



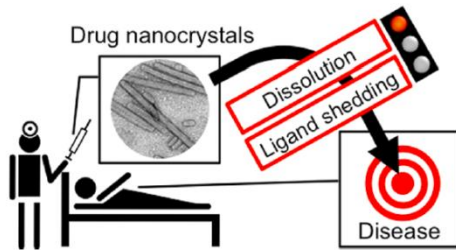
Nouveaux développements en dialyse péritonéale “active”

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Department of Chemistry and Applied Biosciences
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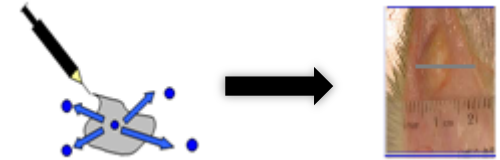
Drug formulation at the ETH

Colloids



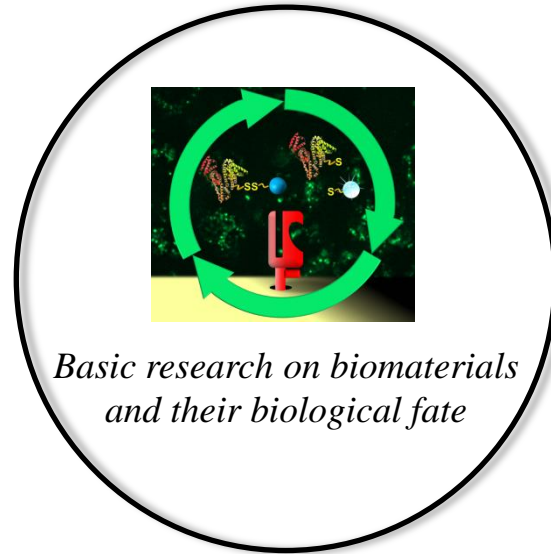
Targeted delivery of drugs and nucleic acids

Gels and microparticles



Parenteral sustained release formulations

← - - - Delivery - - - →



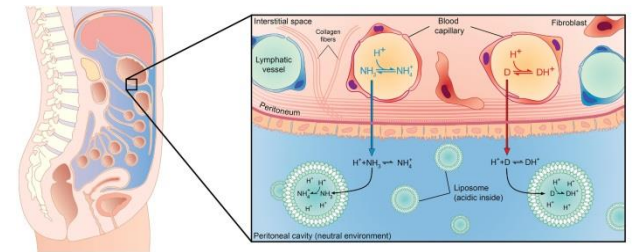
Basic research on biomaterials and their biological fate

Proteins



Inactivation of toxic exogenous proteins

Small molecules



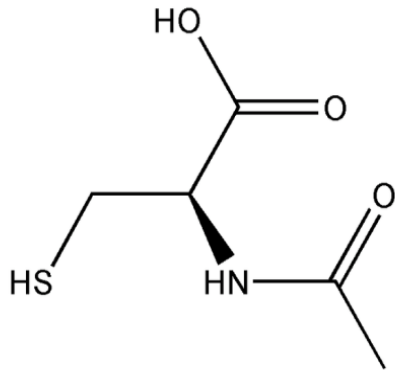
Treatment of intoxications to drugs and metabolites

← - - - Removal - - - →

Biodetoxification

Nano/microvesicles

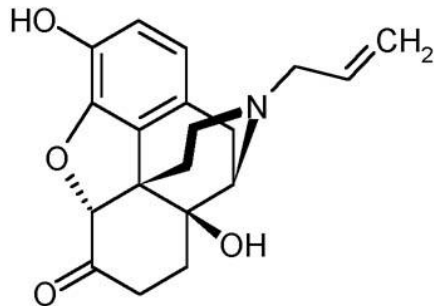
Specific antidotes



- ***N*-acetylcysteine**

Used to counter paracetamol overdose.

Hepatotoxicity caused by *N*-acetyl-*p*-benzoquinoneimine upon depletion of glutathione.

