



# Epichlorohydrin-crosslinked Cyclodextrin Polymers for Drug Delivery

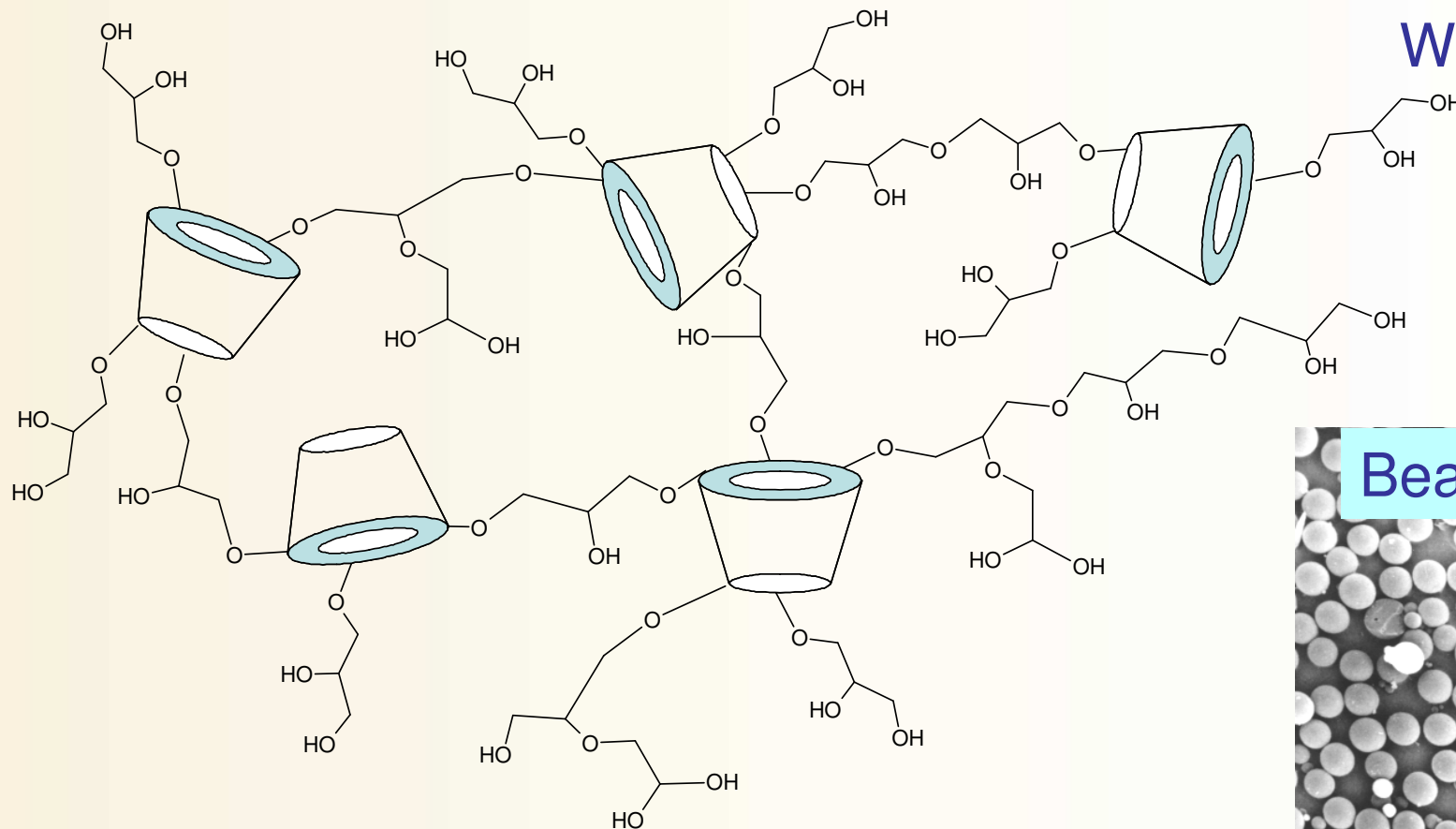
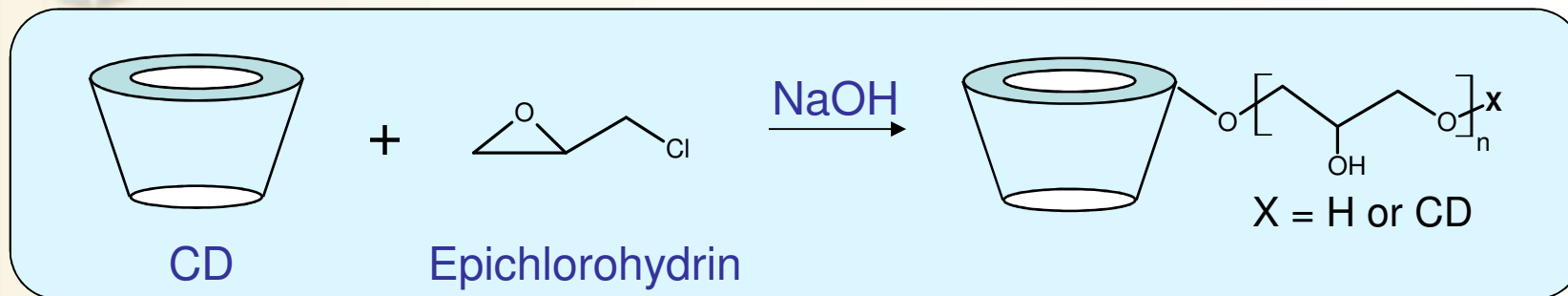
Éva Fenyvesi, M. Malanga, I. Puskás, K. Csabai,  
G. Benkovics & Lajos Szente

