlagh Feeney from Monash Institute of Pharmaceutical Sciences for her presentation "Using PEGylated Surfactants to Control the Digestion of Lipid-Based Formulations" and Tzu-Yu (Vicky) Liu from University of Queensland for her presentation "Synthesis of Nanoparticle-Based Delivery System for Vaccine Against Cervical Cancer." You may see them around the conference in Hawaii!

An industry podium soapbox-like session was also held for the first time, with representatives from Malvern, Perkin Elmer, ATA Scientific, and Johnson & Johnson given an opportunity to describe more industrially relevant research with a technique

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Australian Chapter continued from page 27

focus to provide a break from the intensive research-focussed sessions and a nice transition to the conference dinner held on the Monday night.

The band Cheek to Cheek Trio, who played for us at the conference dinner in 2010 held at the Melbourne Zoo and were a huge hit, were fortunately available again for DDA2012. The dinner was held at the Carlton Football Club overlooking the Aussie rules football ground. The entertainment kept delegates busy with fun and dancing into the night.

Delegates enjoy the conference dinner and entertainment.

The meeting was strongly supported by continuing sponsors ATA Scientific, Davies Collison Cave, Monash Institute of Pharmaceutical Sciences, TrendBio, and University of Technology Sydney School of Pharmacy and by new sponsors Pall Life Sciences and In Vitro Technologies. Their generous and continued support is much appreciated.

Corporate sponsors of DDA2012.

The election of office bearers was held at the chapter annual general meeting. All current office bearers were re-elected into their positions for the coming year: Ben Boyd (president), Leab Sek (treasurer), Dany Traini (secretary), Paul Young (scientific secretary), and Pavla Simerska (vice president).

In summary, this high-quality two-day meeting was a great success, with a number of collaborations arising from discussions and networking, as well as great exposure for the students involved. The quality of the meeting was again testament to the growing significance of drug delivery research across Australia. There is high anticipation for DDA2013, to be held overlooking the magnificent Sydney Harbor at the Woolcock Institute for Medical Research in Sydney on October 24–25, 2013. See www.crsaustralia.org for more information. ■

UKICRS 2013

Dr. Vitaliy Khutoryanskiy, University of Reading, United Kingdom

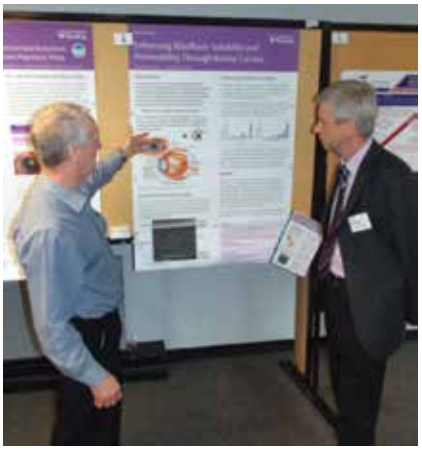
Industrial Workshop

The annual United Kingdom-Ireland Local Chapter of the Controlled Release Society (UKICRS) symposium "Future Pharmaceutics—Innovation in Controlled Release" was hosted by the University of Reading on April 15–16, 2013. The first day of the symposium was geared toward industrial exhibitors, including Stable Micro Systems, NanoSight, Surface Measurement Systems, Caleva Process Solutions, Meritics, Fisher Scientific, Presearch, Merrow Scientific, and Biopharma Process Systems, who showcased their products and technologies through a series of talks and exhibitions.

Harry Schimanski from Stable Micro Systems presented their texture analyser instrument and described how it can measure mechanical characteristics and adhesion of various pharmaceutical, cosmetic, and food products. Philip Attwool from Surface Measurement Systems discussed the application of their dynamic vapour sorption instruments for characterising various pharmaceutical materials. Patrick Hole from NanoSight described their nanoparticle tracking analysis instruments for studying pharmaceutical nanomaterials. Richard Paszkowski from Fisher Scientific talked about specialty chemicals they are able to supply. Steve Robinson from Caleva Process Solutions demonstrated the range of their instruments for extrusion, spheronisation, and encapsulation. Brian Miller from Meritics talked about their nuclear magnetic resonance-based instrument and its use for characterisation of pharmaceutical nanomaterials. Richard Lewis from Biopharma Process Systems presented an overview of lyophilisation technologies. Ben Proudlove from Merrow Scientific described their instruments for measuring viscosity.

Annual Symposium

The scientific programme of the symposium included two keynote speakers, 11 talks from postgraduate students and postdoctoral researchers, and 51 poster presentations. The first morning session began with a keynote lecture from Prof. Wim Hennink (Utrecht University, The Netherlands). The lecture covered many aspects of his research, mainly focussing on the development of novel biodegradable polymers for protein delivery. He discussed the possibility of using these polymers



Peter Morrison discussing his poster with Prof. John Smart.

Postgraduate speakers and session chairs.

as *in situ* gelling temperature-responsive systems for delivery via injections. This lecture was followed by two short presentations from Gayle Wilson (Keele University), speaking about targeted drug delivery via the PepT1 transporter, and Nooshin Daveshpour (Queens University Belfast), focusing on the development of novel sialic acid-coated PLGA nanoparticles for the treatment of acute lung injury.

Three short presentations were delivered after the coffee break. Jitinder Singh Wilkhu (Aston University) discussed the effect of vesicle size on uptake of bilosomes and antigen by the Peyer's patches. Dolores Serrano Lopez (Universidad Complutense de Madrid, Spain) talked about novel amphotericin B controlled release formulations and their *in vitro/in vivo* studies. Hamid Merchant (University College London) described the application of an automatic pH control system to simulate the entire gastrointestinal pH.

Following the lunch and poster presentations, the afternoon session was opened by a keynote lecture from Prof. John Smart (University of Brighton) that provided an excellent overview of

Prof. Karl Malcolm, Prof. Wim Hennink, and Dr. Vitaliy Khutoryanskiy during the poster session.

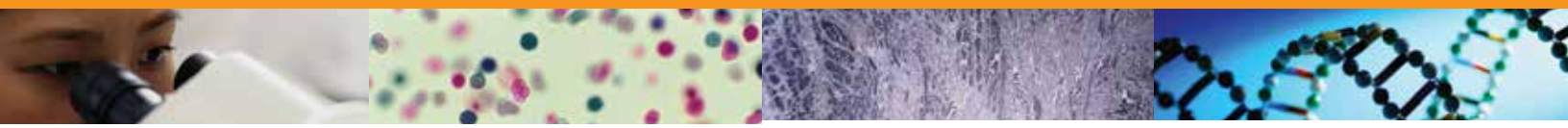
Prof. Wim Hennink answering questions.

drug delivery via the oral cavity with the use of mucoadhesive polymers. He highlighted that a wide range of formulations has been developed for buccal drug delivery (tablet, patch, liquids, and semisolids) over the last 30 years, but only a few have found their way onto the market.

This lecture was followed with a talk by Charlie Chen (University of Cambridge), who discussed the application of direct multinuclear magnetic resonance imaging for the study of controlled drug release. Giovanna Sicilia (University of Nottingham) presented the synthesis of a novel dual stimuli-responsive polymer-DNA hydrogel, cross-linked via DNA base pairing and disulphide bonds. Samuel Bizley (University of Reading) described the application of the layer-by-layer deposition approach for the development of novel enterically coated microparticles.

Following the coffee break and poster presentations, the final session of the symposium included three postgraduate talks. Sukrut Somani (University of Strathclyde) gave a presentation on transferrin-targeted dendrimers for gene delivery to the brain. Louise Harris (University of Sunderland) discussed some opportunities in formulating slow release products for farmed ruminants and also talked about knowledge-transfer partnership schemes. Fiona McCartney (University College Dublin) described her investigation of sugar esters as novel intestinal permeation enhancers.

The meeting concluded with symposium chair Dr. Vitaliy Khutoryanskiy (University of Reading) announcing the winners of the best talk and poster awards. The best talk prize was awarded to Giovanna Sicilia, and the best poster award was presented to Jitinder Singh Wilkhu. ■



Pioneers in Microencapsulation: Harlan Hall and Fluid Bed Coating

Charles Frey, Coating Place, Inc., U.S.A.

Harlan Hall

Harlan Hall began work in the fluid bed coating labs of the Wisconsin Alumni Research Foundation (WARF) in 1971 and has remained active in fluid bed coating to this day. Harlan has a tremendously innovative and practical nature, which has served him in his pioneering efforts. This article offers a historical perspective on Harlan's career and fluid bed coating, based on an interview and personal acquaintance.

Prior to joining the WARF labs, Harlan was employed in his first postcollege position as an analytical chemist at Tee-Pak, a sausage casing manufacturer in Illinois. His work at Tee-Pak was somewhat far removed from the Wurster fluid bed coating process that he would come to know intimately; however, it involved elements of coating and controlled release that he would find useful in his developing career. Sausage casing manufacturing involves unique packaging requirements both for the finished packaging and the sausage casings. His analytical work involved competitive analysis of laminated packaging barriers with five to nine layers designed for optimal product preservation on store shelves. Various coatings were used in meat casings to provide properties such as easy release of the casing from the meat. This easy release was sometimes coupled with a need for good adherence through curing processes that resulted in shrinkage—a loose casing on a sausage has never been a desirable feature. Polyvinylidene chloride oxygen barriers were used to minimize oxidation that would cause some sausages (such as liverwurst) to turn green.

In 1971, his position at Tee-Pak became questionable because of company acquisition, which resulted in his move to the WARF coating labs in Middleton, Wisconsin, U.S.A. These labs were involved in the study and commercialization of the air-suspension coating processes recently invented by Dr. Dale Wurster at the University of Wisconsin through the 1950s and 1960s. The bottom spray process, which was the focus of Harlan's attention, is commonly referred to as the Wurster fluid bed coating process.

Harlan acknowledges the mentors, contacts, and relationships that he found at WARF as the most profound and influential of his career. Tom Hinkes, WARF coating lab director, was his boss and the person who hired him. Tom introduced him to Dr. Wurster. Through industry interest in the Wurster fluid bed coating process, Harlan came to know many individuals, including Dr. Yegnaswami Raghunathan, with whom he worked closely on the coating of controlled release drug/ion resin complexes for liquid suspension technology (known as Pennkinetic™).

The work at WARF focused primarily on commercialization of the fluid bed coating processes. Harlan became involved with projects from many companies, including Upjohn Corporation, Eli Lilly, Tennessee Eastman, Shaklee Corporation, Miles Laboratories, Ball Seeds, and Glatt Air Techniques. These projects involved primarily microencapsulation for various controlled release or delivery objectives. Goals included taste masking and application of protective and controlled release barriers for enhanced stability or controlled delivery. These projects involved both formulation development and design/manufacture of equipment for client needs.

As projects came to fruition, the needs of the developing industry became apparent. An Upjohn project involving a vitamin product was successful; however, Upjohn's 12 in. diameter Wurster unit was only fired up once or twice per year to meet the needs. Upjohn was frustrated with the situation because this limited use was inadequate for maintaining a good working knowledge of the process. As spray nozzle technology improved, the yearly needs of this product at Upjohn could be produced in around eight days at the WARF labs. Upjohn offered to pay handsomely for this service; however, as a tax-exempt entity, WARF could not take on commercial work. Harlan offered to rent the facility to run their process two weeks each year, but it was not considered a viable option by WARF. Other contract coating operations were not commercially available at that time.