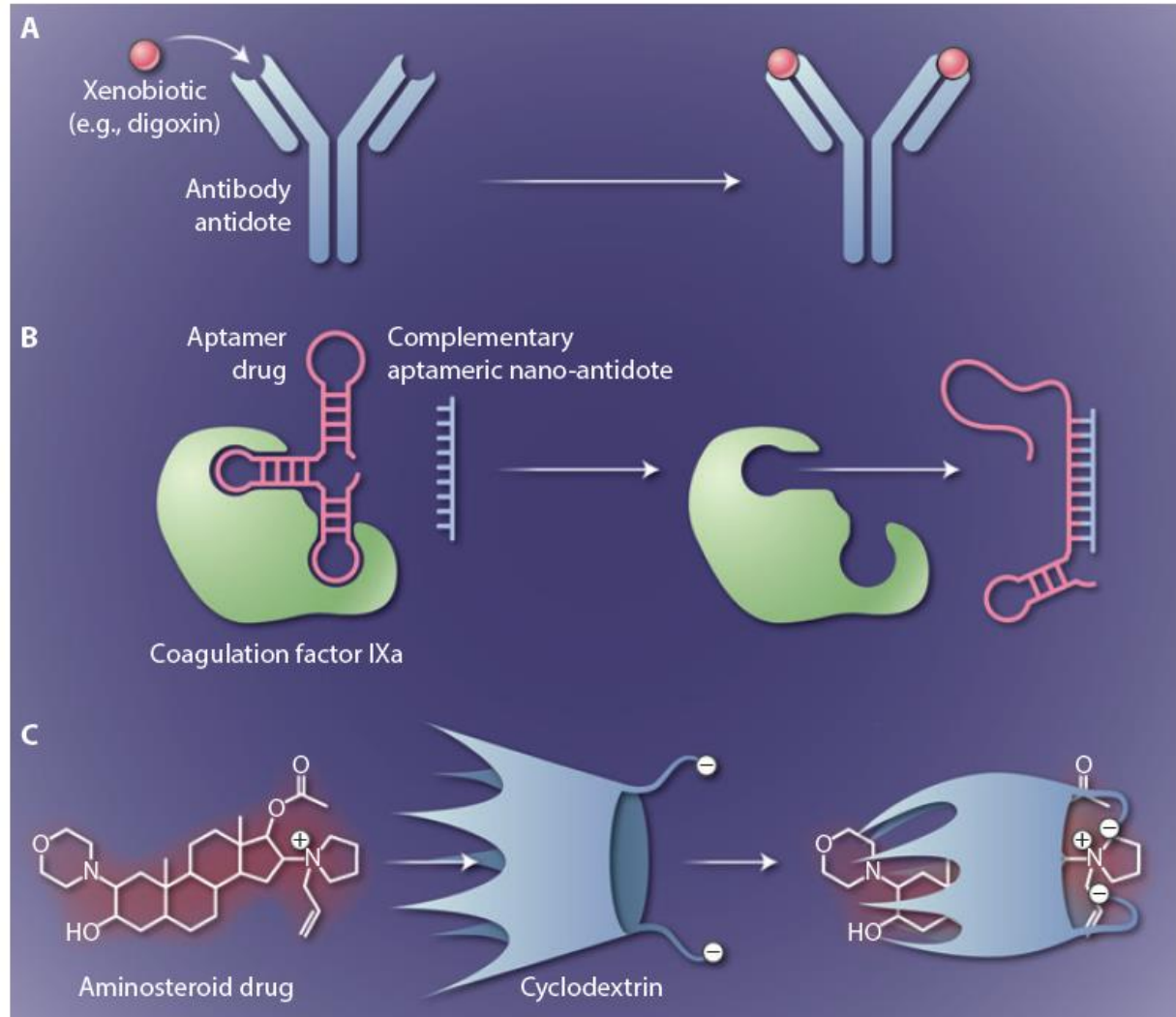


- **Naloxone**

