Osmotic Water Transport Induced by Icodextrin
Occurs Independently of Water Channels and Resembles Colloid Osmosis

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Introduction

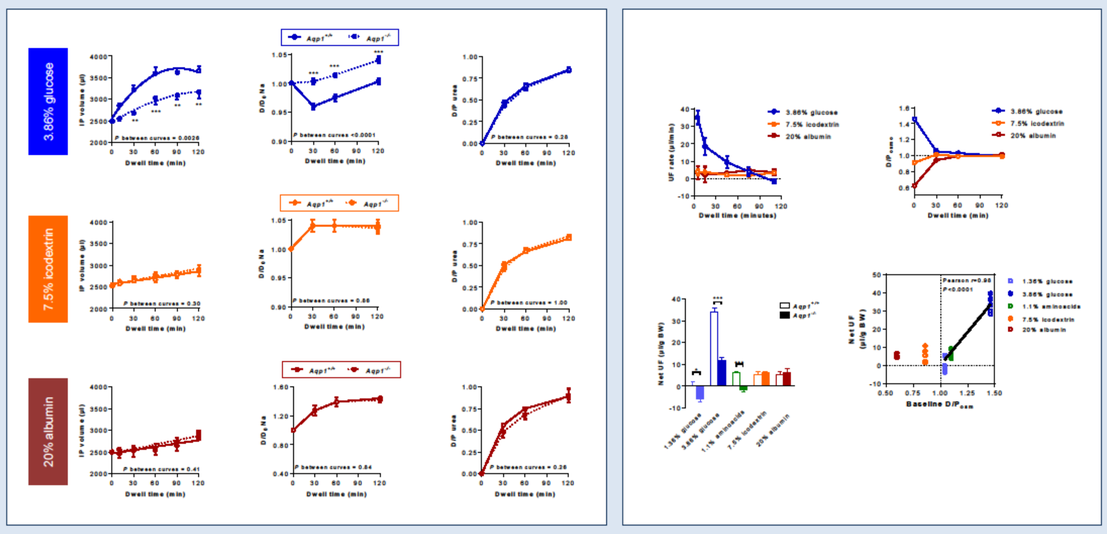
- The principle of osmosis has been applied for more than 50 years to generate ultrafiltration (UF) across the peritoneum of peritoneal dialysis (PD) patients. Aquaporin-1 (AQP1) water channels mediate free-water transport and half the UF during PD with hypertonic glucose[1].
- In recent years, icodextrin has emerged as a useful alternative to glucose to achieve UF during long dwells and improve water balance in PD patients[2]. However, the mechanisms underlying icodextrin-induced osmosis have not been investigated.

Methods

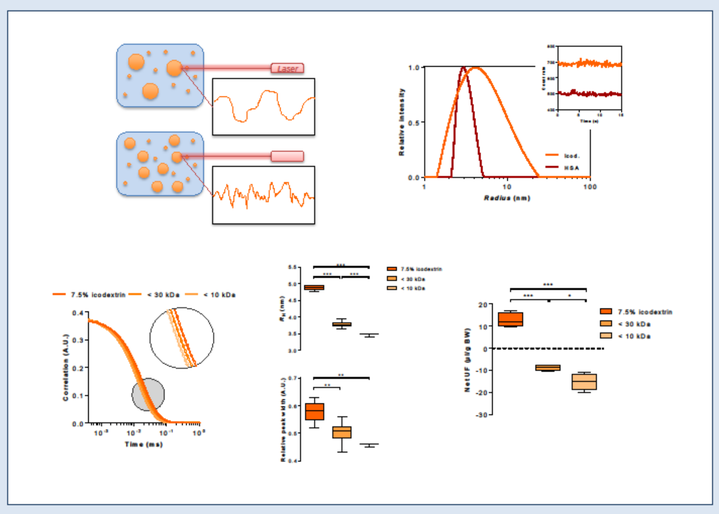
- The effects of icodextrin on peritoneal solute and water transport were compared to glucose-, aminoacids and albumin-based dialysis solutions, in a well-established mouse model of PD and in transgenic *Aqp1* mice.
- Hydrodynamic radius (R_H) of icodextrin and albumin were assessed by dynamic light scattering.
- The impact of icodextrin subfractions and bimodal osmosis on water transport was investigated *in vivo,* after selective removal of large polymers or with combinations of icodextrin and glucose, respectively.