*CycloLab, Budapest*

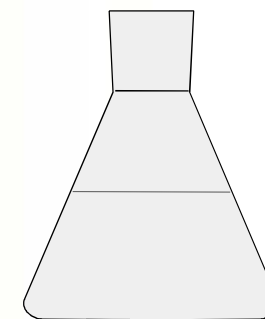


The Cyclodextrin Company

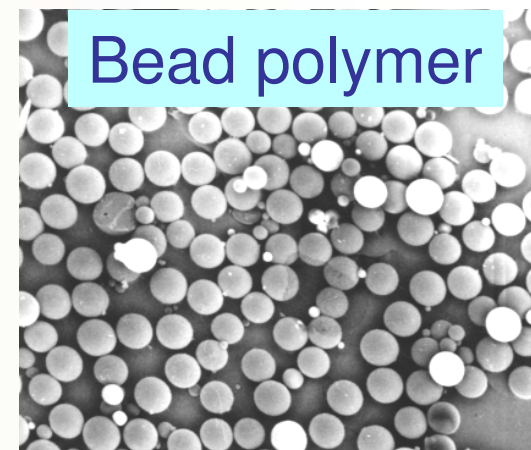
# Crosslinking with epichlorohydrin



Water-soluble

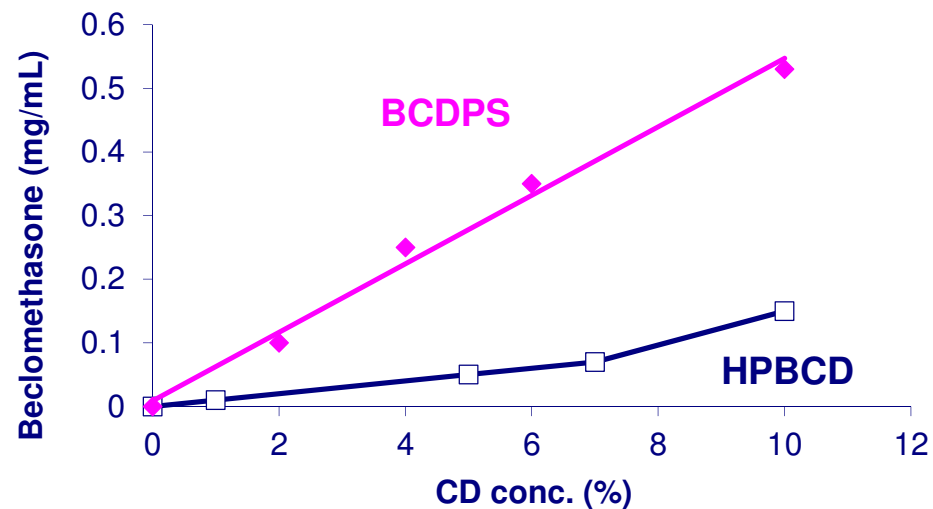
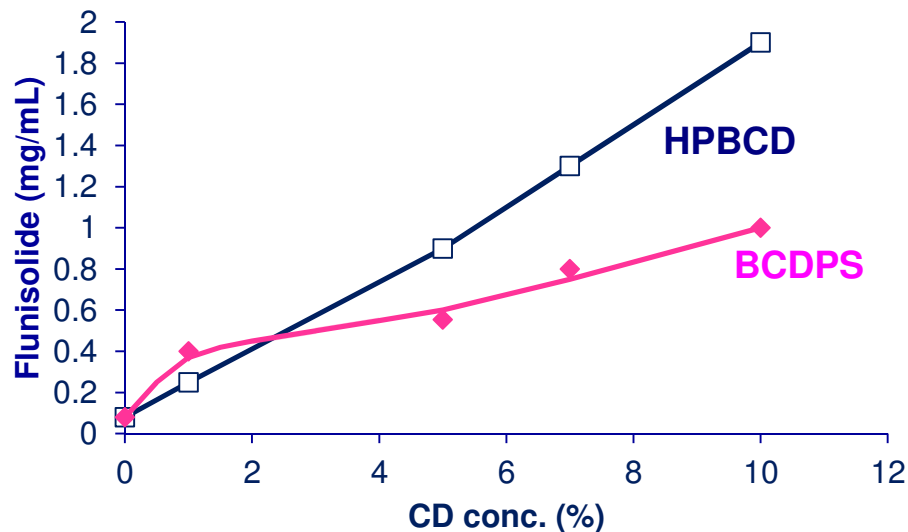


Bead polymer

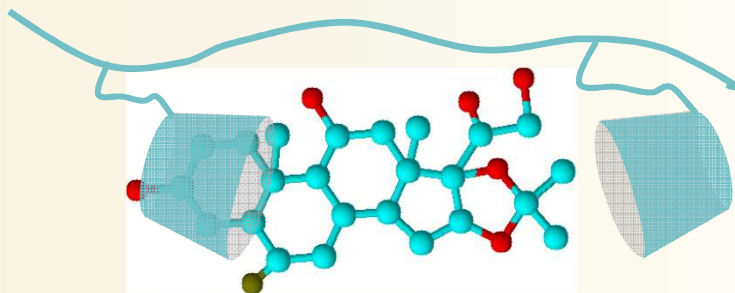




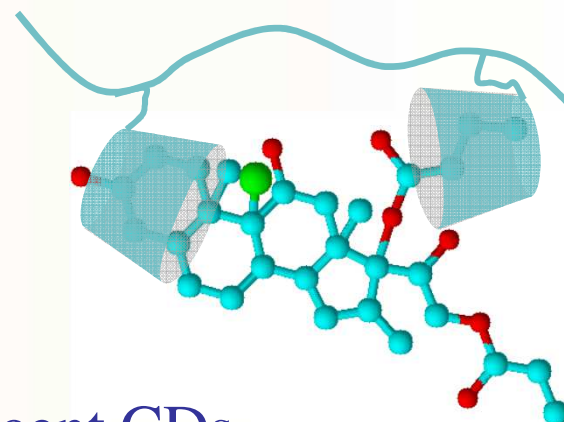
# Enhancement of solubility



CD : Flunisolide 1:1



CD : Beclomethasone 2:1

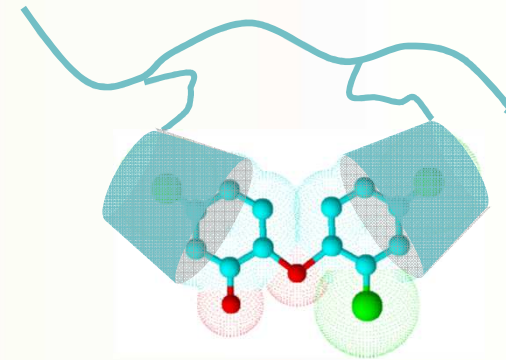
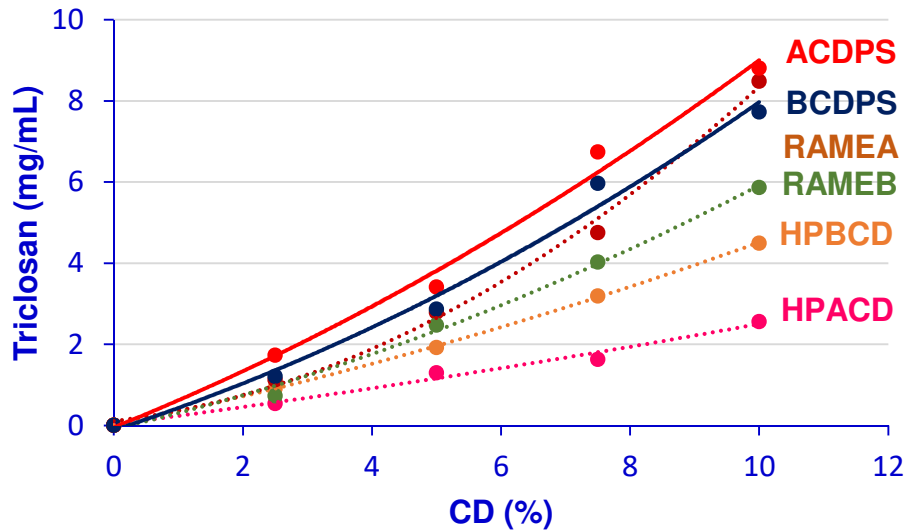


Cooperative action of the adjacent CDs



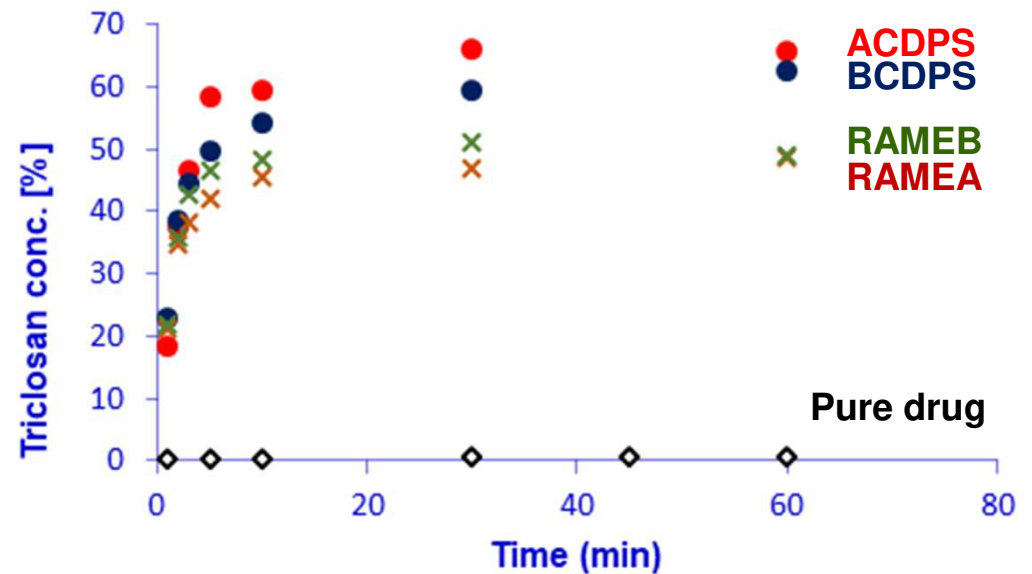
# Enhancement of solubility and dissolution