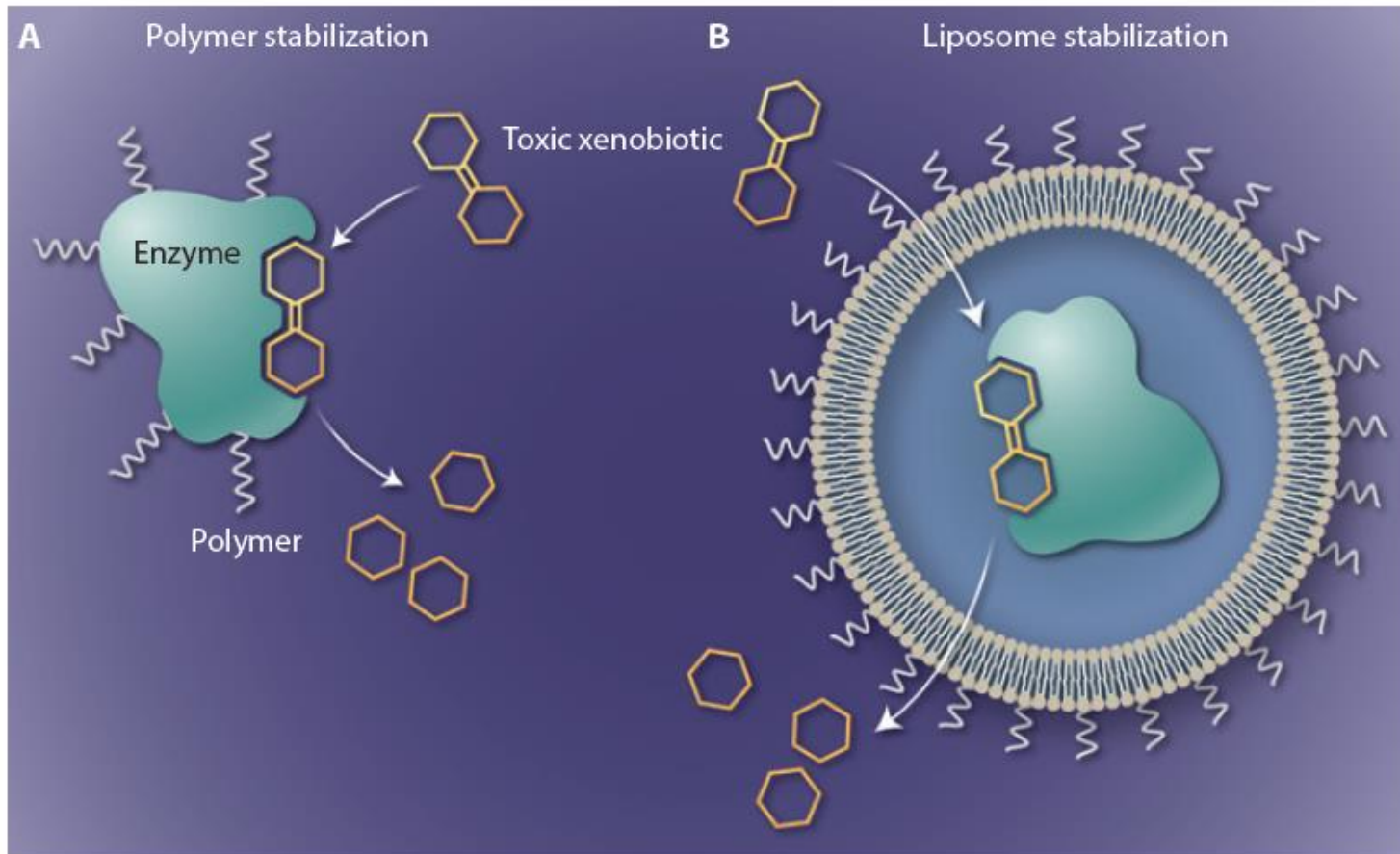
μ-opioid receptor competitive antagonist.