Soon after this, Harlan and colleagues from WARF including Ralph Pondell wrote a letter to the WARF administration explaining the lost opportunity of such contract arrangements. They received no immediate response. One to two years later, in 1976, as the WARF coating labs were preparing to move out of the existing facility into storage, WARF remembered the letter and asked Harlan if there was still interest in running a contract operation. Harlan and Ralph negotiated with Tom Hinkes, who encouraged and facilitated the deal, which included a coater, an old boiler, a compressor, and support equipment. An offer to buy was made in December 1976, and the WARF board accepted the offer before year end. The arrangement involved a note to be paid off in three years and included a license to sell product.

Coating Place "A" research unit.

Coating Place, Inc., became a reality in an old concrete facility in Verona, Wisconsin, that had a building tall enough to house a single-nozzle unit with an 18 in. coat chamber. This was designated as the "B" unit, and it was operational by April 1, 1977. In May 1977, they bought back and renovated a research unit that had been built for Ball Seeds; this was designated as the "A" unit. Both units remain in operation at the facility today. Harlan and Ralph were the only employees at the beginning, and they had a goal of clearing around $100 a week per person for the first full year, which they were almost able to achieve. A principal product during that year was a pharmaceutical taste-masked warfarin for the WARF labs.

Harlan and Coating Place carried on the work that had been underway at WARF. WARF was a passive marketer of the Wurster process. Their work with Miles Laboratories and others reduced nonvented pan coating processes from days to minutes. There was tremendous potential, and WARF appeared to be cold to foreign involvement. They had granted an English company the exclusive right to sell Wurster equipment in Europe, but to Harlan's knowledge, this company never sold anything. Glatt Air Techniques approached WARF to buy rights to the technology, but the English agreement prevented any transaction.

Arial view of Coating Place, Inc., 1985.

Dr. Dale Wurster (left) and Harlan Hall (right) admire a Wurster coater at Coating Place during a recognition event for Dr. Wurster cosponsored by the University of Wisconsin Pharmacy Department, Wisconsin Alumni Research Foundation, and Coating Place in October 2002.

Glatt went on to build and sell some units in Europe without significant attention from WARF. Nevertheless, when some units were sold in the United States, it was picked up on WARF's "radar." Marv Woerpel from WARF confronted Herr Glatt on the issue, and the response from Glatt was something like "What took you so long?" This led to a licensing arrangement with Glatt in the early 1970s.

WARF shared the technology openly with Glatt Air Techniques, but Glatt engineers did not appear to receive it well. They built to their own specifications on an existing chassis. Eventually, many WARF innovations were incorporated by Glatt and other equipment manufacturers; however, from what might have been a firm mindset on both sides, the relationship was uncomfortable. Attempts to reconcile in the late 1970s had minimal success.

Coating Place has continued to grow with a focus on contract Wurster fluid bed coating services. Principal ownership of Coating Place changed in 1999, but it remains a privately held company with Harlan as a part owner actively working in the operation.

Harlan has found the greatest rewards in problem solving through formulation or equipment and nozzle design. He helped design Coating Place Wurster units that are linearly scalable to three- and seven-nozzle configurations. He has been involved in the development of many commercial formulations in pharmaceutical, food, nutritional, agricultural, industrial, and many other areas. Many of these formulations

Consumer and Diversified Products continued on page 32

Consumer and Diversified Products continued from page 31

Arial view of Coating Place, Inc., 2007.

did not stay at Coating Place, and Harlan helped client companies install equipment. Harlan has enjoyed working with good people and the relationships he has developed along the way. When comparing the problem-solving work of the 1970s to today, Harlan acknowledged the greater challenges imparted by increased regulatory constraints. There are more regulatory hurdles to cross, which can dampen enthusiasm and progress.

The greatest challenges, in Harlan's opinion, include company expansion to service needs only to see the needs disappear. Contract business requires equipment availability in a timely manner; thus, it must exist before the work. To this day, Coating Place's model is to expand before need is imminent.

There have been some disappointments in Harlan's career. Regarding CRS, he regrets that he had to let his membership expire in the early days of Coating Place (and lose his two-digit membership number). Tom Hinkes was at the first CRS meeting back in the mid-1970s when CRS was a symposium. Harlan attended years two and three but dropped out because of a limited budget. His most significant disappointment at Coating Place was a process incident that caused the beer tent at the local festival to close early.

Harlan's contributions to controlled release technology and CRS have been recognized with both a CRS Distinguished Service Award and a CRS College of Fellows Award.

Harlan voiced a concern about the perceived loss of nonpharmaceutical interests in CRS. Although these interests remain and are even growing, they are overshadowed by the robust presence of the pharmaceutical industry. Harlan loves technology and would like all controlled release technologies and applications to be shared broadly in CRS. He pointed out that, for example, he does not recall encountering the "e-ink" technology used in electronic display screens in CRS or at a CRS meeting.

Harlan offers researchers the following advice:

1. Look outside your area of expertise to find solutions.
2. Be concise and simplify.

On that second point, Harlan, who enjoys computer games, recalled a computer adventure game called "Zork" from the early days of computer gaming. It involved no graphics, only words. A significant challenge of the game was to say only what needed to be said, concisely. ■

Patent Watch

Charles Frey, Coating Place, Inc.

Selected U.S. patents related to controlled release or delivery and issued from July through December 2012 are briefly summarized. The reader can find full patent disclosures in the U.S. Patent Database at http://patft.uspto.gov/.

Multifunctional and Biologically Active Matrices from Multicomponent Polymeric Solutions; U.S. Patent 8,338,390

This invention uses heparin covalently bound to PEG in an electrospun matrix for linear release of a growth factor over at least seven days.

Pharmaceutical Formulation Containing Gelling Agent; U.S. Patent 8,337,888

This invention involves use of a polyethylene oxide in an extended release oxycodone formulation as an abuse deterrent. Attempts to extract drug also extract polymer, which imparts sufficient viscosity to prevent injection.

Hydrophilic Vehicle-Based Dual Controlled Release Matrix System; U.S. Patent 8,333,989

Use of a hydrophilic vehicle and a hydrogel polymer provides a controlled release matrix for capsules. Since presence of the hydrogel makes drug extraction difficult, this platform offers an abuse deterrent feature.

Dual Controlled Release Dosage Form; U.S. Patents 8,329,217 and 8,241,667

Osmotic dosage forms containing two drug layers that release independently through preformed channel arrangements are disclosed.

Shell and Core Dosage Form Approaching Zero-Order Drug Release; U.S. Patent 8,329,215

This invention involves a swellable, controlled release shell on a drug-containing core. The formulation is sized such that shell swelling is sufficient to promote gastric retention.

Compositions Comprising a Dispersant and Microcapsules Containing an Active Material; U.S. Patent 8,329,154

The use of controlled release microcapsules of antimicrobials and perfume agents prepared by coacervation, interfacial polymerization, and the like for fabric treatment is disclosed.

Preparation of Biodegradable Polyesters with Low-Burst Properties by Supercritical Fluid Extraction; U.S. Patent 8,324,343

This patent describes the use of supercritical fluid extraction to extract a poly(lactide-glycolide) isolates with reduced initial burst strength compared with the bulk polymer.

Compositions and Methods of Making Sustained Release Liquid Formulations; U.S. Patent 8,318,210

Suspension of controlled release microbeads in thixotropic media and the process to prepare such suspensions is disclosed.

Cyclodextrin-Based Polymers for Therapeutics Delivery; U.S. Patents 8,314,230 and 8,252,276

These patents disclose the use of cyclodextrin polymers with covalently attached amino acid, oligopeptide, or other therapeutic agents for delivery by hydrolysis or enzymatic cleavage.

Encapsulation of Sensitive Liquid Components into a Matrix to Obtain Discrete Shelf-Stable Particles; U.S. Patent 8,313,757

A process to prepare and extrude dough containing sensitive encapsulants for a variety of controlled release applications is described. Encapsulants may include enzymes or probiotics or other products such as herbicides, fungicides, insecticides, rodenticides, detergents, flavorants, fragrances, and the like.

Method of Delivering an Implantable Medical Device with a Bioabsorbable Coating; U.S. Patent 8,313,521

This invention discloses an expandable stent containing a bioactive base layer under a poly(lactide-glycolide) or parylene controlled release layer.

Fragmented Polymeric Compositions and Methods for Their Use; U.S. Patent 8,303,981

A two-syringe system is described for mixing drug with a hydrogel to form a controlled release hydrogel/drug matrix and injecting the matrix at a target therapeutic location.

Controlled Release of Nitric Oxide and Drugs from Functionalized Macromers and Oligomers; U.S. Patent 8,303,978

This invention involves the linking of nitric oxide–releasing moieties or other drug molecules to macromers or oligomers of glycolic acid, lactic acid, caprolactone, and *p*-dioxanone. The varying hydrolysis rates of the drug-monomer links are used to formulate and control drug release.

Matrix Compositions for Controlled Delivery of Drug Substances; U.S. Patent 8,298,581

Polyethylene glycols or polyethylene oxides are combined with ethylene oxide or propylene oxide polymers and poorly soluble drugs to form matrix tablets that both preserve an amorphous drug state with stable, enhanced bioavailability and provide a zero-order release profile.

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Patent Watch continued from page 33

Osmotic Device Containing a Venlafaxine Salt and a Salt Having an Ion in Common; U.S. Patent 8,293,799

This patent discloses use of a single core consisting of drug and an osmotic salt with a common counterion to provide an osmotic device with a zero order, pseudo-zero order, or sigmoidal release profile depending on the counter-ion amount.

Lipophilic Vehicle-Based Dual Controlled Release Matrix System; U.S. Patent 8,293,270

Use of a lipophilic vehicle and a hydrogel polymer provides a controlled release matrix for capsules that is useful for low-dose and moisture-sensitive drugs.

Reshapable Device for Fixation at a Dental Site; U.S. Patent 8,287,277

A device designed for fixation to a dental site and delivery of a predetermined portion of active material over a predetermined time around and between teeth is described.

Cleaning Implement with Erodible Foam Substrate and Controlled Release System of Active Agent; U.S. Patent 8,283,305

A cleaning device consisting of an erodible foam substrate and a controlled release system for delivery of surfactant, bleaching agent, limescale reducing agent, or biocide is disclosed.

Short Duration Depot Formulations; U.S. Patent 8,278,330

This invention describes an injectable depot composition for delivery of bupivacaine anesthetic over one to seven days.

Scent-Emitting Patch and/or Bandage; U.S. Patent 8,277,940

Microcapsules of perfume or cologne are incorporated in to a patch or bandage whereby pressure or scratching breaks capsules to release contents.

Topical Herbal Formulation for Treatment of Acne and Skin Disorders; U.S. Patent 8,268,367

This invention takes advantage of a reservoir effect achieved by nano-emulisfying lemon juice and/or rose water herbals in essential oils for sustained delivery in treatment of acne, eczema, psoriasis, and age scaring.