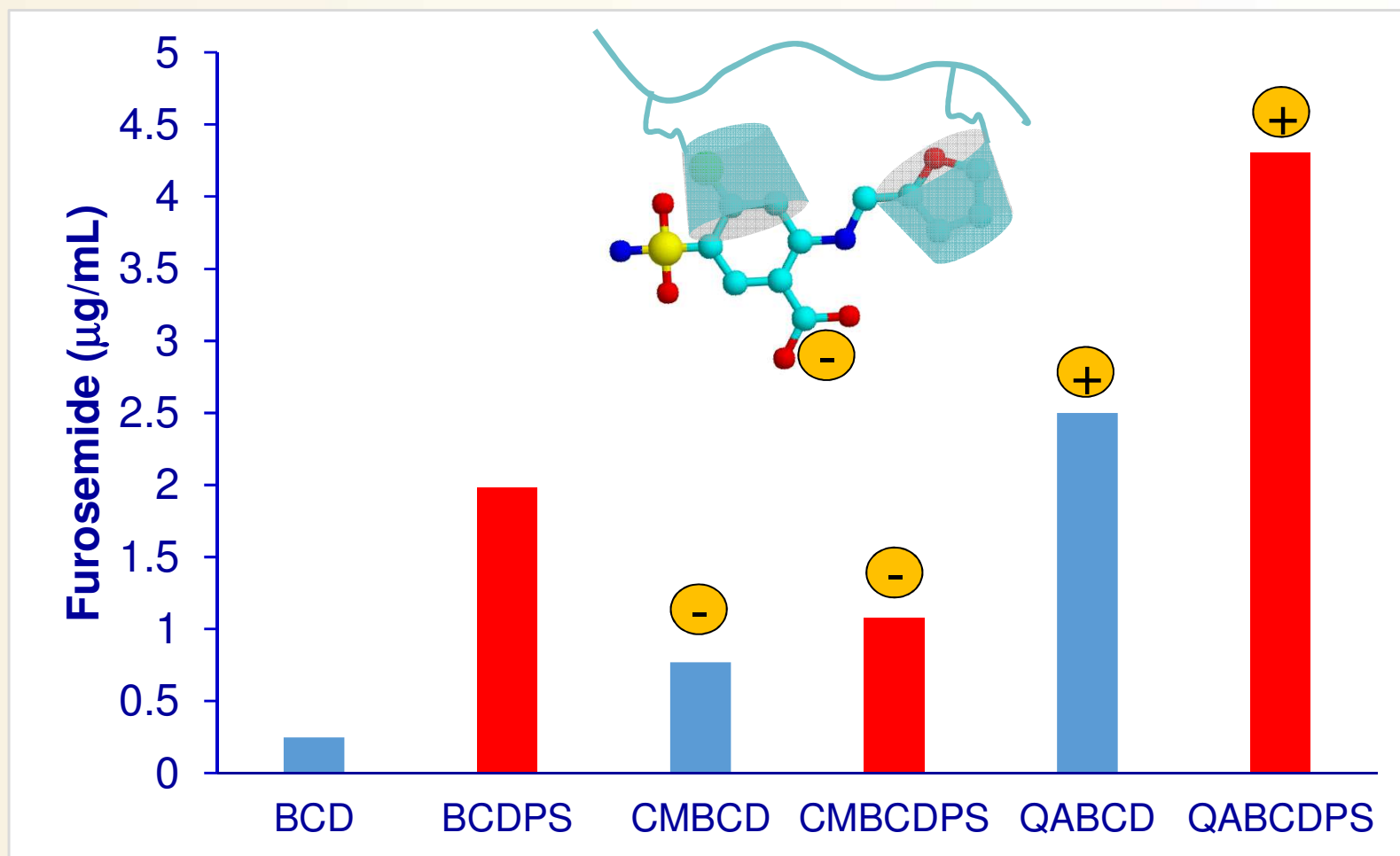
The Cyclodextrin Company



## Release profiles

Phase-solubility curves at r.t.

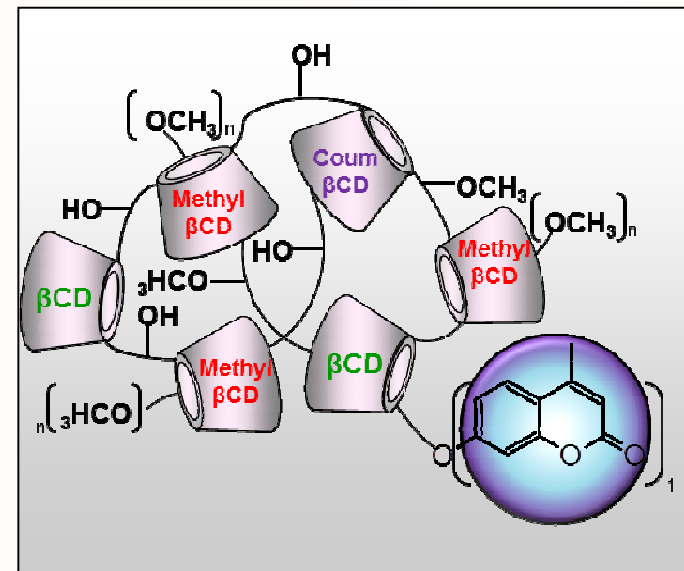
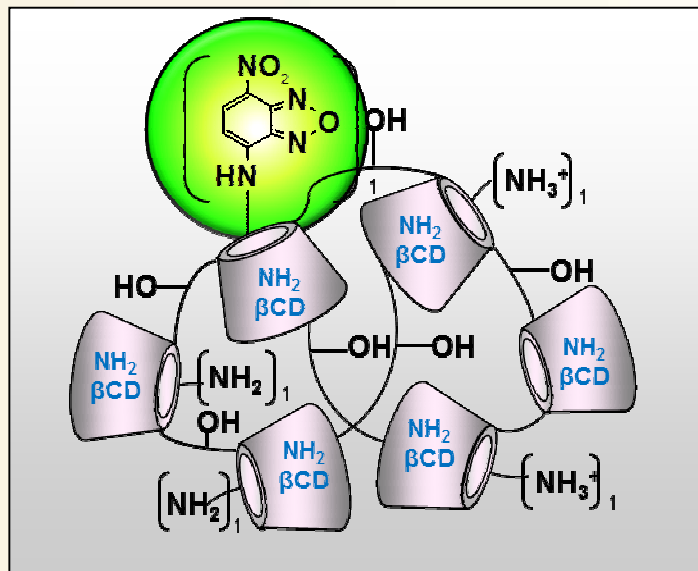
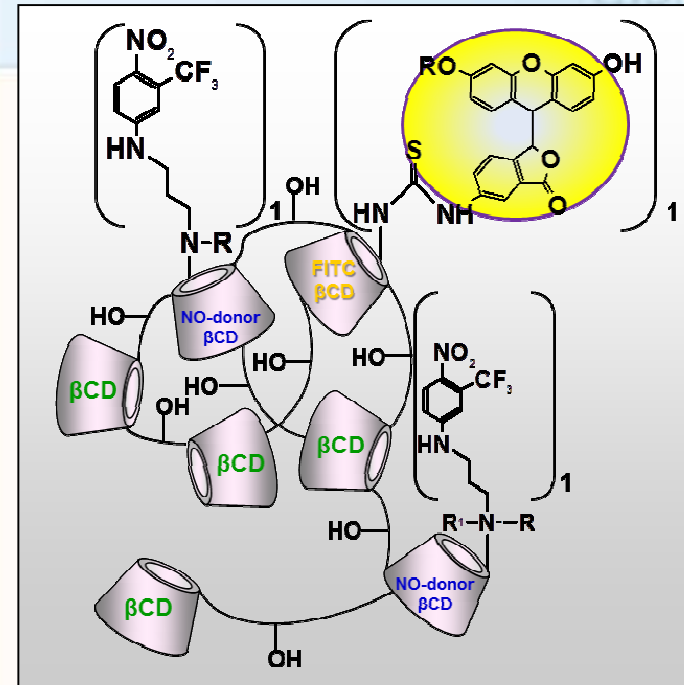
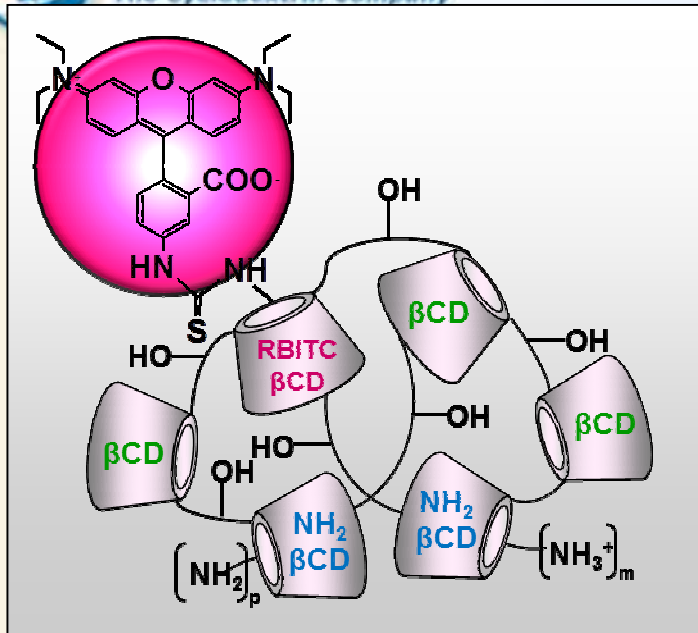