Used to counter opioid overdose (heroin, morphine).

Specific antidotes



Specific antidotes

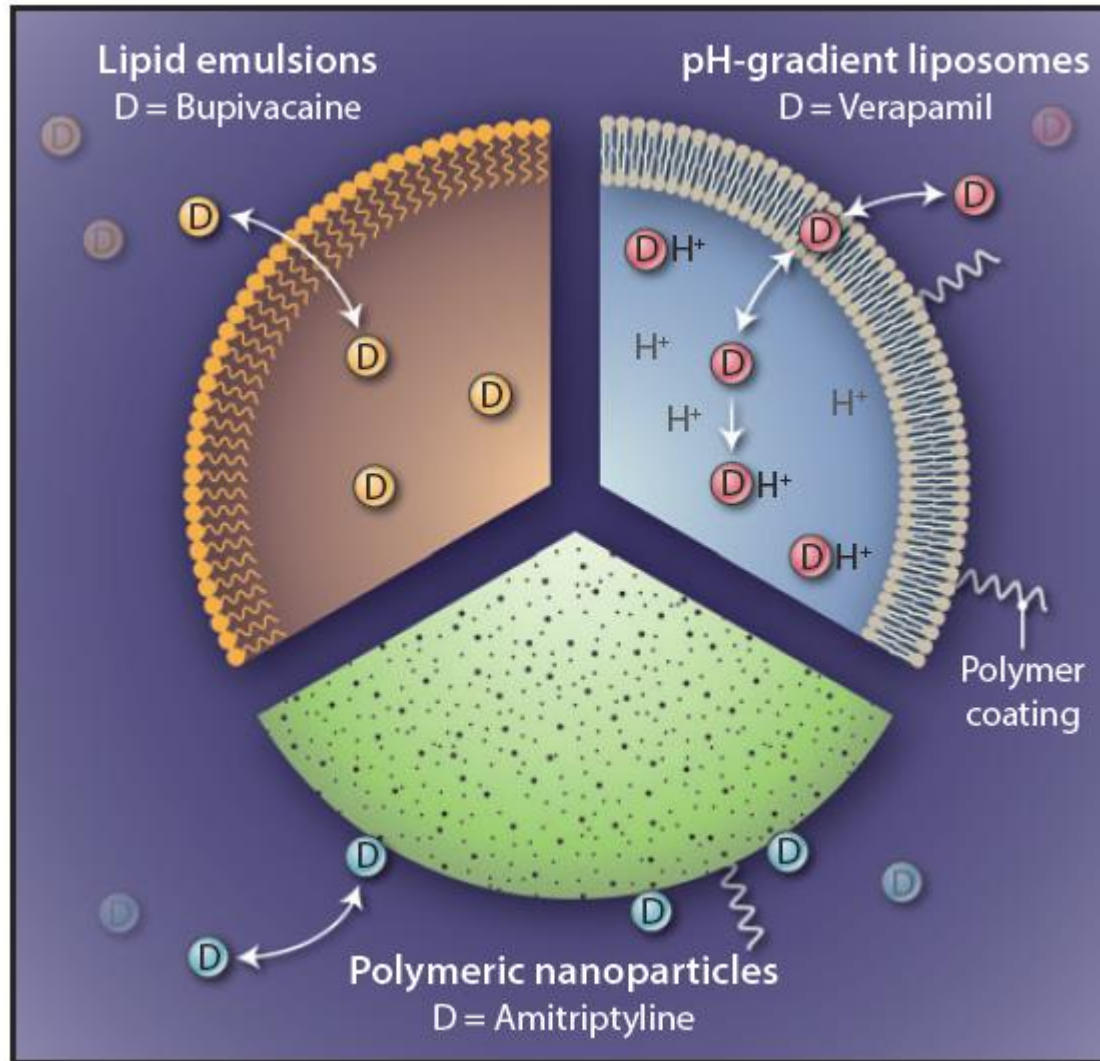


Non specific treatments

- Activated charcoal
- Gastric emptying
- Whole bowel irrigation
- Hemodialysis & hemoperfusion
- Corrections of electrolyte disturbances
- Breathing assistance, etc.



