



# APV Focus Group Drug Delivery

Combining Science & Technology to Create Advanced Drug Delivery Systems

INTERNATIONAL ASSOCIATION FOR PHARMACEUTICAL TECHNOLOGY

NEWSLETTER | ISSUE 3/2007

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## DRUG DELIVERY EVENTS

Provided by Christoph Blümer

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- ◇ **APV course: Novel excipients or novel use of known excipients from technical feasibility to registration** [Details](#)  
Berlin (D), December 11<sup>th</sup> - 12<sup>th</sup> 2007
- Drug Delivery to the Lungs 18 (DDL18)** [Details](#)  
Edinburgh (UK), December 12<sup>th</sup> - 14<sup>th</sup> 2007
- 9<sup>th</sup> US-Japan Symposium on Drug Delivery Systems** [Details](#)  
Lahaina, Maui, Hawaii (USA), December 16<sup>th</sup> - 20<sup>th</sup> 2007
- The 12<sup>th</sup> Annual Drug Delivery Partnerships** [Details](#)  
San Diego, CA (USA), January 21<sup>st</sup> - 23<sup>rd</sup> 2008

**[Suggest a meeting to be announced!](#)**

## DRUG DELIVERY PRODUCTS

Provided by Dr. Louise Rosenmayr-Templeton

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**Exelon® Patches** (Novartis AG; manufactured by LTS Lohmann Therapy-Systems)

In July the FDA approved Exelon® transdermal patches for the treatment of mild to moderate dementia in Alzheimer's and Parkinson's disease. The product is also earmarked for EU approval having recently received a positive opinion from the Committee for Medicinal Products for Human Use. The approvals come at a time when worldwide demand for Alzheimer therapeutics is estimated to grow 11 % per annum to approximately \$3.05 billion in 2009.

The patches, which are 5 cm<sup>2</sup> and 10 cm<sup>2</sup> in size, contain 9 or 18 mg of the dual acetylcholinesterase and butyrylcholinesterase inhibitor, rivastigmine, and are designed to release respectively 4.6 and 9.5 mg of active over 24 hours. They are comprised of a four-layer laminate consisting of a backing film, an acrylic drug-containing co-polymer matrix, a silicon based adhesive layer and a release liner that is removed prior to use.

The transdermal formulation offers patients a number of advantages over the existing Exelon® Capsule and Oral Solution products. Firstly, drug release is smooth and continuous resulting in steady plasma drug levels, and patch use has already been shown to reduce rivastigmine related gastrointestinal side-effects. Secondly, because it is applied to the skin and its presence can be visually checked, the patch overcomes some of the problems associated with giving medicines to elderly dementia patients. These include difficulties swallowing and missed doses through forgetfulness. Its use, thus, eases rivastigmine administration and allows carers to monitor compliance.

The patches were developed and are manufactured as a result of a collaboration between Novartis and LTS Lohmann Therapy-Systems.

Further information at : [www.novartis.com/](http://www.novartis.com/); <http://www.exelon.com/>; <http://www.ltslohmann.com/>

## Somatuline® Depot (Ipsen Pharma)

Somatuline® Depot injection (containing 60, 90 and 120 mg of lanreotide base as the acetate salt) was approved in August by the FDA for the long-term treatment of acromegaly in patients unsuitable or unresponsive to surgery and/or radiotherapy. Acromegaly occurs in about 60 adults per million and is caused by excessive growth hormone secretion usually as a result of a pituitary gland tumour. Lanreotide, a cyclical, octapeptidic somatostatin analogue, acts via a negative feedback mechanism to normalise circulating growth hormone and insulin growth factor-1 (IGF-1) levels, the overproduction of the latter being the cause of many acromegalic symptoms. The product is already sold as Somatuline® Autogel® in nearly 60 countries and had sales of €92 million in 2006. The formulation will be marketed in North America by Tercica.