Method and Apparatus for AC Electrospray; U.S. Patent 8,267,914

This patent discloses an alternating current electrospray device for creating micron-sized droplets. The device can be applied to create aerosol droplets for respiratory delivery or as a microencapsulation technique for controlled drug delivery.

Method of Preparing a Controlled Release Fertilizer; U.S. Patent 8,262,765

Ammonium in amino acid fermentation byproducts is converted to magnesium ammonium phosphate. The low solubility of this salt provides a controlled release nitrogen source.

Multilumen Heat Transfer Catheter Systems; U.S. Patent 8,257,340

A heat transfer catheter system for controlled delivery or removal of heat at remote internal body locations is disclosed.

Biocompatible Polymers for Medical Devices; U.S. Patent 8,252,887

New classes of novel biodegradable and bioresorbable polymers and copolymers are described with radiopaque properties for use in medical devices and controlled release formulations.

Charged Mesoporous Silica Nanoparticle-Based Drug Delivery System for Controlled Release and Enhanced Bioavailability; U.S. Patent 8,252,337

Negatively charged bioactive materials are loaded in the pores and channels of positively charged mesoporous silica nanoparticles. Deprotonation at pH above the pI of the positively charged surface leads to controlled release of the negatively charged bioactive.

Bioadhesive Drug Formulations for Oral Transmucosal Delivery; U.S. Patent 8,252,328

Bioadhearing tablet formulations of either hydrogel or eroding nature for buccal and sublingual controlled delivery of sufentanil are disclosed.

Multiphasic Biofunctional Nano-Components and Methods for Use Thereof; U.S. Patent 8,241,651

Multiphasic nano-components comprised of at least two phases are described for potential use in diagnostics, pharmaceutical, personal care, and many other systems. These components can be designed for controlled release of one or more compatible or incompatible active ingredients and can contain a targeting moiety for improved efficacy. Components can be formed by electrified jetting of polymers.

Poly(tetrafluoroethylene) Polymer with Nitric Oxide Donating Surface; U.S. Patent 8,236,341

Poly(tetrafluoroethylene) surfaces are modified for controlled release of nitric oxide from implants.

High-Molecular-Weight Polymers, Devices, and Method for Making and Using Same; U.S. Patent 8,232,322

Tailored anhydride polymers with preselected molecular weight, flexibility, hardness, adhesiveness, and other properties are disclosed for use as delivery systems, formulations, and devices.

Controlled Release System; U.S. Patent 8,231,903

This invention involves the use of glycerol formal or Solketal (isopropylideneglycerol) as solvents for sucrose acetate isobutyrate (SAIB)/drug injectable controlled release systems.

PDGF Fusion Proteins Incorporated into Fibrin Foams; U.S. Patent 8,226,942

Wound healing compositions for enhanced controlled delivery of platelet-derived growth factor from fibrin matrices administered as gels or foams are disclosed.

Bone Implants for the Treatment of Infection; U.S. Patent 8,221,396

Devices for controlled delivery of antimicrobial silver to infections in bone tissue are described.

Dispenser and Method for Storing and Dispensing Sterile Product; U.S. Patent 8,220,507

A hermetically sealed dispenser for delivery of controlled amounts of substances such as medicaments, pharmaceuticals, cosmetics, food products, or oxidatively unstable materials to humans or animals is disclosed.

Controlled Release of Phenolic Opioids; U.S. Patent 8,217,005

This invention discloses prodrug forms of phenolic opioids that release active ingredient through an enzymatic cyclization reaction.

Methods of Treating Disease with Nitric Oxide (NO)–Releasing Polymers and Soluble NO-Releasing Nitrosamines; U.S. Patent 8,211,459

Nitric oxide–releasing polymers and low-molecular-weight compounds that may be used through local or systemic dosing for the treatment of medical conditions associated with nitric oxide deficiency are disclosed.

Implantable or Insertable Medical Devices for Controlled Delivery of a Therapeutic Agent; U.S. Patent 8,211,455

Novel, implantable/insertable medical devices composed of maleic anhydride polymer and copolymer combinations are described for controlled release of therapeutic agents.

Controlled Release Fertilizers and Methods of Manufacture; U.S. Patent 8,211,201

Controlled release fertilizers are prepared by sandwiching deposited fertilizer between two polymer films.

Controlled Release Nitrogeneous Fertilizer Composition System; U.S. Patent 8,211,200

Tannins are employed as nitrification inhibitors to control release of nitrogenous fertilizer.

Containment Device with Multilayer Reservoir Cap Structure; U.S. Patent 8,211,092

Devices for controlled release of reservoir contents via electrically disintegrable caps are provided. ■

Drug Delivery and Translational Research

Vinod Labhasetwar, Ph.D., Editor-in-Chief

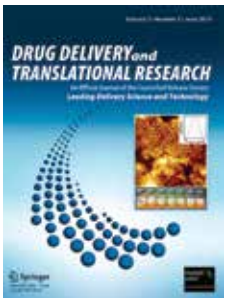
2012 *DDTR* Outstanding Research Paper Award Winner

The *DDTR* Outstanding Research Paper Selection Committee, Springer, and CRS are pleased to announce the following paper published in *DDTR* during 2012 for the award. The award will be presented at the Tuesday, July 23, plenary session during the 2013 CRS annual meeting. Please join CRS in congratulating the authors of the paper for their outstanding achievement.

> Alireza Shalviri, Ping Cai, Andrew M. Rauth, Jeffery T. Henderson, and Xiao Yu Wu. Evaluation of new bi-functional terpolymeric nanoparticles for simultaneous *in vivo* optical imaging and chemotherapy of breast cancer. Drug Deliv. Transl. Res. 6: 437-453 (2012).

In this paper, authors have developed self-assembled bi-functional nanoparticles as nanotheranostics and evaluated their efficacy in a murine model of breast cancer using doxorubicin as a therapeutic agent. The bi-functional nanoparticles conjugated to both near-infrared dye, which helped evaluate biodistribution and tumor targeting efficiency of different formulations via imaging, and doxorubicin to achieve tumor growth inhibition.

Corresponding author Xiao Yu (Shirley) Wu received her Ph.D. in chemical engineering from McMaster University, Canada. After a postdoctoral fellowship at the University of Toronto, she joined the Faculty of Pharmacy. Her research interests include novel nanomedicine for enhanced therapy of multidrug-resistant and metastatic cancer, multifunctional polymers and nanocomposites for theranostics and CNS drug delivery, closed-loop insulin delivery, mechanism of controlled drug release and excipient–drug interactions, and mathematical modeling and computer-aided design of controlled release dosage forms. Dr. Wu and coworkers have published over 300 papers, book chapters, proceedings, and abstracts and hold 16 issued or pending patents.



Join the leading scientists who are publishing their work in *DDTR* and compete for the 2013 *DDTR* outstanding research paper award. It will be selected from research articles published in *DDTR* during 2013. The award will be given during the 2014 CRS Annual Meeting, to be held July 13–16, 2014, at The Hilton Chicago, U.S.A. Visit the CRS website for award criteria (controlledreleasesociety.org).

Upcoming *DDTR* Special Issues

Nano Biointerface, with guest editors Subhra Mohapatra, Srinivas Nagaraj, and Shyam S. Mohapatra, Morsani College of Medicine, University of South Florida, Tampa, FL, U.S.A.

This special issue is partly based on the NanoBio Collaborative International Conference 2012 (NBCIC 2012), which was organized by the University of South Florida Nanomedicine Research Center and was held March 22–24, 2012. NBCIC 2012 brought together engineers, chemists, physicists, biologists, and clinicians from across the globe to discuss recent advances, opportunities, and barriers in nanoscience and nanotechnology and its applications to diagnosing and treating diseases.

RNA Interference-Based Therapeutics and Diagnostics, with guest editors Prof. Ken Howard, Aarhus University, Denmark, and Prof. Dan Peer, Tel Aviv University, Israel.

The capability to control and study cellular gene expression by the process of RNAi interference (RNAi) has provided researchers with an unprecedented tool for investigating functional genomics and the potential to harness the RNAi mechanism as a potent therapeutic. The special issue will cover the processes, molecules, and delivery solutions relevant for the clinical translation of RNAi.

DDTR Policy for Conflict of Interest

Conflict of interest affects everyone with a stake in the integrity of scientific research, including institutions, academia, industry, funding agencies, individual researchers, and of course journals publishing manuscripts sharing the output of this research.

When an author or the institution of the author has a relationship, financial or otherwise, with individuals or organizations that could influence the author's work inappropriately, a conflict of interest may exist. Examples of potential conflicts of interest may include but are not limited to academic, personal, or political relationships; employment; consultancies or honoraria; and financial connections such as stock ownership and funding. Although an author may not feel that there are conflicts—and certainly having a competing interest does not, in itself, imply wrongdoing—disclosure of relationships and interests that could be viewed by others as conflicts of interest affords a more transparent and prudent process in the publication of scientific research.

Accordingly, *DDTR* is asking that *all* authors of an article include statements in their manuscripts declaring whether there are any such conflicts of interest with their article; *DDTR* will no longer publish articles that do not contain such statements from all listed authors. For more information, please visit the instructions for authors (www.springer.com/biomed/pharmacology+%26+toxicology/journal/13346).

In addition, all contributing authors will receive an e-mail once the manuscript is submitted. All authors are required to verify via embedded link that they have read and approved the final version of the manuscript. ■

People in the News

Compiled by Steven Giannos, University of Maryland, Baltimore, MD, U.S.A.
Industrial Editor

Tris Pharma's Ketan Mehta Among Ernst & Young Entrepreneur of the Year® 2013 Finalists in New Jersey

PRNewsire: May 2, 2013 – MONMOUTH JUNCTION, NJ, U.S.A. – Tris Pharma, a specialty pharmaceutical company focused on developing innovative drug delivery technologies, today announced that Ketan Mehta, the company's founder, president, and chief executive officer, has been named a finalist for the Ernst & Young Entrepreneur of the Year® 2013 Award in the New Jersey region. The awards program recognizes high-growth entrepreneurs who demonstrate excellence and extraordinary success in such areas as innovation, financial performance, and personal commitment to their businesses and communities. Finalists were selected by a panel of independent judges. Award winners will be announced at a special gala event on June 13 at the Hyatt New Brunswick.

Tris has achieved significant growth since Mr. Mehta founded the company in 2000. Under his leadership, Tris has developed multiple proprietary drug delivery technologies that fulfill an unmet need among people who have difficulty swallowing pills. Tris has launched several important products and continues to partner with key pharmaceutical companies such as Pfizer to bring innovative products to market. Tris's active development pipeline consistently targets unmet patient medical needs, complementing its drive for continued corporate growth. The company is now more than 300 employees strong and steadily growing.

"I'm thrilled to be a finalist for the Ernst & Young Entrepreneur of the Year award in New Jersey," said Mehta. "It's truly an honor to be recognized among such an impressive group of peers. I'm proud of Tris's success and look forward to continuing to instill the entrepreneurial spirit in our employees."