Large spectrum antidotes



Large spectrum antidotes

■ CASE REPORTS

Anesthesiology 2006; 105:217-8

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Successful Use of a 20% Lipid Emulsion to Resuscitate a Patient after a Presumed Bupivacaine-related Cardiac Arrest

Meg A. Rosenblatt, M.D.,* Mark Abel, M.D.,† Gregory W. Fischer, M.D.,† Chad J. Itzkovich, M.D.,‡ James B. Eisenkraft, M.D.§



Anaesthesia, 2007, 62, pages 516-518

doi:10.1111/j.1365-2044.2007.05065.x

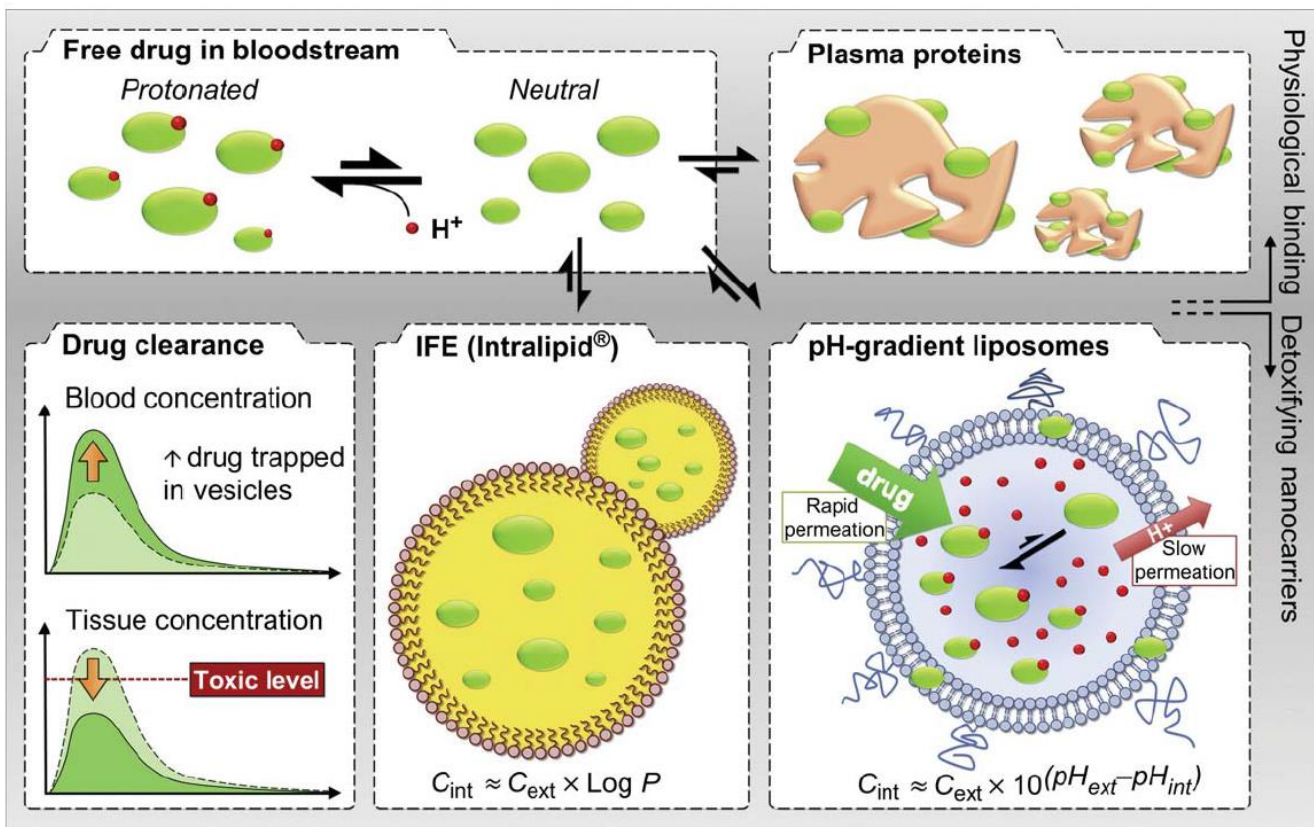
CASE REPORT

Levobupivacaine-induced seizures and cardiovascular collapse treated with Intralipid[®]

G. Foxall,¹ R. McCahon,² J. Lamb,³ J. G. Hardman⁴ and N. M. Bedford³

*1 Fellow in Regional Anaesthesia, 2 Specialist Registrar, 3 Consultant Anaesthetist, Department of Anaesthesia,
4 Associate Professor and Reader in Anaesthesia, University Department of Anaesthesia, Queen's Medical Centre,
Nottingham NG7 2UH, UK*