Somatuline® Depot injection is supplied as a white to pale yellow semi-solid formulation in pre-filled syringes for deep subcutaneous administration. The product is unusual in that it consists of an aqueous supersaturated solution of lanreotide acetate (concentration corresponding to 24.6 % w/w base) with no other added excipients. Following injection, the formulation is thought to form a drug depot on interaction with physiological fluids, with the active being released steadily over 4 weeks. The mechanism of depot formation is not described in the product literature. However, it is known that the Ipsen processed peptide self-aggregates in water to form nanostructures, whose packing and thermodynamic stability depends on drug concentration (C. Valéry et al). The formulation is patented until 2015 in both the US and Europe.

Further information at <http://www.ipсен.com/> and in C. Valéry et al, *Biophysical Journal* 86:2484-2501 (2004).

## DRUG DELIVERY COMPANIES

Provided by Gerben Moolhuizen

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**to-BBB technologies B.V. (NL-Leiden)** develops a unique CNS drug targeting solution, called 2B-Trans™, which takes care of the delivery of drugs into the CNS. The 2B-Trans™ technology uses a well characterized and effective transport system with a specific carrier protein that has an excellent proven safety profile in human.

to-BBB started as a spin-off company from the renowned Blood-Brain Barrier Research Group of the Leiden/Amsterdam Center for Drug Research from Leiden University in The Netherlands. The company recently secured Euro 4 million of venture funding from Aescap Ventures for the development of its internal product pipeline.

### Fact sheet

Founded: 2003

Location: Leiden, The Netherlands

Employees: 8

Ownership: Privately funded  
Investors, besides management and informal investors:  
Aescap Venture  
Antea Participaties  
BioPartner Start-up Ventures  
Libertatis Ergo Holding  
VenGen

Key technologies: **2B-Trans™ technology**

to-BBB technology is based on the use of the well characterized internalizing transport receptor for diphtheria toxin, which to-BBB has newly identified for the targeting of drugs to the brain. This 2B-Trans™ receptor has several unique advantages:

- it makes use of an effective and safe, non-toxic transport mechanism called receptor-mediated endocytosis, with proven cargo-carrying properties across the blood-brain barrier (e.g. brain delivery of large proteins and liposomes containing drugs and genes)
- the receptor has no endogenous ligands and thus neither competition from endogenous ligands, nor blockade of transport to the brain of essential nutrients is to be expected
- it is constitutively expressed on the blood-brain barrier, neurons and glial cells
- the receptor expression is highly amplified in disease conditions and thus allows for site-specific disease targeting

In order to utilise the 2B-Trans™ receptor for delivering drugs to the CNS, to-BBB makes use of a well characterized carrier protein that specifically binds to the receptor: the non-toxic mutant diphtheria toxin protein, CRM197. Delivery into the CNS is achieved by linking the drug of interest to this carrier protein.

The carrier protein has an extensive history of safe use in humans as it has already been successfully marketed for human use for other indications in vaccines for many years with a proven carrier efficacy and excellent safety profile. It is well characterized (i.e. known receptor binding domain, conjugation sites, manufacturing process)

Product pipeline: **Lead product: 2B3-101.**

to-BBB aims to make use of the 2B-Trans™ technology for the rapid delivery of ribavirin to the brain as a novel therapy for viral encephalitis, in particular infection with Japanese Encephalitis Virus (JEV)

Every year about 50,000 patients end up in intensive care units worldwide after being infected with JEV, a common mosquito-transmitted flavivirus in Asia. Within a week after hospitalization, the lack of an effective therapy results in the death of about 30% of these patients, whereas the vast majority of survivors are left with severe neurological damage.

Intravenous ribavirin is marketed as combination therapy with alpha-interferon for Hepatitis C and as an inhalation solution for respiratory syncytial virus (RSV), and extensively used off-label for a wide range of RNA virus infections for which there currently is no treatment available. This broad-spectrum drug has antiviral activity against a wide range of encephalitis-causing viruses (including Japanese & St.Louis Encephalitis Virus, West Nile Virus, Dengue Virus), and also against a number of potential bioterrorism viruses, but CNS penetration is too slow to reach therapeutic concentrations in time.

to-BBB is currently pursuing the preclinical development of 2B3-101, heading for a human phase 1 / 2 clinical trial in JEV in 2009.

Partner products: to-BBB has established R&D partnerships with GenMab and Biogen-Idec.

