

Report on EuroCD European Cyclodextrin Conference

Oct. 6-9, 2015, Lille

The conference organized by the French Cyclodextrin Society, Bernard Martel, Sophie Fourmentin and Eric Monflier was a significant event with 170 participants from 4 continents. The 9 invited, 37 oral, 18 flash presentations and 66 posters covered various fields of cyclodextrin research and applications. Most of the presentations, however, focused on pharmaceutical applications.

There were a few on the antibiotic drug delivery.

CyclonHit presentations:

Penicillins were successfully stabilized by positively charged CD derivatives which form complexes of 10-fold enhanced association constants compared to the uncharged CDs suggesting that the electrostatic interactions contribute to the stabilization¹. On the other hand, the anionic EDTA-type CDs having chelating properties toward metal cations were found to be able to inhibit metallo- β -lactamases, the enzymes responsible for antibiotic resistance of Gram-negative bacteria². In vitro studies proved that these EDTA-type CDs significantly enhanced antimicrobial activity of the antibiotic Imipenem against metallo- β -lactamase-producing *K. pneumonia*. The poster won the **Best Poster Prize**.

Fluorescent labeled CD derivatives substituted with xanthene dyes useful for the delivery of antibiotics were prepared³. A bichromophoric BCD derivative bearing a nitroaniline moiety as a nitric oxide (NO) donor and an anthracene moiety as a fluorescence label was presented in a flash presentation⁴.

Monosubstituted cationic cyclodextrins were prepared and labeled with rhodamine B or fluorescein⁵. Their complex forming ability was studied using acridine orange, a fluorescent dye using capillary electrophoresis. The skin penetration was proved by two photon confocal microscopy.

Further, non-CyclonHit presentations related to antibiotic delivery

Antibacterial hydroxyapatite/chitosan/CD polymer spongy hybrid was prepared for bone regeneration⁶. The hydrogel was obtained by self-association of chitosan and CD polymer crosslinked by citric acid in the presence of hydroxyapatite and impregnated with Ciprofloxacin, as model antibiotic. Enhancing the CDP content in the hydrogel resulted in decreased swelling and faster rate of drug release. The antibacterial activity was confirmed on *E. coli* and *S. aureus*.

Nanofibers with antibacterial properties were fabricated by electrospinning inclusion complexes of hydroxypropyl-beta-cyclodextrin (HPBCD), hydroxypropyl-gamma-cyclodextrin (HPGCD) and methylated-beta-cyclodextrin (MeBCD) with natural antibiotics: geraniol, limonene and linalool without using polymer matrix⁷.

A hot-melt extrusion process was demonstrated in flash presentation awarded by the **Best Flash Presentation prize**. Itraconazole/HPBCD system was used to study the efficiency of the technology⁸. Granulate-like, amorphous product was obtained.

Nanofibers were produced by electrospinning ACD- and BCD-epichlorohydrin polymer using poly(ϵ -caprolactone) or poly(N-vinylpyrrolidone) matrices and Fluconazole as antifungal drug⁹. Good thermal stability and sustained drug release characterized the nanofiber formulation.

The mixture of antibacterial agent Triclosan with chitosan itself and blended with HPBCD or CD polymer crosslinked with citric acid were also transferred to nanofibers by electrospinning to obtain drug delivery systems with high surface area and porosity¹⁰.

HPBCD and MeBCD were used to prepare Cefixime complex in order to improve its poor (40%) oral bioavailability. The HPBCD complex prepared by kneading showed enhanced solubility and permeability¹¹.

Textiles were modified with multilayer CD polyelectrolites (citric acid-CD polymer and quaternary amino CD polymer) using Layer-by-Layer technique to obtain textiles with antibacterial properties to be applied as wound coatings, prostheses etc¹². Sustained release of three model drugs such as tert-butyl benzoic acid, methylene blue and Triclosan was presented.

References

- ¹ **Marco Agnes**, Angelos Thanassoulas, Polychronis Stavropoulos, George Nounesis, **George Miliotis**, **Vivi Miriagou**, **Konstantina Yannakopoulou**: Enhancement of cyclodextrin-penicillin complexation through designed host-guest interactions. Abstract Book FP10
- ² **Georgios Miliotis**, Maria Lampropoulou, Marco Agnes, Stathis D. Kotsakis, Leonidas S. Tzouvelekis, **Konstantina Yannakopoulou**, **Vivi Miragou**: Polycarboxylated EDTA-type Cyclodextrins as inhibitors for metallo-beta-lactamases produced by Gram-negative pathogens. Abstract Book P38
- ³ Mihaly Balint, **Milo Malanga**, Tamas Sohajda, **Gabor Benkovics**: New Synthetic Strategies for Xanthene Dye-Appended Cyclodextrins. Abstract Book P20
- ⁴ **Gabor Benkovics**, **Milo Malanga**, **Eva Fenyvesi**, **Salvatore. Sortino**: Fluorescent cyclodextrins as photoactivable nanoplatfoms. Abstract Book FP5
- ⁵ **Milo Malanga**, **Gabor Benkovics**, Tamas Sohajda, **Hanna Thomsen**, **Marica B. Ericson**, **Éva Fenyvesi**: Synthesis and Characterization of Cationic Cyclodextrins and their Use as Skin Penetration Enhancer. Abstract Book O26
- ⁶ Claudia Flores, Jean Christophe Hornez, Feng Chai, Gwenael Raoul, Nicolas Tabary, Frédéric Cazaux, Joel Ferri, Hartmut F. Hildebrand, Bernard Martel, Nicolas Blanchemain: Cross linking reaction between chitosan and poly-CTR cyclodextrine for the formation of a hybrid material for bone regeneration. Abstract Book O4
- ⁷ Fatma Kayaci, Zeynep Aytac, Tamer Uyar: Electrospun Nanofibers from Flavor/Fragrance-Cyclodextrin-Inclusion Complexes. Abstract Book O29
- ⁸ Annika Heel, Hartwig Steckel: Development of Hot-Melt Extrusion Process with β -Cyclodextrin and Itraconazole for Inclusion Complex Formation – A First Approach. Abstract Book FP2

⁹ Alejandro Costoya, Florencia Montini Ballarin, Gustavo Abraham, Carmen Alvarez-Lorenzo, Angel Concheiro: Polycyclodextrin electrospun fibers for antifungal treatment. Abstract Book P36

¹⁰ Safa Ouerghemmi, Stéphanie Degoutin, Nicolas Tabary, Frédéric Cazaux, Ludovic Janus, F. Chai, Nicolas Blanchemain and Bernard Martel: Electrospun cyclodextrin functionalised chitosan nanofibres for triclosan release. Abstract Book O31

¹¹ Nurten Celen¹, Naile Ozturk¹, Erem Bilensoy¹, Sema Calis: Cefixime oral bioavailability improved by cyclodextrin inclusion complex: In vitro - in vivo evaluation. Abstract Book P63

¹² Jatupol Junthip, Nicolas Tabary, Bernard Martel, Nicolas Blanchemain, Feng Chai, Alain Hedoux, David Landy, Laurent Leclercq: Dual cyclodextrin polyelectrolyte multilayer coatings on textile for controlled drug delivery. Abstract Book O15