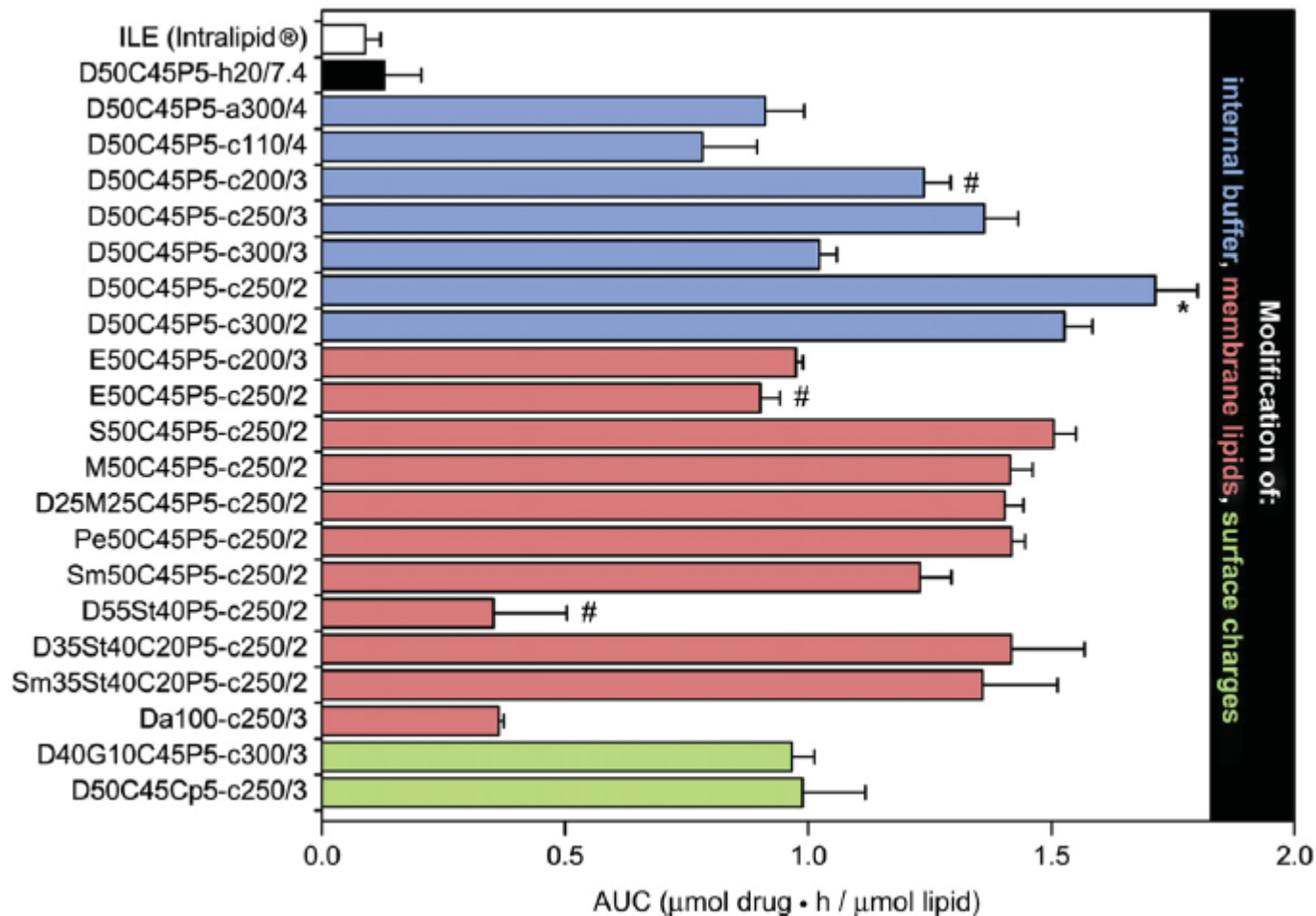
Large spectrum antidotes



Bertrand *et al.* *ACS Nano* **4** (2011) 7552-7558.
 Forster *et al.* *Biomaterials* **33** (2012) 3578-3585.

Screening of formulations