Website: <http://www.tobbb.com>

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## DRUG DELIVERY TERMINOLOGY

Provided by Prof. Dr. Karsten Mäder

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The main processes involved in the clearance of a polymer from the body are [POLYMER EROSION](#) and [POLYMER DEGRADATION](#). **Erosion** is the mass loss from a polymer matrices. Polymer **degradation** is the process of chain cleavage and therefore, leads to a decrease of the molecular weight [1].

Polymers might leave the body by a pure erosion processes (e.g. PEG, PVA). In contrast, for many polylactides or poly(lactide-co-glycolides) a significant degradation might take place before any erosion occurs [2]. The incorporation of PEG into the polyesters leads to similar kinetics of the erosion and degradation process [2].

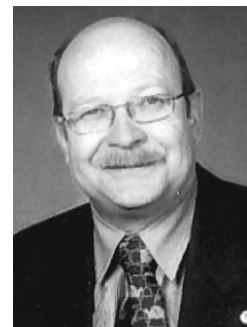
[1] F. v. Burkensroda, L. Schedl, A. Göpferich: Why degradable polymers undergo surface erosion or bulk erosion. *Biomaterials* 23 (2002) 4221–4231.

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[Write a comment on this definition](#)

[Suggest a term to be defined](#)  
[Suggest a definition](#)

**JÖRG KREUTER**, an outstanding scientist and imminent proponent of the application of nanotechnology to drug delivery and targeting, is Full Professor of Pharmaceutical Technology at the University of Frankfurt (Germany).



Prof. Kreuter is a trained pharmacist, and graduated from Philipps-University of Marburg (Germany) in 1971. He received his doctoral training at the Swiss Federal Institute of Technology (ETH) in Zurich (Switzerland), graduated in 1974, and received the ETH medal for his outstanding thesis on "New adjuvants on a poly methyl (methacrylate) base" in 1975. He then pursued his scientific career at ETH, combined with two postdoctoral visits to the University of Kansas (Lawrence, KS), and the University of Michigan (Ann Arbor, MI). In 1982, Prof. Kreuter submitted his habilitation thesis on the "Evaluation of nanoparticles as drug delivery systems" at ETH. After a Visiting Associate Professorship at the University of Wisconsin (Madison, WI), he assumed the post of Professor in Pharmaceutical Technology at the University of Frankfurt (Germany), serving as dean of the faculty of Biochemistry, Pharmaceutical Sciences and Food Sciences twice, in 1988-1989 and 1997-1998.

Prof. Kreuter has received numerous awards and recognitions, including the International Association of Pharmaceutical Technology (APV) prize for scientific contributions on "Nanoparticles as adjuvants for vaccines and particulate drug carrier systems" in 1981, the election to the Board of Governors to the Controlled Release Society (CRS) in 1987, and the election as Fellow of the American Association of Pharmaceutical scientists (AAPS) in 1995. In 2005, he received the Distinguished Service Award of the CRS, having coordinated the installation of Local Chapters of the society in various countries, which allows students a better access to the scientific drug delivery community.

In the current discussion on "(bio)nanotechnology" and "nanomedicine" it is often overlooked that very early on, pharmaceutical scientists have largely developed and adapted nanoscale systems to the safe and efficient delivery of active principles. The contributions of these scientists have made technologies such as self-assembling colloidal systems, non-viral gene delivery, or cell-specific drug and vaccine targeting possible. From the beginning of his scientific career, Prof. Kreuter has focused on the interface between the technology of colloidal drug delivery systems and the biological environment these systems are exposed to. These studies have resulted in more than 250 publications on:

- Nanoparticulate and liposomal drug delivery systems
- Drug targeting
- Skin permeation studies and transdermal delivery
- Formulation of parenterals
- Stability studies using microcalorimetry

One of the outstanding achievements of Prof. Kreuter and his co-workers has been overcoming the blood-brain barrier using surface-modified nanoparticles and delivering active compounds, including peptides, to the central nervous system. His group at Frankfurt University is currently further pursuing this research.

Under Prof. Kreuter's supervision, more than 50 Ph.D. students graduated from Frankfurt University. The interdisciplinarity and international orientation of Prof. Kreuter's group has enabled former students to succeed in their various careers in academia and industry.