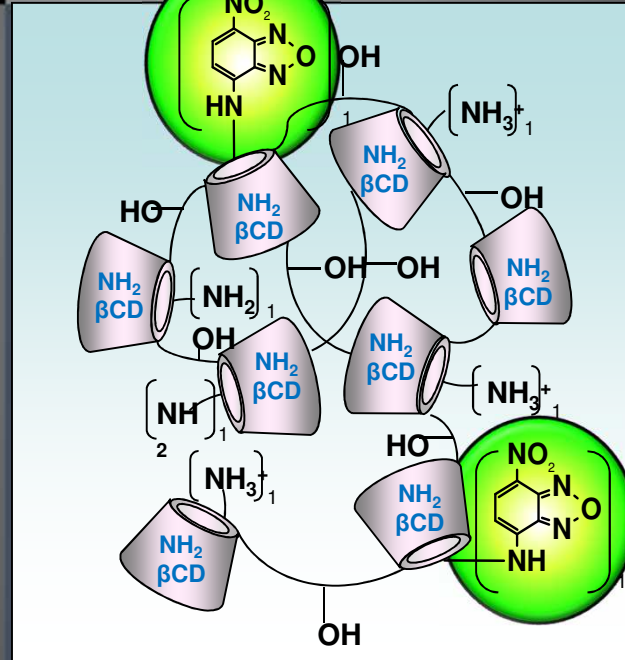
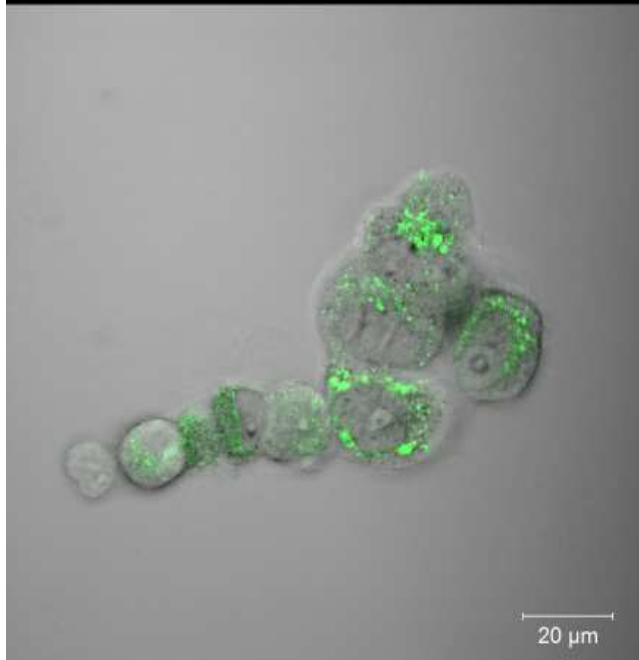
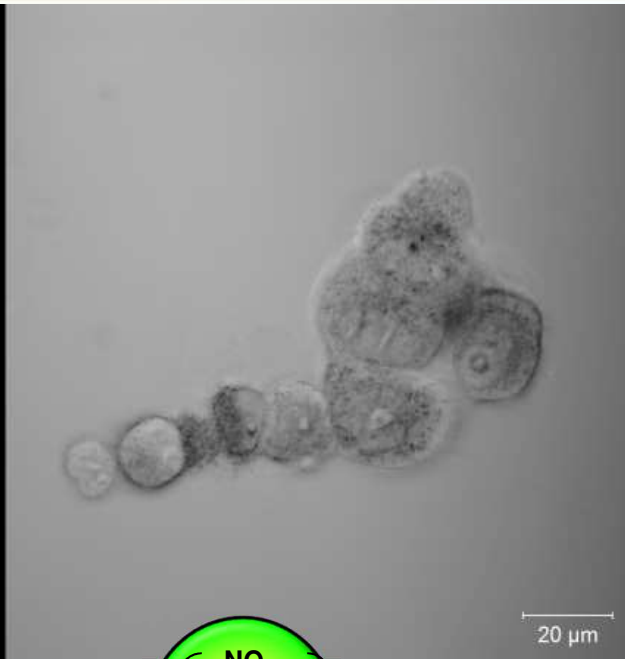
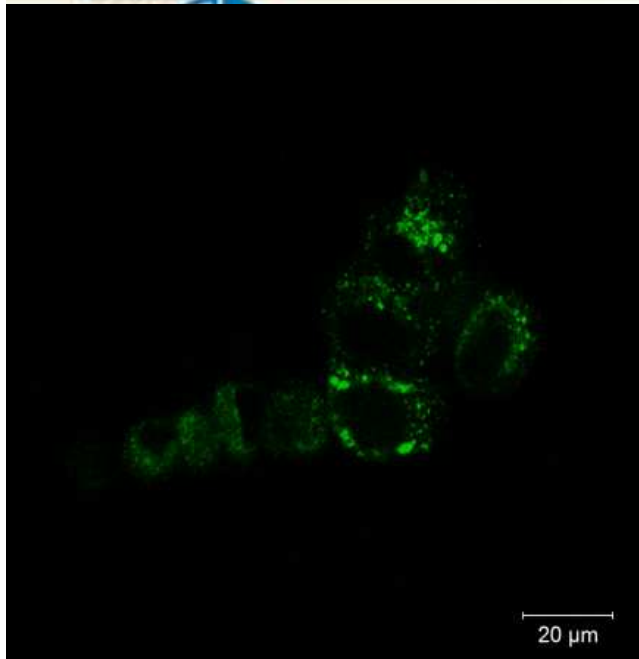
Solubility of Furosemide in CD solutions (5%)  
 CM = carboxymethyl, QA = quaternary ammonium