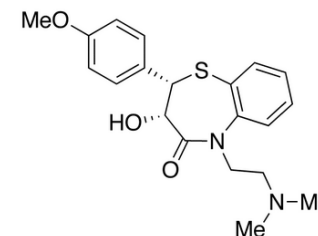
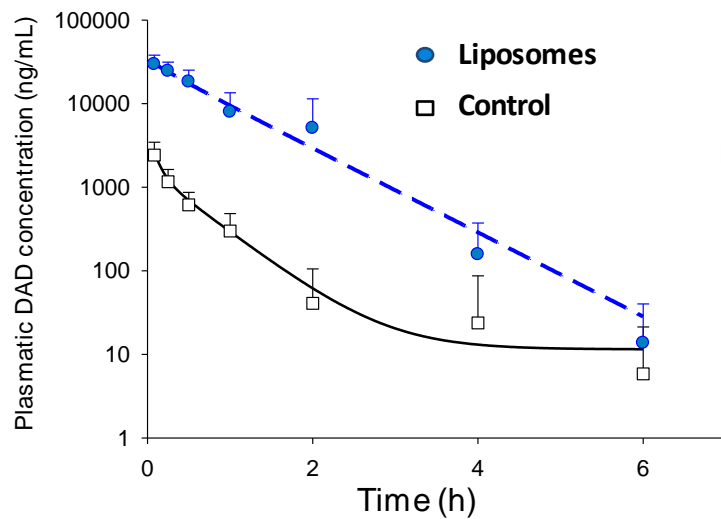
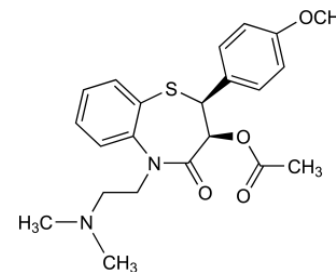
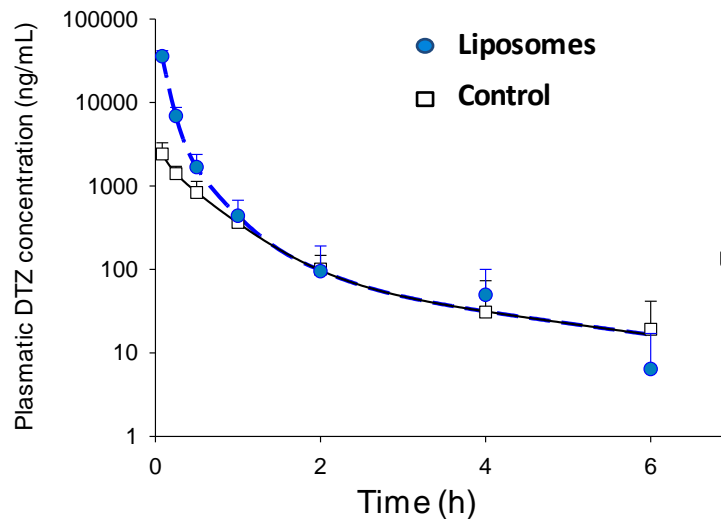
Uptake of diltiazem in 50% FBS