Now in its 27th year, the Entrepreneur of the Year Program has expanded globally to recognize company builders in over 140 cities and in more than 50 countries throughout the world. Regional award winners go on to compete at the national level. Award winners in several national categories, as well as the National Ernst & Young Entrepreneur of the Year Overall Award winner, will be announced at the annual awards gala in Palm Springs, California, on November 16, 2013. The awards are the culminating event of the Ernst & Young Strategic Growth Forum®, the nation's most prestigious gathering of high-growth, market-leading companies.

A.P. Pharma Appoints New Management Team

Business Wire: May 2, 2013 – REDWOOD CITY, CA, U.S.A. – A.P. Pharma, Inc. (OTCBB: APPA.OB), a specialty pharmaceutical company, today announced that its Board of Directors has appointed a new management team to lead the company. Effective today, Barry D. Quart, Pharm.D., will join the company as chief executive officer, Robert Rosen, who joined A.P. Pharma in October 2012 as senior vice president and chief commercial officer, will be promoted to the role of president, and Steve Davis will join the company as executive vice president and chief operating officer. Each executive joined A.P. Pharma's Board of Directors in 2012 and will continue to serve as directors.

"We are very excited to assemble a team with such extensive industry experience and impressive track records to maximize the value of A.P. Pharma's lead drug candidate, APF530, and capitalize on the company's Biochronomer™ drug delivery platform," said Kevin C. Tang, chairman of the A.P. Pharma Board of Directors. "Barry was instrumental in building two biopharmaceutical companies, Ardea Biosciences and Agouron Pharmaceuticals, that were acquired by major pharmaceutical companies for more than $1 billion each. Rob brings deep experience in the commercialization of oncology drugs and was responsible for the launch of two products, Nexavar and Eloxatin, that each achieved sales of more than $1 billion only a few years following market introduction. Steve most recently was the chief architect in the transaction resulting in the sale of Ardea Biosciences to AstraZeneca for more than $1 billion."

"I would also like to extend my thanks to John Whelan and Michael Adam, Ph.D., each of whom made valuable contributions to A.P. Pharma and will be stepping down from their current positions," continued Mr. Tang.

"I am very excited to join A.P. Pharma and to work with the stellar management team the company has assembled. APF530 and the Biochronomer drug delivery technology, which has the potential to be used for a broad range of drugs, provide a solid platform for building a successful company," said Dr. Quart.

Dr. Quart was most recently president and chief executive officer of Ardea Biosciences, Inc., a biopharmaceutical company, since its founding in December 2006. Ardea was acquired by AstraZeneca PLC for $1.26 billion in June 2012. Previously, he was with Pfizer as senior vice president, Pfizer Global Research and Development and the director of Pfizer's La Jolla Laboratories, where he was responsible for approximately 1,000 employees and an annual budget of almost $300 million. Prior to Pfizer's acquisition of the Warner-Lambert Company, Dr. Quart was president of research and development at Agouron Pharmaceuticals, Inc., a division of the Warner-Lambert Company. Agouron was acquired by Warner-Lambert for $2.1 billion in 1999. Dr. Quart joined Agouron in 1993 and was instrumental in the development and registration of Viracept, which went from the lab bench to new drug application approval in 38 months. Dr. Quart received his Pharm.D. degree from University of California, San Francisco.

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Prior to joining A.P. Pharma as senior vice president and chief commercial officer, Mr. Rosen served as global head of oncology at Bayer HealthCare, where he was responsible for the development of the global oncology business unit for regions that included the Americas, Europe, Japan, and Asia Pacific from 2005 to 2011. During his tenure at Bayer Healthcare, he led the launch of Nexavar for the treatment of renal cell carcinoma and hepatocellular carcinoma. Nexavar's worldwide sales in 2011 were $1.0 billion. He also led premarket activities for Stivarga for gastrointestinal stromal tumors and colon cancer and Alpharadin for prostate cancer. From 2002 to 2005, Mr. Rosen was vice president of the oncology business unit at Sanofi-Synthèlabo, where he was responsible for the development of Sanofi's U.S. oncology business and the launch of Eloxatin for colon cancer. Eloxatin U.S. sales in 2005, its third full year on the market, were $1.1 billion, ranking it among the industry's most successful oncology drug launches. Mr. Rosen received a bachelor of science degree in pharmacy from Northeastern University.

Mr. Davis was most recently executive vice president and chief operating officer at Ardea Biosciences, Inc. He has completed numerous strategic transactions between biotechnology and pharmaceutical companies, including the recent $1.26 billion acquisition of Ardea by AstraZeneca PLC. Prior to Ardea, Mr. Davis served as president and chief executive officer of Neurogen Corporation, a biopharmaceutical company acquired by Ligand Pharmaceuticals. Before becoming Neurogen's chief executive officer, Mr. Davis served in numerous executive roles at Neurogen, completing multiple collaboration and asset acquisition and sale transactions with global pharmaceutical companies. Previously, Mr. Davis practiced as a corporate and securities attorney with a Wall Street law firm and as a certified public accountant with a major accounting firm. Mr. Davis received his B.S. in accounting from Southern Nazarene University and a J.D. from Vanderbilt University.

A.P. Pharma is a specialty pharmaceutical company developing products using its proprietary Biochronomer™ polymer-based drug delivery platform. This drug delivery platform is designed to improve the therapeutic profile of injectable pharmaceuticals by converting them from products that must be injected once or twice per day to products that need to be injected only once every one or two weeks. The company's lead product candidate, APF530, is being developed for the prevention of both acute- and delayed-onset chemotherapy-induced nausea and vomiting. For further information, please visit the company's web site at www.appharma.com.

Zosano Pharma, Inc. Expands Board of Directors with Addition of Kleanthis G. Xanthopoulos, Ph.D.

PRNewswire: April 15, 2013 – Freemont, CA, U.S.A. – Zosano Pharma, Inc., a privately held pharmaceutical company developing products based on its novel transdermal delivery technology, announced today the appointment of Kleanthis G. Xanthopoulos, Ph.D., to its Board of Directors. Dr. Xanthopoulos is president and chief executive officer of Regulus Therapeutics Inc. (NASDAQ: RGLS), a leading company developing microRNA therapeutics.

"I am pleased to welcome Dr. Xanthopoulos as our independent board member," said Vikram Lamba, chief executive officer of Zosano Pharma. "He is a veteran life sciences industry CEO whose extensive healthcare, execution, and IPO experience will provide Zosano with valuable insight as we pursue potential public options for financing our extensive clinical development program."

Prior to joining Regulus in 2007, Dr. Xanthopoulos was a managing director of Enterprise Partners Venture Capital. He cofounded and served as president and chief executive officer of Anadys Pharmaceuticals and remained a director until its acquisition by Roche. He was vice president at Aurora Biosciences (acquired by Vertex Pharmaceuticals) and participated in The Human Genome Project as a section head of the National Human Genome Research Institute. Previously, he was an associate professor at the Karolinska Institute, Stockholm, Sweden, after completing a postdoctoral research fellowship at The Rockefeller University, New York. An Onassis Foundation scholar, Dr. Xanthopoulos received his B.Sc. in biology with honors from Aristotle University of Thessaloniki, Greece, and received both his M.Sc. in microbiology and Ph.D. in molecular biology from the University of Stockholm, Sweden. Dr. Xanthopoulos is a member of the Board of Directors of the Biotechnology Industry Organization (BIO), Apricus Biosciences, Sente Inc., and a member of the board of BIOCOM, Southern California's life science industry association.

"I am delighted to join the Zosano board," said Dr. Xanthopoulos. "Zosano's ZP Patch technology has the potential to provide novel drug delivery solutions for many therapeutic indications—and I look forward to working with the other board members and management team to shape the company's future."

Fuisz LLC Announces Induction of Richard C. Fuisz, M.D., into Georgetown University's 1789 Society

PRNewswire: March 21, 2013 – MIAMI, FL, U.S.A. – Fuisz LLC announced the induction of Richard C. Fuisz, M.D., into Georgetown University's 1789 Society.

The induction statement, signed by university president Jack DeGioia, read as follows: "A prolific inventor, visionary inventor and dedicated philanthropist, Richard C. Fuisz, M.D. (C'61, M'65), has distinguished himself as an alumnus of Georgetown College and Georgetown School of Medicine…. Dr. Fuisz's longstanding support of the university—particularly for the School of Medicine and Georgetown Lombardi Comprehensive Cancer Center—has greatly strengthened teaching, research and patient care at Georgetown."

Donors who contribute $1 million or more to the university are members of the 1789 Society, named for the year in which the university was founded. They are honored for their generosity at

the spring semester faculty convocation (http://giving.georgetown.edu/recognitionsocieties/).

Fuisz LLC is a private technology company originated by the Fuiszes. The Fuiszes have made substantial contributions in drug delivery including orally dissolving tablets and novel particle coating systems at Fuisz Technologies; inventing and developing thin film drug delivery technologies at Kosmos Pharma and MonoSol Rx; as well as independently developing extruded sheet technology and diagnostic applications. Fuisz has extensive experience working with big and specialty pharma, as well as large consumer products companies. Fuisz has its headquarters in Miami. www.fuisz.com

BD Announces Appointment of Dr. Ellen Strahlman as Chief Medical Officer and Senior Vice President, Research and Development

PRNewswire: March 13, 2013 – FRANKLIN LAKES, NJ, U.S.A. – BD (Becton, Dickinson and Company) (NYSE: BDX), a leading global medical technology company, today announced the appointment of Ellen Strahlman, M.D., M.H.Sc., to the newly created position of chief medical officer and senior vice president, research and development, effective April 22, 2013. Dr. Strahlman will report to chairman, CEO, and president Vincent A. Forlenza and will serve as a member of the company's management committee and leadership team. In her new role, Dr. Strahlman will oversee the company's medical affairs and research and development functions.

"I am very pleased that Dr. Strahlman will be joining BD at a time when we are strategically focused on driving growth through innovation and customer focus," said Mr. Forlenza. "She brings extensive experience as a senior physician and leader in the pharmaceutical and medical device industries, and her patient-centric approach aligns with our focus on providing innovative solutions to address the healthcare needs of customers and patients."

Dr. Strahlman joins BD from GlaxoSmithKline, where she served as senior vice president and chief medical officer since 2008 and more recently worked in the office of the CEO as senior medical advisor and global head of neglected tropical diseases. As GSK's chief medical officer, Dr. Strahlman had accountability for safety and patient matters for all programs in development and commercialized products in the vaccines, pharmaceutical, and consumer businesses, as well as organizational responsibility for medical affairs, regulatory affairs, clinical safety, and other areas. Prior to GlaxoSmithKline, Dr. Strahlman has held executive leadership roles at Merck, Novartis, Pfizer, and Bausch & Lomb that included oversight of the development and commercialization of proprietary and generic pharmaceuticals, drug delivery systems, and medical devices.