# Derivatization of CD polymers



# Enhanced cell penetration



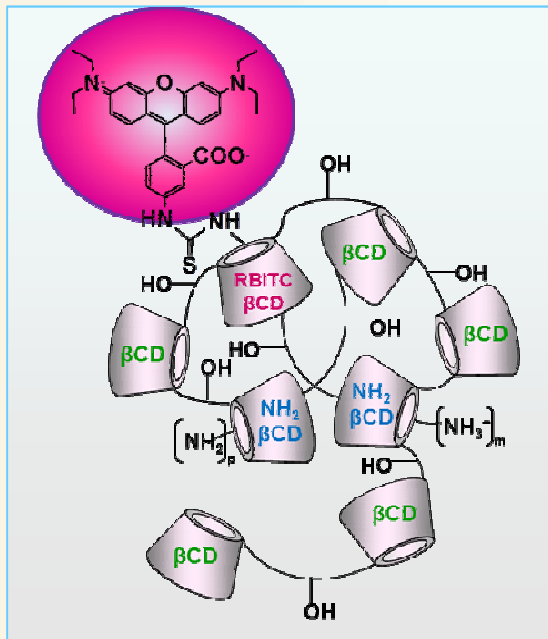
- Cell targeting with  $\text{NH}_2$
- human squamos carcinoma cells (A 431)
- Imaging
- Anticancer drugs delivery

*Unpublished results  
in cooperation with groups  
M. Ericson and S. Sortino*

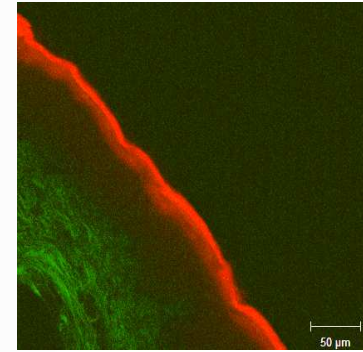
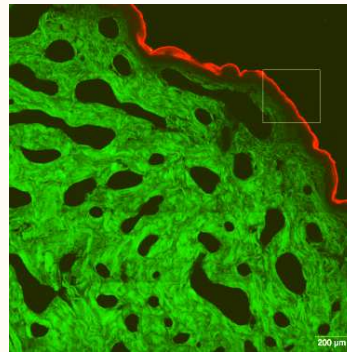


Targeting with  $\text{NH}_2$  function

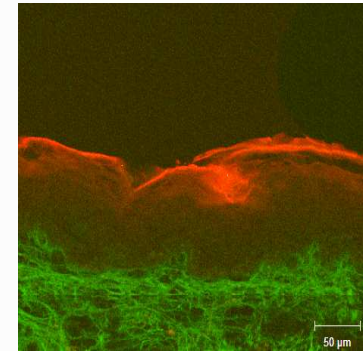
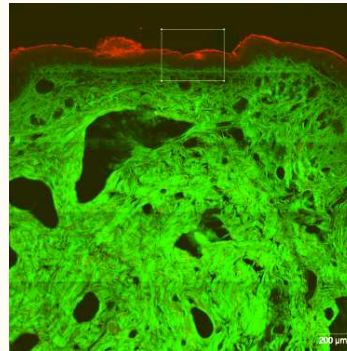
Imaging through fluorescent substituents (rhodamine-B, RBITC)



RBITC in MiliQ



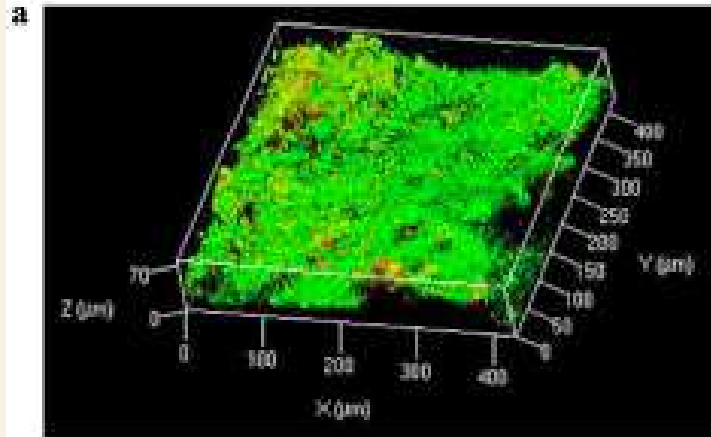
BCDPS-RBITC in  
MiliQ



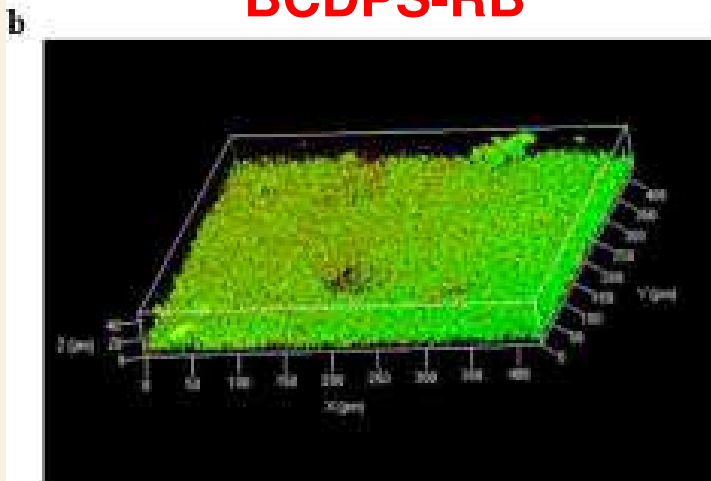
Two-photon microscopy of  
cryosections of human skin

Topical delivery with  $\beta$ -cyclodextrin polymer labeled with Rhodamine B  
(in cooperation with group of M. Ericson)