Results

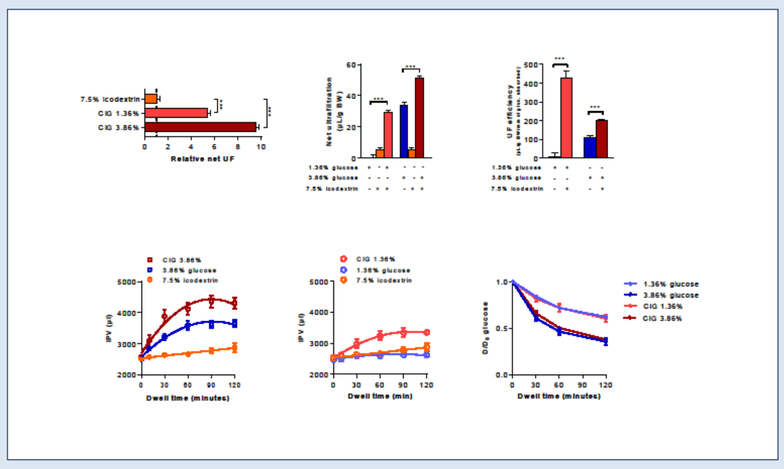
- Contrarily to PD solutions containing glucose or aminoacids, glucose polymer icodextrin and albumin induce a sustained water transport across the peritoneal membrane, independently of water channels, as indicated by the same net UF in *Aqp1* knockout and wild-type mice.



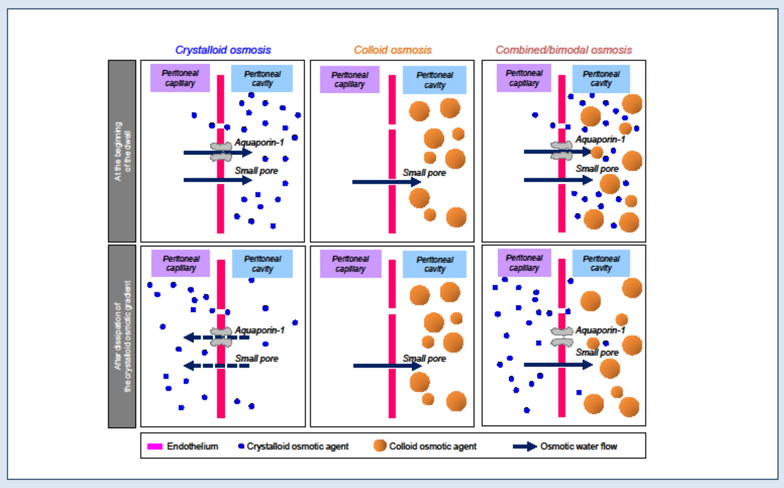
- The presence of large polymers allows icodextrin (mean R_H 5.0 nm, range 1-23 nm, *versus* 3.6 nm for albumin) to generate an osmotic water transport even when the solution is hypotonic. Removal of large (> 30 kDa/4.0 nm or > 10 kDa/2.5 nm) icodextrin polymers completely abolishes osmosis, but has no or little effect on dialysate osmolality.



- Combining icodextrin with glucose in the same solution synergistically enhances UF.



- The synergistic effect of bimodal osmosis results from the complementary mechanisms of osmotic water transport:
  - glucose induces a fast, AQP1-mediated, transcapillary UF during the first part of the dwell,
  - while large icodextrin molecules maintain a colloid osmotic gradient and prevent backfiltration when the crystalloid gradient has dissipated because of solute absorption.



Conclusions

- **Icodextrin induces a colloidal osmotic water transport across the peritoneum, like albumin, thanks to the presence of large fractions with a R_H that exceeds the functional *radius* (4.0 nm) of the small pores predicted by the three-pore model[3,4]**
- **Colloidal osmosis occurs independently of water channels and tonicity, contrarily to crystalloid osmosis (glucose and aminoacids)**
- **Combining colloid and crystalloid osmotic agents in the same dwell synergistically enhances water removal during PD, validating predictions from the three pore model[4]**

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