Dr. Strahlman obtained her M.D. from the Johns Hopkins University School of Medicine, her M.H.Sc. from the Johns Hopkins School of Public Health, and her B.A. degree from Harvard University. ■

In the News

Compiled by Steven Giannos, University of Maryland, Baltimore, MD, U.S.A.
Industrial Editor

May

Kala Presents Data on Enhanced Topical Ocular Delivery of a Receptor Tyrosine Kinase Inhibitor

Kala Pharmaceuticals: May 7, 2013 – WALTHAM, MA, U.S.A. – Kala Pharmaceuticals, Inc., a leading developer of innovative products that rapidly and effectively penetrate the mucosal barrier to treat ocular diseases, announced today the presentation of preclinical data demonstrating that topical delivery of a small molecule receptor tyrosine kinase inhibitor (RTKi), which has been formulated utilizing Kala's proprietary mucosal-penetrating particle (MPP) technology, greatly enhanced drug levels in the retina. These data, which were presented at the Association for Research in Vision and Ophthalmology (ARVO) 2013 Annual Meeting, demonstrated that by utilizing its MPP technology Kala could create potential noninvasive treatments for retinal diseases such as wet age-related macular degeneration (wet AMD).

"Today, wet age-related macular degeneration is treated primarily with frequent intraocular injections, which are associated with potential risks to patients, as well as significant discomfort and inconvenience," said Kim Brazzell, Ph.D., chief medical officer at Kala Pharmaceuticals. "By applying our MPP technology Kala has demonstrated the potential to create a first-of-its-kind, noninvasive treatment for wet AMD. In addition, these data further support the significant potential of the MPP technology in creating highly effective topical treatments for a broad range of ocular diseases."

In a poster presentation entitled "Enhanced Topical Delivery of a Small Molecule Receptor Tyrosine Kinase Inhibitor (RTKi) via Mucosal-Penetrating Particle Technology," Kala Pharmaceuticals researchers presented preclinical data which demonstrated that:

- Topical RTKi-MPP showed a fivefold enhancement in retinal drug concentration over a non-MPP nanoparticle control in nonpigmented rabbits.
- A single dose of RTKi-MPP resulted in retinal drug levels that were >40 higher than the drug's IC50 for KDR, an RTK also known as VEGFR2, for up to 24 hours.
- Topical administration of RTKi was well-tolerated and significantly reduced vascular leakage in an *in vivo* VEGF-induced retinal vascular permeability model.

Imugene Granted Patent for Novel Delivery Technology

Imugene: May 7, 2013 – ARMADALE, Victoria, Australia – Australian drug delivery technology company Imugene recently announced the acceptance of a key Chinese patent application for the company's novel drug delivery technology Linguet (Patent No. 200680010802.4).

The Chinese application provides protection around Linguet's formulations and other specific excipients for a class of drugs that prevent the loss of bone mass, known as bisphosphonic acids and bisphosphonates, which are used to treat conditions such as osteoporosis and multiple myeloma.

Osteoporosis affects almost 70 million Chinese over the age of 50, including 22.5% of men and 50.1% of women. The condition causes some 687,000 hip fractures in China, a result of the bones becoming more porous and fragile.

Linguet is now protected in two key markets, with the same patent formulation allowed in Japan last month. Imugene uses its proprietary drug delivery technology to improve the efficacy and safety of a diverse number of existing prescription and over the counter medicines. Its platform technology, known as Linguet, enables the active ingredient of drugs to be absorbed straight into the bloodstream when placed inside the cheek (via the buccal mucosa) or under the tongue (sublingual).

"The expansion of our patent portfolio in Japan and China is a significant step in our commercialization strategy. Not only does it demonstrate the strength of our novel Linguet technology, but it enables us to explore two lucrative Asian markets ahead of the anticipated regulatory approval of Linguet Vitamin D next year," said Dr Nick Ede, executive director of Imugene.

Vitamin D deficiency is associated with a wide range of conditions, including osteoporosis, certain forms of cancer, prediabetes, and cardiovascular health.

Imugene's novel rapid Linguet form of Vitamin D has now completed feasibility testing and formulation development. The company expects to file for regulatory approval in the U.K. and license the product to a third party in 2014.

Imugene Limited is commercializing drug delivery applications based on its novel buccal Linguet technology. Linguet is a patient-friendly and cost-effective system used to deliver established pharmaceutical and nutraceutical products. For more information, visit www.imugene.com.

Injectable Nano-Network Controls Blood Sugar in Diabetics for Days at a Time

FierceDrugDelivery.com: May 6, 2013 – In a promising development for diabetes treatment, researchers have developed a network of nanoscale particles that can be injected into the body and release insulin when blood-sugar levels rise, maintaining normal blood sugar levels for more than a week in animal-based

laboratory tests. The work was done by researchers at North Carolina State University, the University of North Carolina at Chapel Hill, the Massachusetts Institute of Technology, and Children's Hospital Boston.

"We've created a 'smart' system that is injected into the body and responds to changes in blood sugar by releasing insulin, effectively controlling blood-sugar levels," says Dr. Zhen Gu, lead author of a paper describing the work and an assistant professor in the joint biomedical engineering program at NC State and UNC Chapel Hill. "We've tested the technology in mice, and one injection was able to maintain blood sugar levels in the normal range for up to 10 days."

When a patient has type 1 diabetes, his or her body does not produce sufficient insulin, a hormone that transports glucose—or blood sugar—from the bloodstream into the body's cells. This can cause a host of health effects. Currently, diabetes patients must take frequent blood samples to monitor their blood-sugar levels and inject insulin as needed to ensure their blood sugar levels are in the "normal" range. However, these injections can be painful, and it can be difficult to determine the accurate dose level of insulin. Administering too much or too little insulin poses its own health risks.

The new, injectable nano-network is composed of a mixture containing nanoparticles with a solid core of insulin, modified dextran, and glucose oxidase enzymes. When the enzymes are exposed to high glucose levels they effectively convert glucose into gluconic acid, which breaks down the modified dextran and releases the insulin. The insulin then brings the glucose levels under control. The gluconic acid and dextran are fully biocompatible and dissolve in the body.

Each of these nanoparticle cores is given either a positively charged or negatively charged biocompatible coating. The positively charged coatings are made of chitosan (a material normally found in shrimp shells), while the negatively charged coatings are made of alginate (a material normally found in seaweed).

When the solution of coated nanoparticles is mixed together, the positively and negatively charged coatings are attracted to each other to form a "nano-network." Once injected into the subcutaneous layer of the skin, the nano-network holds the nanoparticles together and prevents them from dispersing throughout the body. Both the nano-network and the coatings are porous, allowing blood—and blood sugar—to reach the nanoparticle cores.

"This technology effectively creates a 'closed-loop' system that mimics the activity of the pancreas in a healthy person, releasing insulin in response to glucose level changes," Gu says. "This has the potential to improve the health and quality of life of diabetes patients."

Gu's research team is currently in discussions to move the technology into clinical trials for use in humans.

The paper, "Injectable Nano-Network for Glucose-Mediated Insulin Delivery," was published online May 2 in *ACS Nano*. The paper was coauthored by a team led by Dr. Robert Langer, MIT's David H. Koch Institute Professor, and Dr. Daniel Anderson, the Samuel A. Goldblith Associate Professor of Chemical Engineering and a member of MIT's Institute for Medical Engineering and Science, David H. Koch Institute for Integrative Cancer Research, and Children's Hospital Boston. The research was supported by a grant from the Leona M. and Harry B. Helmsley Charitable Trust Foundation and a generous gift from the Tayebati Family Foundation.

Alliqua to Present Results Demonstrating Antimicrobial Properties of SilverSeal® at SAWC SPRING 2013

PRNewswire: May 2, 2013 – NEW YORK, NY, U.S.A. – Alliqua, Inc. (OTCQB: ALQA) ("Alliqua" or the "company") today announced it will present the results of two *in vitro* studies investigating the antimicrobial properties of the company's SilverSeal® hydrogel dressing. Data from these studies indicate that SilverSeal may be capable of rapid and sustained efficacy in managing the occurrence of wound contamination by reducing the bioburden from multiple bacterial pathogens and by sustaining this activity for up to eight days. Complete data will be presented at the Symposium on Advanced Wound Care and Wound Healing Society (SAWC/WHS) meeting taking place May 1–5, 2013, in Denver, Colorado.

The first study tested the bactericidal activity of SilverSeal against pathogens commonly associated with wound infections, including MRSA and VRE. SilverSeal dressings were exposed for up to 24 hours to methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus faecalis* (VRE), *Escherichia coli*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*. Concentrations of *E. coli*, *P. aeruginosa*, MRSA, *E. faecalis*, and *K. pneumoniae* had been reduced by >99.99%, and of VRE after 24 hours.

"The ability of SilverSeal to control these bacterial pathogens is a very important finding in today's environment where health officials around the globe are voicing concern over the rising prevalence of resistant hospital-acquired infections, including surgical site infections," stated David Johnson, Alliqua's chief executive officer. "The timing of these findings is particularly opportune as we institute plans to increase our marketing of these dressing solutions through our growing sales organization to the acute care and post-acute care marketplace."

The second study measured the time during which silver ions are released from SilverSeal dressings in concentrations sufficient to provide antimicrobial activity. These findings indicate that SilverSeal delivers a sufficient, sustained concentration of silver ions to provide antimicrobial activity for up to eight days in both water and normal saline *in vitro* and supports a seven-day dressing change period.

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The above results are summarized in two posters, both of which will be on exhibit May 2–4 in the Korbel Ballroom: "Silver Ion Release from a Silver Fiber Hydrogel Wound Dressing" (abstract #LB-27) and "Bactericidal Activity of a Silver-Coated Nylon Fiber Hydrogel Wound Dressing" (abstract #LB-45).

Moberg Derma Becomes Moberg Pharma

Business Wire: May 2, 2013 – STOCKHOLM, Sweden – Moberg Derma AB (OMX: MOB) announced today that the Swedish Companies Registration Office has granted the company's application for a name change to Moberg Pharma AB (publ), in accordance with the decision of the AGM on April 23, 2013.

The rationale for the name change is that the business, through the acquisition of Alterna LLC (renamed Moberg Pharma North America LLC), encompasses more than only skin conditions. However, skin conditions and topical drug delivery will remain core areas of the company.

"The name change is a natural step in the company's development. Today, our activities cover other areas than skin conditions, and as we continue to build a different kind of pharmaceutical company, we expect to operate in additional therapeutic areas," said Peter Wolpert, CEO of Moberg Pharma.

Updated contact details and website address are provided below. The company's shares will continue to trade under the ticker symbol MOB on the NASDAQ OMX Nordic Exchange Stockholm.

Moberg Pharma AB (publ) is a rapidly growing Swedish pharmaceutical company with direct sales through its own sales organization in the U.S. and sales through distributors in more than 35 countries. The company's product portfolio includes topical products for the treatment of skin disorders and pain under the brands Kerasal®, Jointflex®, Emtrix®, and Kaprolac®. Emtrix® (Nalox™ in many markets) is the leading product for the treatment of nail disorders in the Nordic market. The portfolio is developed further through acquisitions and in-licensing of products as well as product development with focus on innovative drug delivery based on proven compounds. Moberg Pharma has offices in Stockholm and New Jersey, and the company's share (OMX: MOB) is listed on the Small Cap list of the NASDAQ OMX Nordic Exchange Stockholm. For further information, please visit www.mobergpharma.se.