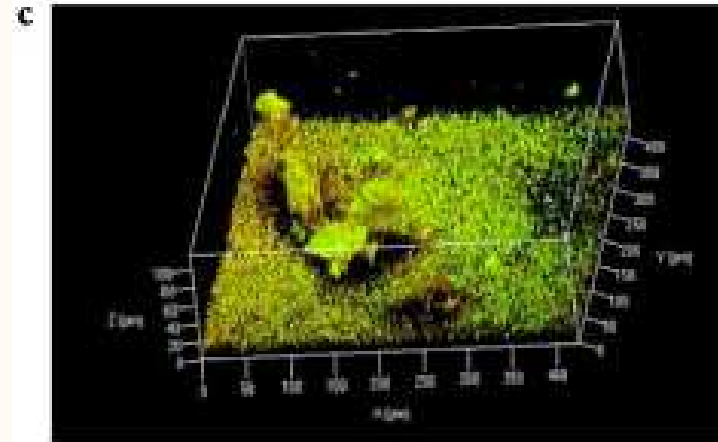




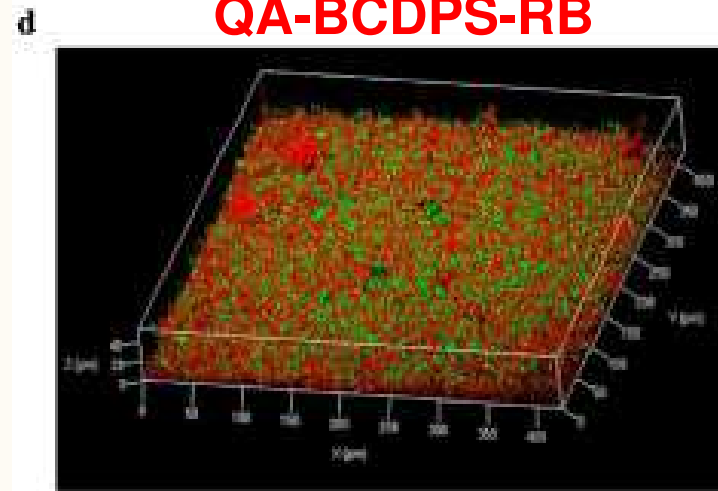
**BCDPS-RB**



**CM-BCDPS-RB**



**QA-BCDPS-RB**



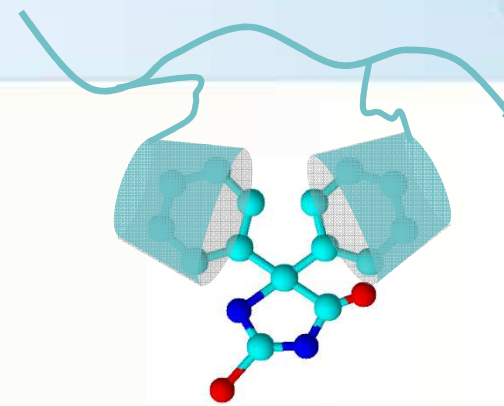
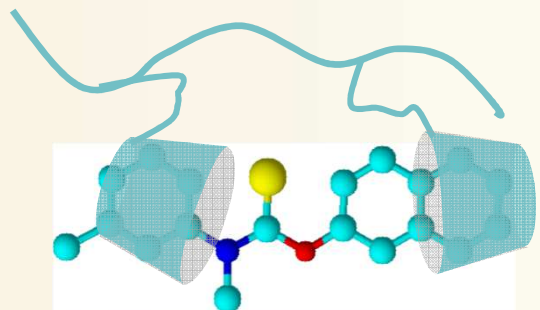
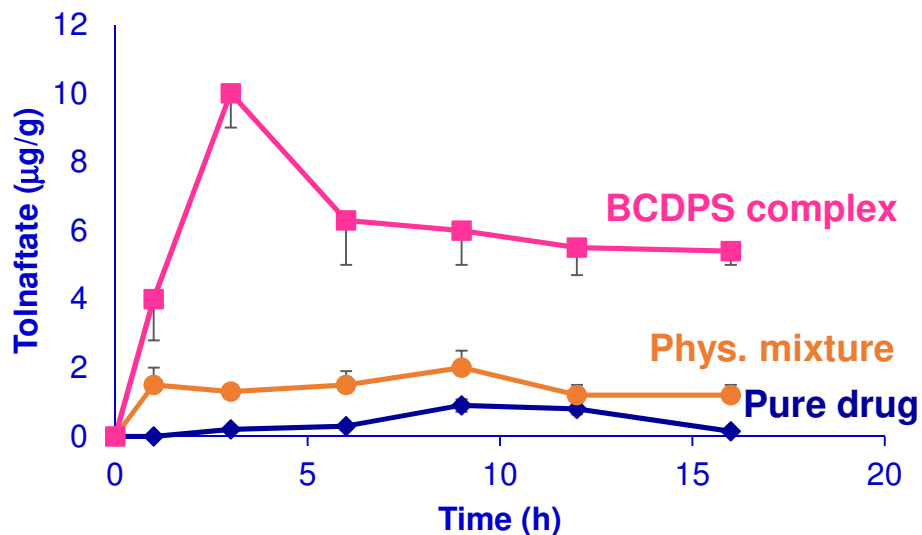
$\beta$ -cyclodextrin polymer labeled with Rhodamine B on *Staphylococcus epidermis* biofilm  
(in cooperation with group of M. Ericson,  
Thomsen et al. *Int. J. Pharm.*, 2017)



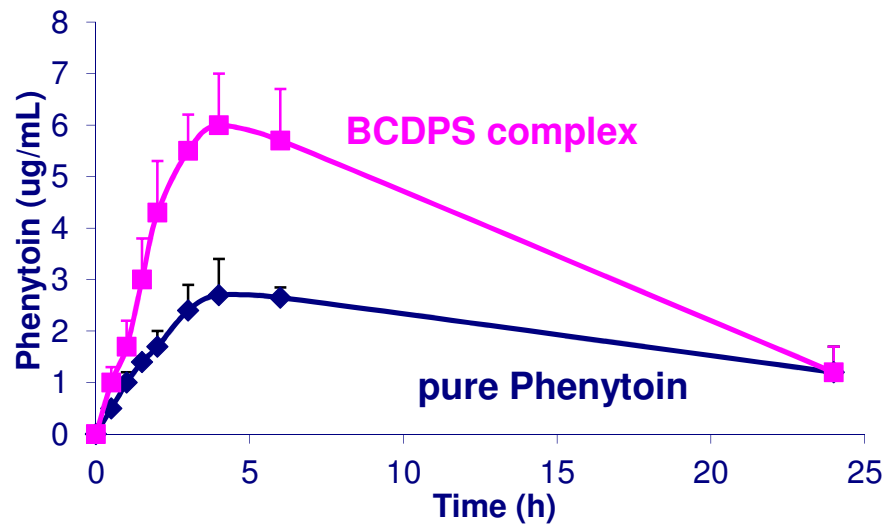
# Enhanced bioavailability

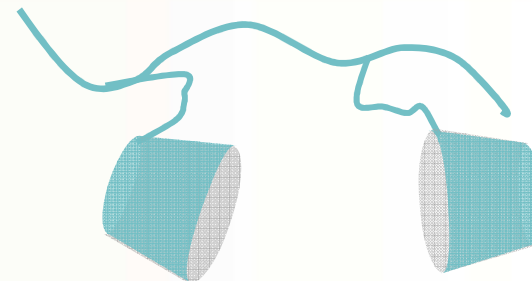


Skin concentration of Tolnaftate after topical administration to mice



Plasma level of Phenytoin after oral administration to dogs





Water soluble polymers with epichlorohydrin:

- ❖ High solubility and solubilizing potential
- ❖ Cooperativity of the CD rings
- ❖ Ionic substituents to add ionic interactions and for targeting
- ❖ Fluorescent substituents for imaging
- ❖ Enhancing the bioavailability of included drugs