To honor Prof. Kreuter's scientific achievements, as well as to celebrate his 60<sup>th</sup> birthday, a symposium on "Nanotechnology and Drug Delivery – from Concepts to Products" is organized on February 15, 2008, at the [Biozentrum of Frankfurt University](#).

## FEATURED ARTICLE

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### BIODEGRADABLE POLYMERS – A CHANGE OF PARADIGMS?

by **Prof. Dr. Achim Göpferich**, **Universität Regensburg, Universitätsstraße 31, D-93053 Regensburg**

#### **1. The early years of biodegradable polymers**

While polymers in general have been an indispensable tool for drug formulation for centuries, biodegradable materials have been used in the pharmaceutical sciences as carriers for the parenteral delivery of biologicals such as peptides and proteins only since the early 1970ies. Questions of the early days of degradable materials were twofold: how biocompatible are the compounds and can they provide suitable release kinetics to comfort pharmacokinetic requirements. Materials that have their roots in this time are definitely poly( $\alpha$ -hydroxyesters) such as the derivatives of lactic- and glycolic acid. Surprisingly these materials of the first hour seem still to be our first choice when we think of developing a new drug delivery system.

The reason why poly(D,L-lactic acid) (PLA) and poly(D,L-lactic-co-glycolic acid) (PLGA) have been so successful is definitely their reasonably good biocompatibility that has been proven over many years in a plethora of studies. Concomitantly it is well documented by the numerous PLA and PLGA derived products that we find on the market. Designing delivery systems using PLA and PLGA provides us hence definitely with a tremendous regulatory advantage that alternate materials lack.

## **2. Degradation and erosion properties: decisive parameters for the performance of degradable polymers**

Although PLA and PLGA seem to be wonderful adjuvants they are far from being 'simple' materials. Even though they are extensively used for the design and development of drug delivery systems, we are far from a complete understanding of how they function. Research that emerged in the 1990ies gave us a glimpse at the complexity of things. First doubts about their broad applicability resulted from the formulation of proteins that were in contrast to small peptides much harder to incorporate since they were prone to degradation either during manufacturing or during release. A close look at the literature reveals that back then, the erosion mechanism emerged as a severe handicap to protein stability [1]. Several studies revealed that even microparticulate systems suffered from low pH values during degradation and high osmotic pressure both of which were known to be a handicap to drug stability [2,3]. Furthermore, what had been underestimated for many years was the continuously changing chemical environment inside delivery systems made of these materials that had tremendous consequences for their internal structure during degradation. Most prominent are findings that amorphous polymers could undergo crystallization due to the formation of homopolymeric degradation products [4] and that degradation products could undergo chemical interactions with peptides such as acylation of amines with monomers [5].

Besides this tremendous complexity of their internal chemistry, PLA and PLGA matrices are subject of distinct but again far from being completely understood erosion mechanisms. Frequently we refer to the materials as bulk eroding, meaning that the polymer chains are degraded throughout a matrix's cross section and not only on its surface. This explains quite well the phenomena that are involved in problems related to incorporated drugs as outlined above and explains quite well the rationale of many outstanding research groups in the late 1980ies and 1990ies to counter steer by developing alternate biodegradable polymer materials. The intention of research at that time from the pharmaceutical point of view was definitely driven by the desire to obtain materials that provided better compatibility with drugs and/or exhibited more favorable degradation kinetics. Polymers tending to be surface eroding such as polyanhydrides [6] or polyorthoesters [7] resulted from this effort, and in general the search for structures set in that allowed shaping the material properties via the type of bonds that underwent hydrolysis. Other material classes such as poly(tartaric acid) or polyphosphazenes followed [8]. Many promising materials have been developed during this time, and concomitantly we eventually developed a little better understanding of the erosion process such that surface and bulk erosion are erosion pathways that are open to every degradable polymer. Which of both is predominant mainly depends on the size of a matrix in relation to the reactivity of the hydrolysable bonds such that increasing dimension and fast hydrolysis favor surface erosion [9]. Regardless of our continuously increasing understanding of the basic processes we have still no universal theory that would explain polymer erosion completely.

