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# Controlled Release Society Annual Meeting Report: Dissolution Highlights

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The 2005 Annual Meeting of the Controlled Release Society (CRS) took place in Miami, Florida, USA, on June 18-22. The presentations this year, as in recent years, were varied and useful. Several offered new strategies and developments in the field of *in vitro* release/dissolution testing.

A highlight for attendees interested in the development and *in vitro* characterization of formulations with modified drug release was the "Colon Targeting for Local and Systemic Action" workshop.

The Saturday session of the workshop was co-chaired by CRS President (2004-2005) **Professors Jennifer B. Dressman, of the University of Frankfurt, Germany**, and **Clive Wilson of the University of Strathclyde, United Kingdom**. Prof. Wilson also opened the morning session. In his presentation "Physiological Opportunities for and Challenges to Colonic Delivery", Professor Wilson gave an overview of the colonic anatomy and physiology in health and disease. He highlighted various physicochemical parameters to drug release and absorption in the colon and reviewed common pitfalls in designing delivery systems for targeted drug delivery to/in the colon. He pointed out that based on the knowledge on colonic transit times, pH, mixing and dispersion of particles in the colonic lumen, particularly the intra- and interindividual variability of these parameters is a challenge for the design and evaluation of future colon-delivery systems.

The next speaker was **Dr. Oliver Schroeder, of the University of Frankfurt, Germany**. His talk "Colonic Diseases and Physiological Targets" focused on the etiology and pathogenesis of inflammatory bowel diseases (IBD) that currently present the main target for colon delivery systems containing local acting drugs. He explained that IBD can present very similarly in terms of clinical symptoms but their inflammation patterns are distributed differently in the gastrointestinal (GI) tract. Colonic drug delivery systems therefore should be selected on an individual basis.

The topics of the talks that followed were the different colon delivery concepts that are available today. **Professor Andrea Gazzaniga from the University of Milan, Italy** presented "Time-Controlled Systems for Colonic Delivery." He pointed out that most of the preclinical formulations are highly sophisticated systems and therefore difficult to scale up. In describing the development of Chronotopic™ he highlighted the importance of process parameters on both the *in vivo* and *in vitro* performance of the formulation. He also mentioned that adequate *in vitro* test parameters are essential to select the optimal formulation for *in vivo* studies and to distinguish between different product qualities.

**Dr. Brigitte Skalsky from Degussa Pharma Polymers, Germany** introduced a new formulation representing "A Combination of pH- and Time-controlled Release for Drug Delivery to the Colon." She gave an overview of dosage form development and drug release mechanism. She also presented *in vitro* data that could be verified in a subsequent proof of principle study performed in healthy volunteers. Based on these data, she concluded that the formulation is very promising for time controlled drug release in the proximal colon.

**Professor Avri Rubinstein of the Hebrew University of Jerusalem, Israel,** one of the pioneers in colonic drug delivery, talked about "Colonic Mucosa Targets: Therapeutic and Oral Delivery Contemplation." He explained historical and new types of colonic drug delivery systems used for the treatment of IBD and colorectal cancer (CRC). Further, he presented case examples of dosage forms with drug release triggered by the gastrointestinal milieu; for example enzymes and bacteria. For the treatment of IBD and CRC, he stated that "arrival at the colon is only the beginning of the journey." It is followed by the attempt to adequately target the specific site in the colonic epithelium.

**Dr. Abdul Basit, of the University of London, United Kingdom,** gave an overview of "Enzymatic Approaches to Selectively Deliver Drugs to the Colon." He presented *in vitro* and *in vivo* results from alpha-amylose-ethylcellulose-coated colonic delivery systems. As drug release of these types of formulations is initiated by amylase degradation by the colonic microflora, bacterial activity in the colon is a parameter that has to be addressed in the *in vitro* test system. Since the species and number of bacteria in the proximal colon underlies a huge intra- and inter-individual variability, it became obvious that the design of an optimal test system is very difficult.

Following Dr. Basit's talk, **Cassie Mahanes from Procter & Gamble Pharmaceuticals, USA,** presented the "Formulation and Development and Scale-up of Colon Targeted Systems" by means of a case example of an enteric coated single unit dosage form.

**Professor Jennifer B. Dressman** concluded the first day of the workshop with her presentation titled "*In vitro* Release Tests – Can We Predict Behavior in the GI Tract?" She first gave an overview of the physiological parameters that can affect drug release from colon delivery system during their passage through the GI tract and then discussed which dissolution test systems can be used to reflect these changing GI conditions. In her talk she emphasized the advantages of USP Apparatus 3 (BioDis™). This setup offers multiple advantages, such as using a gradient of media to simulate the passage through different sections in the GI tract and varying hydrodynamic conditions and residence

times in different media to simulate motility patterns and passage times in fasted and fed states. Prof. Dressman presented case studies involving simple pH gradient methods as well as sophisticated gradients using biorelevant test media. She concluded that the USP Apparatus 3 combined with appropriate test media is a convenient and discriminating method for comparing the drug release behavior from site specific dosage forms containing drugs for either local or systemic action. However, she emphasized that it is very important to address intra- and inter-individual variability in the test system and that it is also important to determine the robustness of the release profile, in other words, the influence of different gastric residence times on drug release in more distal parts of the small intestine.

**Dr. Ian Wilding, of Pharmaceutical Profiles, United Kingdom,** was the first speaker of the Sunday morning session. His talk was entitled "Using Scintigraphy to Visualize the *in vivo* Targeting Properties of Colonic Delivery Systems". He described how to perform pharmacoscintigraphic studies and presented several case examples where pharmacoscintigraphy was successfully applied in dosage form design and evaluation.

**Professor Werner Weitschies, of the University of Greifswald, Germany,** gave a presentation titled "Magnetic Moment Imaging to Track Dosage Form Progress Through the GI Tract". He explained how to perform Magnetic Moment Imaging studies and impressed the auditorium with various real time and fast motion video demonstrations showing how a dosage form passes through the GI tract.

**Dr. Gunther Hochhaus, of the University of Florida, USA,** gave a talk titled "Pharmacokinetic Evaluation of Dosage Forms for Colonic Delivery" in which he presented results from traditional PK studies but also introduced alternative techniques to determine and evaluate drug release in different sections of the GI tract. He concluded that in addition to scintigraphic studies, PK studies are essential for the characterization of formulations for local and systemic drug delivery.

**Dr. Oliver Schroeder** gave a second talk, in which he introduced "Clinical Endpoints to Assess Efficacy of Targeting Approaches." Before the workshop ended with a panel discussion, **Professor Jennifer B. Dressman** gave an overview, where she highlighted the importance of fitting drug release profiles of site-specific release systems to the chronopathology. She ended her presentation with an outlook on optimized oral vaccination products and summarized that for an optimal colon delivery system, the drug has not only to be released but moreover to be absorbed in the colon.

During the two workshop days, the participants received a detailed update on the state of the art in dosage form design and *in vitro*/*in vivo* evaluation. However, speakers and participants agreed that the tip of the iceberg is just been shown and that considering intra- and interindividual variability of physiological GI parameters is crucial in both the design and characterization of colon specific delivery systems.