# Acknowledgement



**Univ. Gothenburg**



**Univ. Catania**

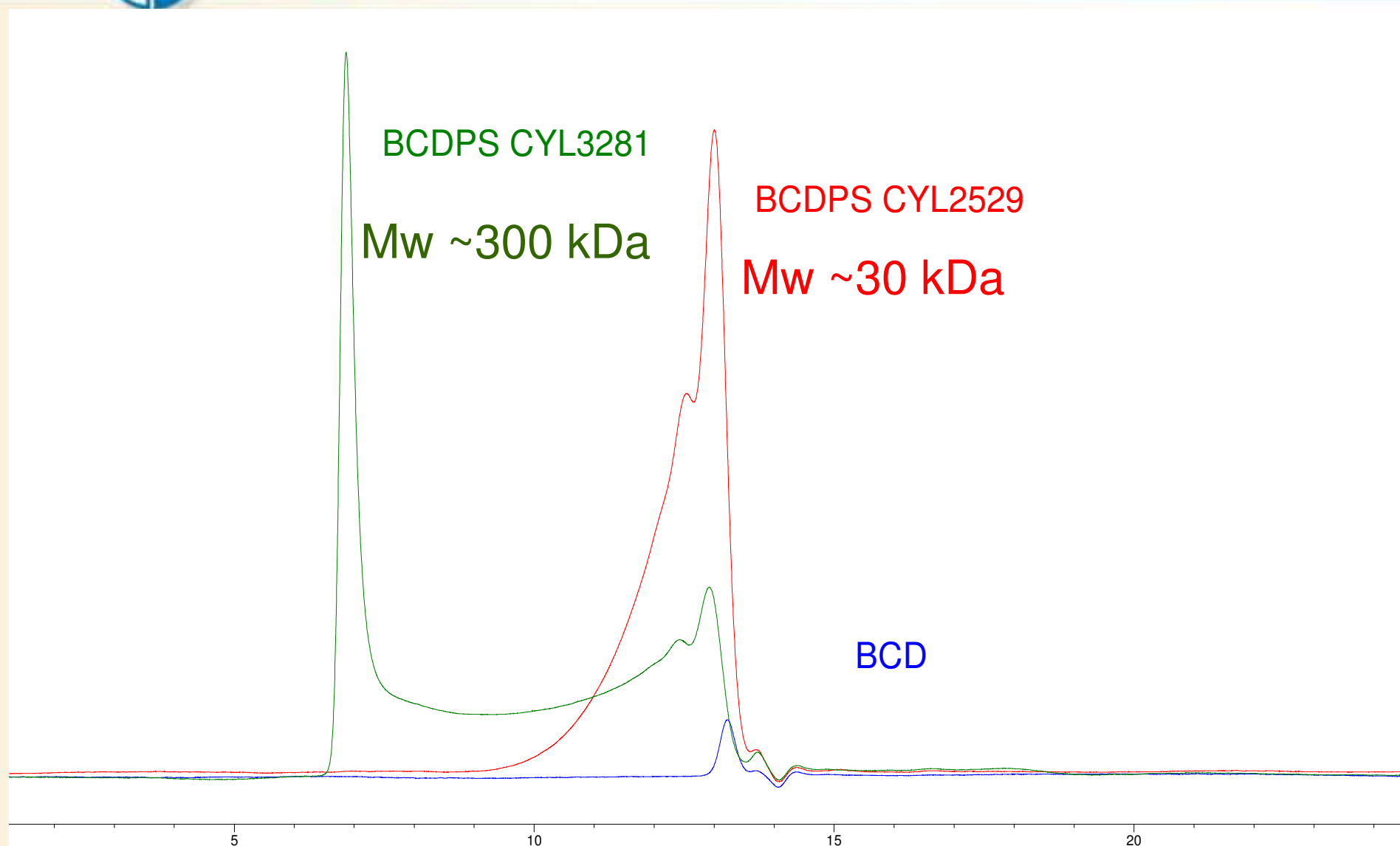
## **EU grants**

CYCLON (EU Marie Curie ITN-2008 237962)

CyclonHit (EU Marie Curie ITN-2013 608407)