April

Pharmaco-Kinesis Corporation Develops First Combinatorial Nano-Drug TNT™

Business Wire: April 30, 2013 – LOS ANGELES, CA, U.S.A. – Pharmaco-Kinesis Corporation (PKC), an advanced medical device company developing smart implantable pumps and medications for local drug delivery, today reported development of the first combinatorial nano-drug product candidate, a combination of temozolomide (Merck & Co.) and thalidomide (Celgene) nanoparticles to be tested for treatment of gliomas and other cancers.

Based on the collaboration with University of California, San Diego's Department of NanoEngineering at the Moores Cancer Center, PKC is planning development and testing of the nano-droplet TNT™, a combination of temozolomide, an anticancer drug from Merck & Co., Inc., and thalidomide, an anticancer drug from Celgene Corporation, in a formulation with ratio of 50% temozolomide and 50% thalidomide.

If this potentially groundbreaking achievement by PKC proves effective, pharmaceutical companies may seek to use this technique in a manner that allows them simultaneously to dissolve at body temperature in their nano-format. PKC believes 2,000 to 20,000 molecules of each type of drug can be packaged in one nano-droplet, and preliminary tests indicate that the ratio of these different drugs can be precisely controlled. PKC intends that these nano-droplets will be produced with special affinities for cancer cells, attaching to and destroying such cells with enhanced efficacy compared to traditional drug treatment. PKC has commenced *in vivo* lab tests of TNT™, and preliminary results indicate that the nano-drug combination has substantially more efficacy than formulations of these drugs currently in use by physicians.

PKC predicts that direct local site delivery will be required to achieve the potentially high efficacy of the nano-drugs. PKC is in the process of developing a microminiaturized Metronomic Bio-feedback Pump Nano (MBPn) version, a fully implantable infusion pump that enables programmable, metronomic, local delivery and sampling via a multi-channel catheter that has the potential to avoid elimination by the liver. PKC hopes that the MBPn will increase therapeutic efficacy of drugs while reducing their side effects in comparison with current systemic delivery methods.

"We are conducting ongoing development and testing in order to prove the efficacy of delivering proprietary nano-droplet formulations of anticancer medications using our MBP," said Frank Adell, CEO of PKC. "If these tests are successful, we believe PKC will produce a major advance in treating gliomas and potentially other types of cancer as well."

Impax Pharmaceuticals and GlaxoSmithKline Terminate Their Collaboration on IPX066 (RYTARY™)

Business Wire: April 29, 2013 – HAYWARD, CA, U.S.A. – Impax Pharmaceuticals, the brand products division of Impax Laboratories, Inc. (NASDAQ: IPXL) today announced that Impax and GlaxoSmithKline (GSK) are terminating their collaboration for the development and commercialization of IPX066 outside the U.S. and Taiwan. IPX066 (known as RYTARY™ in the U.S.) is an investigational extended-release capsule formulation of carbidopa-levodopa being developed for the symptomatic treatment of adult patients with idiopathic Parkinson's disease and is not approved anywhere in the world.

Under the terms of the agreement entered into in December 2010, GSK's right to develop and commercialize IPX066 outside the U.S. and Taiwan will transfer back to Impax effective at the end of July 2013. The decision has been reached because of delays in the anticipated regulatory approval and launch dates in countries in which GSK has rights to commercialize the product.

Impax intends to initiate activities to find a partner or partners for markets outside the U.S. looking to grow their non-U.S. neurology franchise.

Besins Healthcare, Shin Nippon Biomedical Laboratories, Ltd., Announce Delivery Technology Licensing Agreement for Intranasal Progesterone

PRNewswire: April 18, 2013 – BANGKOK, Thailand – Besins Healthcare (Besins) and Shin Nippon Biomedical Laboratories (SNBL), a global leader in hormonal products, announced today that they have completed a licensing agreement to use SNBL's proprietary intranasal drug delivery system, Muco™ System, to further develop its BHR-310 investigational agent containing progesterone for treating mild traumatic brain injury (TBI).

Under the terms of the licensing agreement, Besins gains access to SNBL's delivery technology, along with associated patents and know-how for delivery of progesterone. Besins will be responsible for completing the development of the product, seeking regulatory approval, and commercializing the product. SNBL will be entitled to certain undisclosed milestone payments and royalties on sales.

"The overwhelming need for a treatment for concussions or mild TBI cannot be overstated," said Thomas W. MacAllister, J.D., Ph.D., Besins chief development officer. "The condition is a huge unmet medical need, especially in theaters of war and on sports fields. Partnering with SNBL will allow us to quickly accelerate our intranasal progesterone research program. They have a tremendous amount of expertise in nasal delivery, and the platform we are licensing gives far superior performance than the numerous other approaches we have tried."

An intranasal progesterone powder, BHR-310 is designed as a ready-for-use nasal spray treatment for wounded warriors or athletes with TBI at the site of injury. Outcomes from preclinical studies of BHR-310 in rats and monkeys conducted by Besins' research and development affiliate, BHR Pharma, LLC (BHR), support the feasibility of a high-dose, rapidly absorbed intranasal progesterone product able to deliver clinically meaningful doses of progesterone to the brain. BHR anticipates entering the clinic in Q3 2013.

Progesterone (P4) belongs to a class of hormones called progestogens and is the major naturally occurring human progestogen. A potent, naturally occurring neurosteroid hormone, P4 is produced in both male and female brains normally and in response to brain injury. Research suggests that progesterone has a number of mechanisms of action through which it asserts neuroprotective effects by protecting or rebuilding the blood-brain barrier, decreasing development of cerebral edema (brain swelling), down-regulating the inflammatory cascade, and limiting cellular necrosis and apoptosis (programmed cell death).

"As we have seen in the preclinical phase, we expect that our Muco™ System will safely deliver therapeutic levels of progesterone, enabling the drug to be used in a broad population of brain injured patients," said Ryoichi Nagata, M.D., Ph.D., SNBL president and CEO. "We are pleased to partner with a company so dedicated to finding a viable treatment for this unmet medical condition. Establishment of this relationship is another important milestone in using Muco™ System to provide intranasal solutions to biopharmaceutical products. With its versatility to deliver different types of compounds, we expect that there will be many more partnerships to follow."

Despite significant efforts and more than 75 clinical trials over the past 20 years, there is still no approved treatment for TBI.

Impel NeuroPharma Announces the First Ever Successful Neuroimaging Study Demonstrating Peptide Delivery Direct to the Brain Using Precision Olfactory Delivery (POD) Technology

Business Wire: April 18, 2013 – SEATTLE, WA, U.S.A. – Impel NeuroPharma announced today the completion of its human proof of concept study with the POD technology demonstrating nose-to-brain delivery using SPECT imaging, a first in the pharmaceutical and biotechnology industries. The successful trial opens the door for central nervous system (CNS) drugs to be delivered directly to the human brain, allowing potential treatments for complex neurological conditions that were previously excluded by the blood-brain barrier (BBB). Imaging showed that the POD device successfully deposited a therapeutic amount of radiolabeled tripeptide into the deep nasal cavity that then enabled rapid and significant delivery to the central nervous system, bypassing the BBB.

"This is a major milestone for the company and groundbreaking for the industry," says CEO Michael Hite. "We conclusively demonstrated the POD technology can deliver clinically meaningful levels of biologic drug products to the central nervous system (CNS). We plan to discuss the results at BIO 2013 in Chicago next week."

"Our goal is to advance the treatment of CNS diseases by enabling the delivery of molecules that currently can't be developed as therapeutics because of the blood-brain barrier. Nose-to-brain delivery offers an opportunity to bypass the BBB, providing hope for a broad range of CNS conditions that currently lack a good treatment option," Hite added.

Dr. William Frey II, director of the Alzheimer's Research Center and professor of pharmaceutics, neurology, and neuroscience at the University of Minnesota, commented, "Since the discovery in

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1989 that intranasal delivery could be used to bypass the blood-brain barrier, there has been a need for a safe, effective, and reliable device for targeting the upper third of the nasal cavity. The Impel study is exciting because it confirms that the pathway is conserved across animal species and can be utilized clinically to facilitate delivery of drugs. The study demonstrated that the Impel POD nasal device successfully targets the upper posterior portion of the human nasal cavity, resulting in rapid therapeutic delivery to multiple brain regions, including those involved in Alzheimer's, Parkinson's, and stroke."

"We've made great progress in preclinical studies, with multiple successful programs with National Institutes of Health (NIH), the Department of Defense, and several pharma collaborators, but we're really excited to advance the POD technology into the clinic," John Hoekman, Ph.D., Impel's chief scientific officer commented. Furthering its mission, Impel will continue to broaden its clinical experience with two IND-approved human studies later this year, including one at the University of Washington.

Impel has also recently received a >$650,000 Small Business Investigational Research (SBIR) grant from the NIH to develop a cost-effective version of the POD device for use in research labs. "The NIH has recognized the potential in nose-to-brain drug delivery. By expanding the application of the POD technology in basic and applied neuroscience, we are hoping to accelerate development of therapeutics uniquely enabled by this route," Hoekman added.

Impel has focused on collecting additional performance and safety data for the POD technology and expanding its capabilities for clinical support of pharmaceutical and biopharma partners. Impel has recently signed research agreements with two additional pharmaceutical partners with programs targeting neurological disorders. To date, Impel has entered into seven research agreements with pharmaceutical and device partners with active CNS pipelines, including four of the ten largest pharmaceutical companies.

Impel NeuroPharma, Inc., is developing a novel intranasal device to enable drugs to bypass the blood-brain barrier using direct nose-to-brain delivery. Impel's technology can dramatically improve the delivery of drugs, including biologics, into the brain and central nervous system. Nose to brain delivery may enable molecules previously unable to cross the blood-brain barrier to become therapeutics, potentially aiding treatment to some of the most common and devastating neurological conditions such as Alzheimer's and Parkinson's. To learn more, visit www.impelneuropharma.com

Revolutionary Autoinjector Pushes the Limits of High-Viscosity Drug Delivery

Oval Medical: April 17, 2013 – CAMBRIDGE, U.K. – Oval Medical Technologies Ltd. ("Oval"), today have announced that a variety of 1,100 cPs solutions (the thickness of motor oil) have been successfully delivered through a 25G thin wall needle, in less than 7 seconds, using their revolutionary autoinjector. Oval is a cutting-edge autoinjector company based in Cambridge, U.K. Their autoinjector technology solves currently unsolvable problems in the industry for drug containment and for the end user. Oval are highly focussed and agile, and it is therefore not surprising that they are proving to be a global success and are continuously growing their team.

The automatic delivery of high-viscosity drugs is an important milestone for injection delivery, as there is currently no known automatic injection device, with a needle, on the market that can deliver these viscosities. Viscosity has been a huge problem for many biopharmaceutical formulators, as many biologics are very viscous. There has been no effective way of delivering high-viscosity drugs through a prefilled syringe, without extreme pain to the patient (due a large needle bore) and physical discomfort, to the care-giver, when administering the injection (due to high injection forces). Not only does this mean that these wonder drugs (often coined magic bullets) can be administered through the Oval device, but they can be administered by the patient in the comfort of their own home.