## **3. The recent efforts towards the development of biodegradable polymers are mainly application driven**

Despite the progress of developing and providing classes of biodegradable polymers that would serve a multitude of different applications we saw a shift of paradigms in recent years. While in the past it was our intention to develop classes of materials as 'technology platforms' that would fit a multitude of delivery and formulation problems, we are currently in an era where materials are custom made for specific applications. One reason for this development is definitely that we realized that combining the complexity of a degradable polymer with the variability of classes of drug substances such as proteins does hardly allow formulating a new compound by simply transferring an established process. Another reason is that the degradability of polymers became an indispensable property for new applications of this class of material such as tissue engineering, nucleic acid delivery and materials that are applicable in a minimally invasive way to mention just a few.

### *3.1 Polymers for tissue engineering applications need to allow for cell signaling*

In tissue engineering biodegradable polymers provide a temporal spatial support to cells that are intended to develop a tissue [10]. It is obvious that the cell material interactions play a significant role in this process. This became most obvious, when cells were cultured in the presence of natural polymers that are degradable via enzymatic processes. Materials such as collagen, fibronectin, matrigel or hyaluronic acid and their derivatives turned out to be perfect role models for this concept. As a consequence our view on what we expect from synthetic degradable materials changed accordingly. Besides degradability which remained an indispensable property, it is the specific signaling to cells that plays a major role for this application. Besides shaping physicochemical properties such as surface free energy, zeta potential and others it is especially the attachment of receptor ligands such as peptides containing the RGD motif (which known to bind to receptors of the integrin family) that was recently investigated and developed with increased intensity. That brought materials surface chemistry into focus. Numerous materials with surface grafted pharmacologically active proteins and peptides resulted from this development. Since the resulting materials mimic the extracellular matrix of cells, they were termed biomimetic in the contemporary literature [11].

### *3.2 Polymers for nucleic acid delivery necessitate less toxic materials*

Another application for biodegradable polymers with a tremendous impact on material design that emerged in recent years is nucleic acid delivery. Although the genuine intention was DNA delivery mainly of plasmid DNA with the goal of non-viral gene delivery, the spectrum of applications was broadened in recent years significantly by the discovery of short RNA sequences such as silencing RNA (siRNA) for which currently no ideal delivery vehicle exists. All polymers that have been developed for nucleic acid delivery have in common that they are polycations that interact with nucleic acids via electrostatic forces. The formation of nano- and microparticulate condensates so called polyplexes allows then for cellular uptake of nucleic acids. It has long been known that polycations are toxic and that degradable alternate

materials may provide a solution since such materials would degrade inside the cell to small molecules that would cause less damage. However it was not until recently, that such materials could be developed without loss of efficacy [12]. The reason is most likely due the degradation rates that had to be adjusted to the velocity at which intracellular processes, such as lysosomal escape, move. Hydrolytically cleavable materials were too slow, but when reductively cleavable disulfide cations have been used, their degradation was fast enough for causing no harm.

### *3.3 Hydrogels may increase the ease of application significantly*

Research on another class of biodegradable polymers results from the desire to ease the way of application of a drug delivery system and to provide a more robust chemical environment to sensitive drugs especially proteins and peptides. Hydrogels can serve both purposes. Forming an essentially water insoluble but yet hydrophilic three dimensional network of polymer strands, they form a mesh-like skeleton that incorporates tremendous amounts of water and concomitantly hinders the free diffusion especially of larger molecules. The backbone of hydrogels is formed by either classical cross linking or physical interaction of individual polymer strands via electrostatic interactions. Obviously such systems can be designed in such a way that the cross linking process is initiated upon the application of a viscous precursor solution. Currently major effort is underway to make such systems biodegradable which can for example be achieved by introducing either hydrolytically cleavable bonds or short aminoacid sequences that are prone to enzymatic degradation [13].