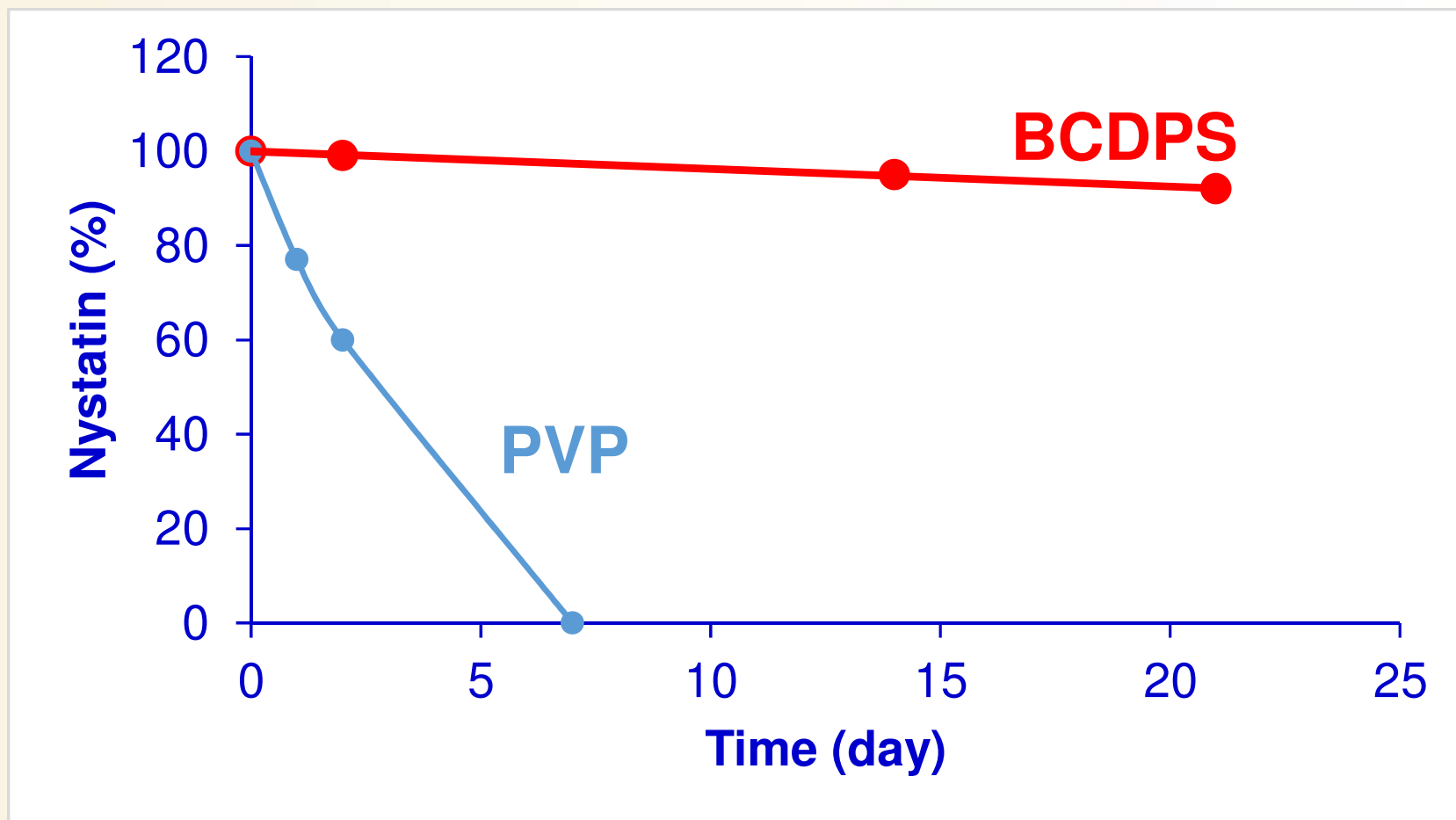
# Molecular weight distribution



HPLC: TSH9 column, eluent: MeOH:water=10:90/1%NaCl, flow: 1 ml/min, RI detector



# Enhancement of stability



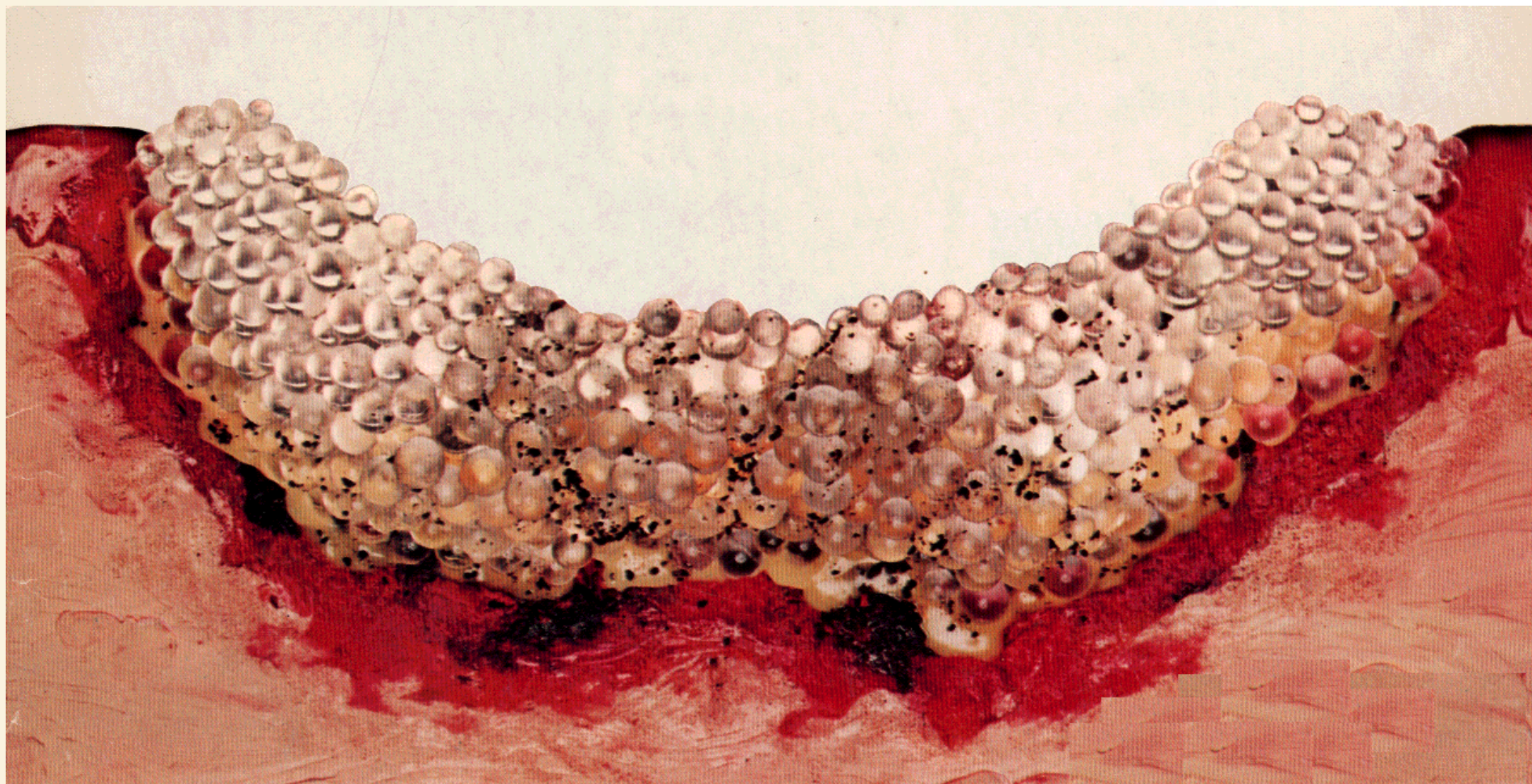
Stability of Nystatin/ $\gamma$ CD complex  
in solutions of lacque-forming polymers



## Wound healing with CD bead polymers

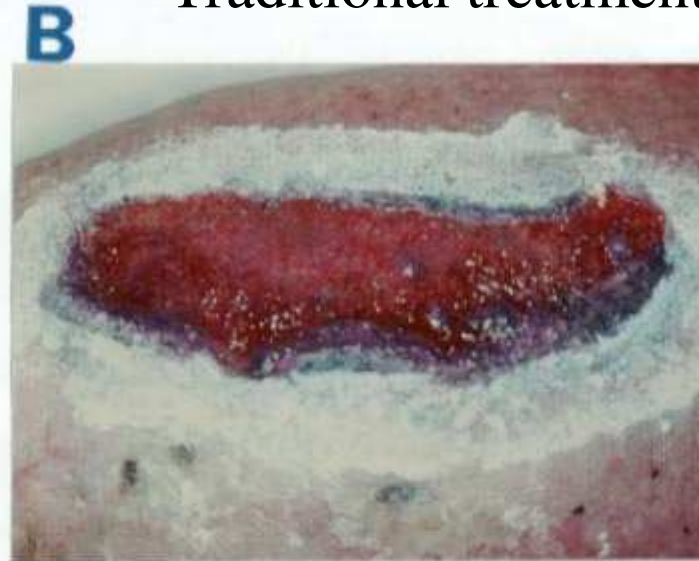


The polymer sucks up the exudate through swelling  
The wound surface is kept dry without being closed from the air  
Safe and easy use



# Wound healing with CDP

Traditional treatment



**C** 14 day-treatment with CDP

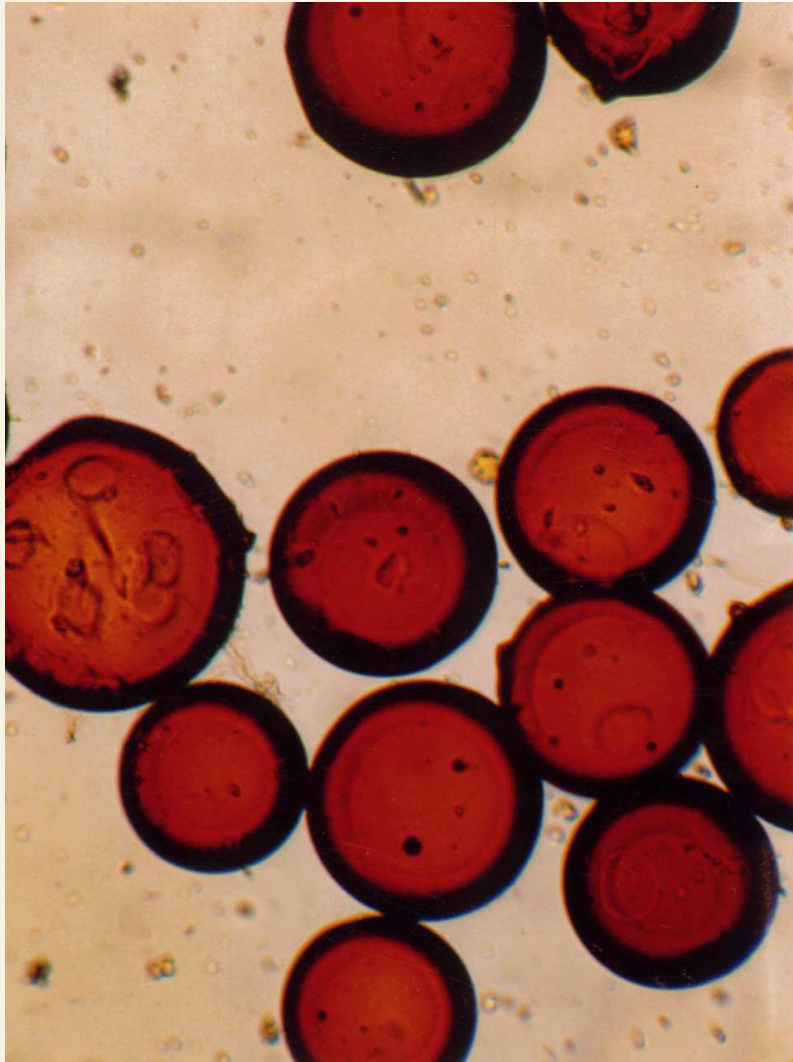
**D** 23 day-treatment with CDP

Woman (58) with ulcer cruris





# CDP with iodine as antiseptic active ingredient



Simultaneous cleansing  
and disinfection

Slow dissolution of iodine



## Tuning drug release by substituents