Oval has wide experimental expertise in the design and testing of primary drug containers, for high-viscosity drugs, in their specifically designed laboratories. Testing of pharmaceutical companies' drugs, to see if they can be delivered in an Oval device, is proving to be a popular service for biopharmaceutical companies. Oval also has a new technology, which should enable much higher viscosities (100,000 cPs) to be administered subcutaneously.

Collegium Pharmaceutical Announces Successful Completion of Clinical Study Evaluating the Impact of Tampering on Oxycodone DETERx®, an Abuse-Deterrent, Extended-Release Opioid Product

PRNewswire: April 17, 2013 – CANTON, MA, U.S.A. – Collegium Pharmaceutical, Inc., a specialty pharmaceutical company focused on the development of innovative treatments for chronic pain, today announced top-line results from its recently completed phase I clinical trial for Oxycodone DETERx®, its extended-release, abuse-deterrent, multiparticulate product in a capsule form. The product utilizes Collegium's DETERx® technology and is designed to be more resistant to tampering and abuse than traditional formulations of the drug and is currently in phase 3 development. The product's abuse-deterrent characteristics are being evaluated in laboratory and clinical studies, consistent with the recently issued FDA Guidance titled "Abuse-Deterrent Opioids—Evaluation and Labeling."

The objective of the recently completed study was to assess the safety and pharmacokinetics of Oxycodone DETERx® following various tampering methods compared to two controls; Oxycodone DETERx®, taken as an intact capsule, and immediate release oxycodone solution. This single-dose, open-label, cross-over comparison study was conducted in 44 healthy subjects. The tampering methods used in this study are commonly employed by

abusers to destroy the time-release mechanism of tablet and capsule formulations to make the drug more abusable. The two tampering techniques that were studied included opening the capsule and chewing the contents as well as crushing the contents. The selected crushing technique was previously identified in the laboratory as the most effective method of reducing the particle size of the product. In addition, chewing was studied, as it a very common method of tampering that has been shown to be effective in compromising the time-release of both conventional and newer, abuse-deterrent formulations.

The top-line results of the study demonstrated the following:

- Both the crushed and chewed contents of DETERx® capsules were bioequivalent to intact DETERx® capsules in the fed state, demonstrating that crushing or chewing the contents of DETERx® capsules does not alter the pharmacokinetics.
- Chewing and crushing the capsule contents in either fed or fasted conditions resulted in mean Cmax values that were lower than the intact capsule when taken fed.
- The mean abuse quotient ("AQ" = Cmax/Tmax) was calculated for all manipulated treatment arms. AQ values for the chewed and crushed Oxycodone DETERx® were similar to when taking the product intact. The AQ for immediate release oxycodone solution was 7-12 times higher than the AQ values for chewed or crushed Oxycodone DETERx®.

The company intends to release detailed study results in the coming weeks. "The results of this study confirm the superior abuse-deterrent properties of our DETERx® technology," said Michael Heffernan, CEO, Collegium Pharmaceutical. "We are not aware of any other product that has demonstrated bioequivalent pharmacokinetics when comparing tampered with intact product. We believe this data differentiates Oxycodone DETERx® from other abuse-deterrent formulations on the market and in development."

Novaliq GmbH Raises €13.9 million ($18.1 million) in 5th Round of Financing

Business Wire: April 11 – HEIDELBERG, Germany – Novaliq GmbH, a drug delivery company with a focus on the efficacious topical application of poorly soluble drugs, today announced the successful completion of a fifth round of financing of €13.9m ($18.1m). Since 2007, the company has raised €27.1m ($35.2m).

Financing was again secured exclusively from the investment company of SAP, cofounder Dietmar Hopp's Dievini Hopp Bio Tech Holding GmbH & Co. KG. With the new funds, the company intends to advance its lead projects into the medical device field to approval, progress its pharmaceutical project CyclASol™ into clinical development, and extend its technology platform.

Dievini is an active investor in life and health sciences companies focusing on innovative therapeutics and diagnostics facilitating novel treatment regimens that will ultimately allow doctors to treat patients with life-threatening diseases better and safer than they can today.

"Novaliq is building an entirely new class of topical drugs for ophthalmic indications, including dry eye, which have the capability to offer compelling alternatives to current products. We are delighted to further invest in Novaliq, with its pioneering ocular drug delivery technology and strong management team," said Mathias Hothum, managing director of Dievini Hopp.

Novaliq GmbH is a drug delivery company developing a superior generation of ocular formulations for poorly soluble drugs. Its patented ocular formulations are based on semifluorinated alkanes (SFAs), which can be easily applied in the form of topical eye drops. A new generation of both prescription and consumer ocular products is possible through the unique and proprietary properties of SFAs as a delivery vehicle.

Novaliq's strategy is to establish a portfolio of consumer and prescription products in the field of evaporative dry eye disease. These products are intended to cover unmet needs, with one major advantage being they will be preservative free.

"We are pleased about the ongoing confidence and support from our investor in order to systematically develop the company with our technology platform. Our leading prescription product, CyclASol, is the first cyclosporine A solution for dry eye disease, while other products are based on emulsions, containing potentially irritating surfactants," said Bernhard Günther, CEO of Novaliq.

This proprietary SFA product is based on the EyeSol™ technology, provided preservative-free in multidose units. The absence of irritating surfactants and preservatives leads to improved tolerability and convenience.

Novaliq is a drug delivery company whose goal is to develop innovative pharmaceutical formulations. Its patented semifluorinated alkanes (SFAs) can be used in various routes of administration for the transport of drugs or oxygen for therapeutic purposes. Based on its unique physicochemical properties, Novaliq currently develops innovative ophthalmic formulations, as well as solutions for organ preservation, and has several product candidates with excellent market potential in various stages of development. Novaliq welcomes invitations from interested parties to enter discussions about significant additional development opportunities.

Agere Announces Novel Technology That Streamlines Polymer Selection for Improved Solubilization

Business Wire: April 10, 2013 – BEND, OR, U.S.A. – Agere Pharmaceuticals, Inc., a leading oral bioavailability contract research and manufacturing organization (CRO/CMO), announced today that it has enhanced the Agere drug delivery

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platform to include prediction technology that identifies best-fit polymer candidates for drug solubilization and formulation. Agere's polymer-selection system for drugs integrates directed experiments with rigorous computations to predict and measure key functions of the drug and candidate polymers. These functions are analyzed to accurately predict and rank order empirically observed behaviors of the drug-polymer compound.

Polymer selection is one of the critical first steps in enhancing the bioavailability of compounds. Identifying the most probable candidates for solubilization allows subsequent formulation design and development efforts to focus on exploration and optimization of likely successful drug-polymer combinations. Agere is unconstrained in the excipients it considers, as the company has no IP ownership of polymers, and therefore clients benefit from a far-reaching and agnostic approach.

"Our new technology further extends the Agere platform to leverage formulation design automation and analysis using fundamental science and proprietary techniques," commented Marshall Crew, president and CEO of Agere. "Our goal was to put a system in place that enables us to quickly consider an expanding spectrum of likely excipients in order to achieve the best bioavailability options for our clients."

Pharmaceutical companies facing solubility challenges with active pharmaceutical ingredients (APIs) depend on Agere's expertise and scientific approach to enhance the bioavailability of their drugs. Agere services span formulation design and development into clinical trial drug manufacturing. All services are offered "à la carte," allowing companies the flexibility to engage with Agere at any stage in their process. Agere provides all services on a fee-for-service basis, in which Agere assumes no intellectual property (IP) ownership over work done on behalf of the company's clients.

Agere is a leading CRO/CMO focused on improving the oral bioavailability of insoluble APIs. The company supports clients from formulation design and development through cGMP manufacturing for phase I, phase II, and phase IIb clinical trials. All services are delivered on a fee-for-service basis, and every project the company undertakes is customized to serve each individual client's requirements. Agere is located in Bend, OR. For information: www.agerepharma.com.

SMARTag™ Advanced Conjugation Technology to be Presented at BIO International

Business Wire: April 10, 2013 – SOMERSET, NJ, U.S.A. – Catalent Pharma Solutions today announced that it has acquired an exclusive license to market Redwood Bioscience's proprietary SMARTag™ precision protein-chemical engineering technology for the development of advanced antibody-drug conjugates (ADCs). Redwood's novel, site-specific protein modification and linker technologies enable the generation of homogenous bioconjugates engineered to enhance potency, safety, and stability. Combined with Catalent's proprietary GPEx® cell line expression system, its brand new state-of-the-art biomanufacturing Center of Excellence in Madison, Wisconsin and broad range of bioanalytical and fill-finish services, this deal marks a further expansion of Catalent's capabilities to help customers develop more and better biologic treatments.

ADCs combine the targeted binding specificity and half-life benefits of monoclonal antibodies with the potency advantages of small molecule chemotherapy or therapeutic agents. With the FDA's recent approval of Genentech's T-DM1 (Kadcycla™) for metastatic breast cancer, and a large and growing list of products in clinical and preclinical development, ADCs are emerging as one of the fastest growing development areas in biologic anticancer treatment.

Redwood's novel protein conjugation and linker technologies overcome the limitations associated with conventional protein chemistries that produce heterogeneous products with variable conjugate potency, toxicity, and stability. The SMARTag technology enables site-specific, controlled drug-protein conjugation and uses only naturally occurring modifications to proteins requiring minimal cell-line engineering. Redwood's technology provides control over conjugate configuration, generating ADCs with optimal efficacy, safety, and stability. The Redwood platform also enables the use of proprietary linker chemistry that prevents systemic drug loss and increases targeted potency. Redwood has developed an array of linkers utilizing this novel chemistry, which are designed for optimal conjugation performance.

Under the terms of the agreement, Catalent will have the exclusive right to sublicense the SMARTag technology to customers and will work with Redwood to comarket the technology and support sublicense programs. As part of the collaboration, Catalent will also take a minority equity stake in Redwood, which may increase over time up to a potential acquisition.

"Our goal is to enable our biologics customers to create more and better treatments through advanced technologies and development solutions," commented Barry Littlejohns, president of Catalent Medication Delivery Solutions. "We believe that Redwood is an industry leader in site-specific conjugation. Their innovative technologies will provide significant value to our customers looking to develop next-generation ADC therapies."

David Rabuka, Ph.D., Redwood's cofounder and chief scientific officer, added, "We are very excited to be closely allied with Catalent. The technical synergy between Redwood and Catalent is a unique opportunity to provide unparalleled access to the next generation of bioconjugates."

For additional information, meetings and presentations with Catalent Biologics are being arranged at the BIO International Convention in Chicago, Illinois, on April 22–25 through the Business Forum partnering system and exhibit booth #4571.

NovaDel Announces the Signing of a Definitive Agreement to Sell Its NovaMist™ Technology and Certain Other Assets

Business Wire: April 8, 2013 – BRIDGEWATER, NJ, U.S.A. – NovaDel Pharma Inc. (NVDL.PK) has signed a definitive agreement to sell its NovaMist™ technology and certain other assets to SUDA LTD, an Australian publicly held pharmaceutical company.