### *3.4 Enzymatically degradable polymers can link the degradation rate to a defined biochemical environment*

Enzymatically degradable materials are another more recent development. In this respect it is the intention to shape the polymer in such a way, that it may undergo an enzymatic breakdown in the presence of a specific enzyme [14]. It is obvious that in many diseases, tissues produce a specific set of enzymes that is intended to break down extra cellular matrix. A well known example is arthritis in the course of which matrix metalloproteinases contribute to the damage of cartilage.

### *3.5 Local drug delivery necessitates materials that fit into a specific environment*

A final example that will highlight that our interests in degradable polymers shifted from one fits all to providing individually tailored materials is local drug delivery. One of the currently most vigorously investigated topics in this field is the development of delivery vehicles for the treatment of the posterior eye [15]. While therapeutic antibodies gave new hope to patients suffering from macula degeneration, the best that we have at our hand for the application are aqueous solutions of the proteins. The consequences are like in other cases that the patient has to undergo repetitive treatments. Nevertheless, materials are under way for drug delivery in the eye [16]. However, their development is tricky since the retina is a highly sensitive tissue raising the biocompatibility level for polymer and its degradation products. Furthermore, the eye bulb is a confined compartment with limited capacities of material exchange.

## **4. Summary**

In summary we can conclude that even though we can make excellent use of degradable polymers for the delivery of proteins and peptides, they are by far not trivial materials. In many cases also well characterized polymers pose the problem of insufficient portability of methods when changing from one drug to another. Even though we intuitively think, that degradation like erosion are simple processes during which a material merely vanishes, they are of significant consequences for drug stability and process kinetics. Finally the latest trends in biodegradable polymer design shifts more towards custom making these materials for individual applications.

## **5. Literature**

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## DRUG DELIVERY LITERATURE

Provided by Dr. Martin Bornhöft

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### RECENTLY PUBLISHED LITERATURE REVIEWS IN THE FIELD OF DRUG DELIVERY

#### **Sumatriptan fast-disintegrating/rapid-release tablets in the acute treatment of migraine.**

Barbanti P, Le Pera D, Cruccu G. *Expert Rev Neurother*. 2007 Aug;7(8):927-34.

#### **Improving vaccines by incorporating immunological adjuvants.**

Fraser CK, Diener KR, Brown MP, Hayball JD. *Expert Rev Vaccines*. 2007 Aug;6(4):559-78.

#### **Targeted therapies in small-cell lung cancer.**

Fernainy K, Saba N. *Expert Opin Ther Targets*. 2007 Aug;11(8):1033-41.

#### **Targeted multifunctional lipid-based nanocarriers for image-guided drug delivery.**

Koning GA, Krijger GC. *Anticancer Agents Med Chem*. 2007 Jul;7(4):425-40.

#### **Extended-release formulations in epilepsy.**

Verrotti A, Salladini C, Di Marco G, Piscella F, Chiarelli F. *J Child Neurol*. 2007 Apr;22(4):419-26.

#### **Targeted pharmaceutical nanocarriers for cancer therapy and imaging.**

Torchilin VP. *AAPS J*. 2007 May 11;9(2):E128-47.

#### **Targeted delivery systems of small interfering RNA by systemic administration.**

Kawakami S, Hashida M. *Drug Metab Pharmacokinet*. 2007 Jun;22(3):142-51.

#### **Novel enhanced delivery taxanes: an update.**

Perez EA. *Semin Oncol*. 2007 Jun;34(3):suppl 1-5.

#### **Extended-release formulation of venlafaxine in the treatment of post-traumatic stress disorder.**

Pae CU, Lim HK, Ajwani N, Lee C, Patkar AA. *Expert Rev Neurother*. 2007 Jun;7(6):603-15.

#### **Matrices and scaffolds for protein delivery in tissue engineering.**

Tessmar JK, Göpferich AM. *Adv Drug Deliv Rev*. 2007 May 30;59(4-5):274-91. Epub 2007 May 3.

#### **Polymer carriers for drug delivery in tissue engineering.**

Sokolsky-Papkov M, Agashi K, Olaye A, Shakesheff K, Domb AJ. *Adv Drug Deliv Rev*. 2007 May 30;59(4-5):187-206. Epub 2007 Apr 27.

#### **Ocular drug delivery: molecules, cells, and genes.**

Liu X, Brandt CR, Rasmussen CA, Kaufman PL. *Can J Ophthalmol*. 2007 Jun;42(3):447-54.

#### **Design of fine particles for pulmonary drug delivery.**

Weers JG, Tarara TE, Clark AR. *Expert Opin Drug Deliv*. 2007 May;4(3):297-313.

#### **Drug delivery via nano-, micro and macroporous coronary stent surfaces.**

Tsujino I, Ako J, Honda Y, Fitzgerald PJ. *Expert Opin Drug Deliv*. 2007 May;4(3):287-95.

**The promise of chitosan microspheres in drug delivery systems.**

Varshosaz J. Expert Opin Drug Deliv. 2007 May;4(3):263-73.

**Programmed drug delivery: nanosystems for tumor targeting.**

Wagner E. Expert Opin Biol Ther. 2007 May;7(5):587-93.

**Iontophoretic drug delivery system: focus on fentanyl.**

Herndon CM. Pharmacotherapy. 2007 May;27(5):745-54.

**Microsponge delivery system.**

Chadawar V, Shaji J. Curr Drug Deliv. 2007 Apr;4(2):123-9.

**pH-sensitive liposomes - principle and application in cancer therapy.**

Karanth H, Murthy RS. J Pharm Pharmacol. 2007 Apr;59(4):469-83.

**Polysaccharide hydrogels for modified release formulations.**

Coviello T, Matricardi P, Marianecci C, Alhaique F. J Control Release. 2007 May 14;119(1):5-24. Epub 2007 Jan 19.

**Gene delivery by cationic lipid vectors: overcoming cellular barriers.**

Zuhorn IS, Engberts JB, Hoekstra D. Eur Biophys J. 2007 Apr;36(4-5):349-62. Epub 2006 Sep 22.

**Nifedipine Gastrointestinal Therapeutic System (GITS) in the treatment of coronary heart disease and hypertension.**

Kragten JA, Dunselman PH. Expert Rev Cardiovasc Ther. 2007 Jul;5(4):643-53.

**Functionalized micellar systems for cancer targeted drug delivery.**

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The APV Drug Delivery Focus Group (APV DD) is a section of the APV (Arbeitsgemeinschaft für Pharmazeutische Verfahrenstechnik e.V. / International Association for Pharmaceutical Technology), a major European society for those sharing a professional interest in pharmaceutical sciences. The Focus Group was established in 2003 in response to the increasing importance of drug delivery within modern pharmaceuticals. [Read more...](#) [Contact us...](#)

**COMBINING SCIENCE AND TECHNOLOGY TO CREATE ADVANCED DRUG DELIVERY SYSTEMS**

**OUR MISSION STATEMENT:**

Modern drug delivery research and development is a truly multidisciplinary approach and must combine all relevant scientific, technical, medical and regulatory aspects required for the design, preparation, testing, manufacturing and registration of drug delivery systems and their components. It is the mission of the APV Drug Delivery Working Group to foster and promote all aspects of research and development required to transform drug molecules into safe, applicable and acceptable drug delivery systems, which provide therapeutic benefit, convenience to the patient and improve patient compliance.

**Our mission includes in particular the following tasks:**

- Thoroughly understanding the physical-chemical and biopharmaceutical properties of the drug substance to be delivered and the components of the drug delivery system
- Understanding the biological barriers and the interactions of the drug molecule and its delivery system with the biological environment and the biological target including PK/PD and PK/safety relationships
- Research on excipients, materials and technologies required for the design, preparation and manufacturing of drug delivery systems for a selected route of administration
- Development and understanding of methods for in vitro and in vivo evaluation of drug delivery systems and their components
- Knowledge of regulatory requirements for clinical testing, manufacturing and registration of drug delivery systems

All disciplines relevant to the above mentioned areas of drug delivery R&D are invited to contribute to the APV Drug Delivery Group:

**Pharmaceutics, Biopharmaceutics, Analytics, Biology, Physical Chemistry, Biochemistry, Physics, Engineering Sciences, Nano Technology, Material Sciences, Polymer Science, Toxicology, Drug Safety, Clinical Research, Drug Regulatory Affairs, etc.** [Read more...](#)

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