The transaction includes the sale of NovaDel's patents and trademarks relating to its NovaMist technology. The sale, as contemplated, does not include the NitroMist® or ZolpiMist™ intellectual property or licenses.

Subject to shareholder approval, NovaDel will receive at closing $400,000 in cash, 50,000,000 shares of SUDA common stock and 10,000,000 options for the purchase of SUDA common shares at $0.05 per share. It is the company's intention to use part of the proceeds from this sale, after transaction expenses, to reduce its outstanding liabilities.

NovaDel continues to seek a purchaser for its remaining assets, the NitroMist and ZolpiMist intellectual property and licenses. As previously reported, the company has appealed to the FDA for a reduction or elimination of the annual fees relating to its licensed marketed products. The amount currently owed to the FDA and the burden of the continuation of these fees has and continues to inhibit the company's ability to find a purchaser for these assets.

Lipocine Reports Positive Clinical Results for Novel Once-a-Day Oral Testosterone

Business Wire: April 8, 2013 – SALT LAKE CITY, UT, U.S.A. – Lipocine Inc. (www.lipocine.com), a biopharmaceutical company focused on developing innovative oral hormone therapies for men's and women's health, today announced favorable phase I results for LPCN 1111. LPCN 1111, a novel prodrug of testosterone, uses the company's proprietary Lip'ral technology to enhance solubility and improve absorption during testosterone replacement therapy. Data from the phase I study established that LPCN 1111 exhibited a strong safety profile and pharmacokinetics, which should allow for once-a-day dosing of this next-generation oral testosterone replacement product. The LPCN 1111 development program complements Lipocine's robust pipeline of potential products including LPCN 1021, a twice-daily oral testosterone replacement, currently entering phase III clinical trials.

"We are very pleased to report that data from the phase I trial indicate that LPCN 1111 appears to be the first once-a-day, orally active testosterone replacement therapy ever advanced into the clinic. This is an important step in the development of this potentially groundbreaking therapy," said Dr. Srinivasan Venkateshwaran, chief technology officer of Lipocine Inc.

"New oral testosterone dosage forms will make a major contribution to the expanding market for testosterone replacement therapy, an established and safe way to treat testosterone deficiency. We believe a once-a-day product will be strongly differentiated and provide a significant advancement in this market. Based on these data, LPCN 1111 is poised to be the first such product in this class," added Dr. Mahesh Patel, president and CEO of Lipocine Inc.

Testosterone replacement therapy (TRT) is an underserved and rapidly expanding segment of health care for men. An independent study in the U.S. indicates that the majority of symptomatic men are not being treated for low testosterone, due in part to the insufficient treatment options currently available. Topical gels currently account for almost 90% of testosterone sales, but carry a boxed warning from the FDA due to concerns about transfer of the gel, and therefore the hormone, to women and infants during use. Lipocine has designed orally available LPCN 1111 specifically to address these issues and provide a safe, effective, and convenient therapeutic option.

In 2012, the U.S. market for TRTs was valued at $2.1B, with double-digit annual growth expected for the foreseeable future.

Lipocine Inc. is a pharmaceutical company leveraging its proprietary drug delivery technologies to commercialize innovative pharmaceutical products. Lipocine is focused on becoming a leading men's and women's health company to develop oral Rx products to improve patient compliance.

March

Sorrento Therapeutics, Inc., and IGDRASOL Announce Three Presentations on Cynviloq™ (IG-001; paclitaxel polymeric micelle) at the American Association of Cancer Research (AACR) Meeting

PRNewswire: March 31, 2013 – SAN DIEGO and FOUNTAIN VALLEY, CA, U.S.A. – Sorrento Therapeutics, Inc. ("STI"; SRNE) and IGDRASOL announced today that IGDRASOL will be presenting updates of its development of Cynviloq™ (IG-001) at the annual meeting of the American Association for Cancer Research (AACR) in Washington, DC (April 6–0). IGDRASOL is a privately held company for which STI was granted an irrevocable option right to acquire. The two companies' combined pipeline features an oncology franchise of potential products with phase 2 data for multiple solid tumor indications as well as two synergistic drug discovery and development platforms, namely the G-MAB® human antibody library and MABiT™, a proprietary technology to generate antibody formulated drug conjugates (AfDC).

Cynviloq™ (or IG-001) is a next-generation, branded, micellar diblock copolymeric paclitaxel formulation currently approved and marketed in several countries as Genexol-PM®. Cynviloq™ has completed phase 1 or 2 trials in MBC, NSCLC, pancreatic cancer, ovarian cancer, and bladder cancer in the U.S. and/or non-U.S. IGDRASOL is preparing for an "End of Phase 2"

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meeting with the U.S. Food & Drug Administration (FDA) targeted for the first half of 2013 regarding Cynviloq™. As an injectable nanoparticle formulation of paclitaxel, Cynviloq™ is potentially eligible for approval via FDA's 505(b)(2) bioequivalence regulatory pathway versus albumin-bound paclitaxel (nab-paclitaxel; Abraxane®) in its currently approved MBC and NSCLC indications. Abraxane® sales exceeded $400 million in MBC in fiscal 2012.

The time, title, authors, and location of the presentations are as follows:

- Monday, April 8, 1:00–5:00 PM (2141/10) – "IG-001 utilization of albumin mediated transport and its potential application in difficult to perfuse tumors." Kouros Motamed, Larn Hwang, Chao Hsiao, Vuong Trieu. IGDRASOL, Fountain Valley, CA. Poster Session, PO.ET01.03. Novel Targeted Therapies 1.
- Tuesday, April 9, 1:00–5:00 PM (3481/27) – "Development of personalized paclitaxel therapy (IG-001) for ovarian cancer." Larn Hwang, Chao Hsiao, Kouros Motamed, Vuong Trieu. IGDRASOL, Fountain Valley, CA. Poster Session, PO.CL13.08. Biomarkers 5: Breast and Gynecologic Cancers.
- Tuesday, April 9, 1:00–5:00 PM (4526/24) – "IG-001—Evaluation as next generation nanoparticle paclitaxel against poorly perfused tumors." Vuong Trieu, Larn Hwang, Kouros Motamed, Chao Hsiao. IGDRASOL, Fountain Valley, CA. Poster Session, PO.CH06.01. Drug Delivery Technology.

Cynviloq™ (or IG-001; a paclitaxel-loaded micellar diblock copolymer) is a next-generation branded paclitaxel formulation currently approved and on the market in several countries as Genexol-PM®.

BioDelivery Sciences Expands Product Pipeline with Acquisition of Patented Topical Clonidine Gel for the Treatment of Painful Diabetic Neuropathy

PRNewswire: March 26, 2013 – RALEIGH, NC, U.S.A. – BioDelivery Sciences International, Inc. (Nasdaq: BDSI) announced today that it has entered into a worldwide licensing agreement with privately held Arcion Therapeutics (Arcion), where BDSI will develop and commercialize topical clonidine gel (formerly ARC4558) for the treatment of painful diabetic neuropathy (PDN) and potentially other indications.

The PDN market is highly underserved by existing products, and there is a strong scientific rationale for developing a topical treatment for PDN that delivers analgesia in a way that avoids systemic side effects.

Under the terms of the agreement, BDSI will make an upfront payment of $2 million to Arcion in the form of unregistered shares of BDSI common stock.

"We are excited about this late-stage product where efficacy has already been demonstrated in a very painful condition with a significant unmet need," said Dr. Mark A. Sirgo, president and chief executive officer of BDSI. "Though we remain focused on preparing our BUNAVAIL NDA for filing in the coming months and completing our BEMA buprenorphine chronic pain phase 3 trials, this product acquisition allows us to build our pipeline, while applying our expertise in pain product development, utilizing the FDA's 505(b)(2) regulatory process, and diversifying outside of opioid therapy and our BEMA technology."

"BioDelivery Sciences makes a great partner for our clonidine program, providing the expertise in developing pain medications and resources to bring this program to patients," stated James Campbell, M.D., chief executive officer of Arcion. "This transaction allows us to now focus our resources on our other pain programs."

Evidence has shown that clonidine stimulates an inhibitory receptor in the skin associated with pain fibers. Arcion has developed a patented topical gel formulation of clonidine and has assessed its effectiveness in reducing pain in PDN in a double-blind, placebo-controlled, phase 2 study where the primary study endpoint was the change in pain intensity over a three month treatment period in diabetic foot pain. A significant treatment difference was seen in the planned subset analysis of diabetic patients who had documented evidence of "functioning pain receptors" in the skin of the lower leg ($p = 0.01$, $n = 63$), thus, at a minimum, supporting the effectiveness of topical clonidine in diabetic patients with functioning pain receptors of the skin. In the overall population that included patients without "functioning nerve receptors," there was a trend favoring topical clonidine gel ($p = 0.07$, $n = 182$), though the overall results did not reach statistical significance.

"These data point to a very clear and compelling therapeutic profile and regulatory strategy as BDSI makes plans to prepare for a confirmatory phase 2b study in the latter part of this year, which would potentially lead to data availability before the end of 2014," stated Dr. Andrew Finn, executive vice president of product development at BDSI. "If this study meets its endpoint, BDSI plans to proceed with the phase 3 placebo-controlled study in the same population."

Additional financial terms of the licensing agreement include a milestone payment to Arcion of $2.5 million in unregistered shares of BDSI stock upon acceptance by the U.S. Food and Drug Administration (FDA) of a New Drug Application (NDA) for topical clonidine gel and a cash payment to Arcion of between $17.5 and $35 million upon NDA approval, depending on certain regulatory and commercial considerations. In addition, the licensing agreement includes sales milestones and low single-digit royalties on net worldwide sales.

Dr. Sirgo concluded, "The use of our equity for initial payment combined with the success-based milestones in this agreement allows us to preserve our capital for the clinical development program, with the majority of the cost falling in 2014 and beyond." ■

Controlled Release Society
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St. Paul, MN 55121
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Calendar of Events

2013

Controlled Release Technology: Polymeric Delivery Systems for Pharmaceuticals, Proteins, and Other Agents
July 8–12
Cambridge, MA, U.S.A.
http://shortprograms.mit.edu/crt

40th Annual Meeting & Exposition of the Controlled Release Society
July 21–24
Hawaii Convention Center
Honolulu, Hawaii, U.S.A.
controlledreleasesociety.org

Advances in Tissue Engineering Short Course
Sponsored by CRS
August 14–17
Houston, TX, U.S.A.
http://tissue.rice.edu/

11th International Nanomedicine and Drug Delivery Symposium (NanoDDS'13)
October 25–27
La Jolla, CA, U.S.A.
http://nanomedicine.ucsd.edu/nanodds13

Mitigating Risks for Patients When Developing Oral Controlled Release Dosage Forms
Sponsored by CRS
November 9–10
San Antonio, TX, U.S.A.
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Introduction to Microencapsulation Technologies
Sponsored by CRS
November 10
San Antonio, TX, U.S.A.
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