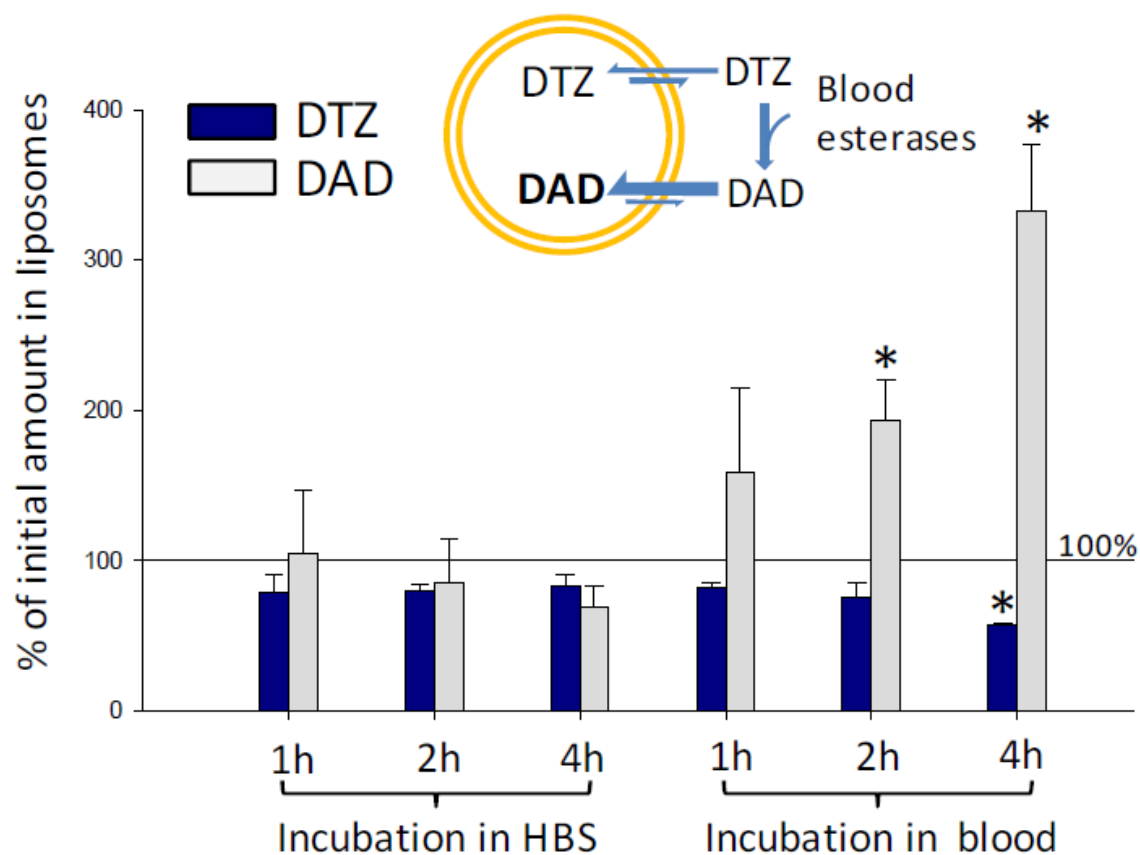
Pharmacokinetics

Liposomes 275 mg/kg i.v.
140 nm

Diltiazem 5 mg/kg i.v.

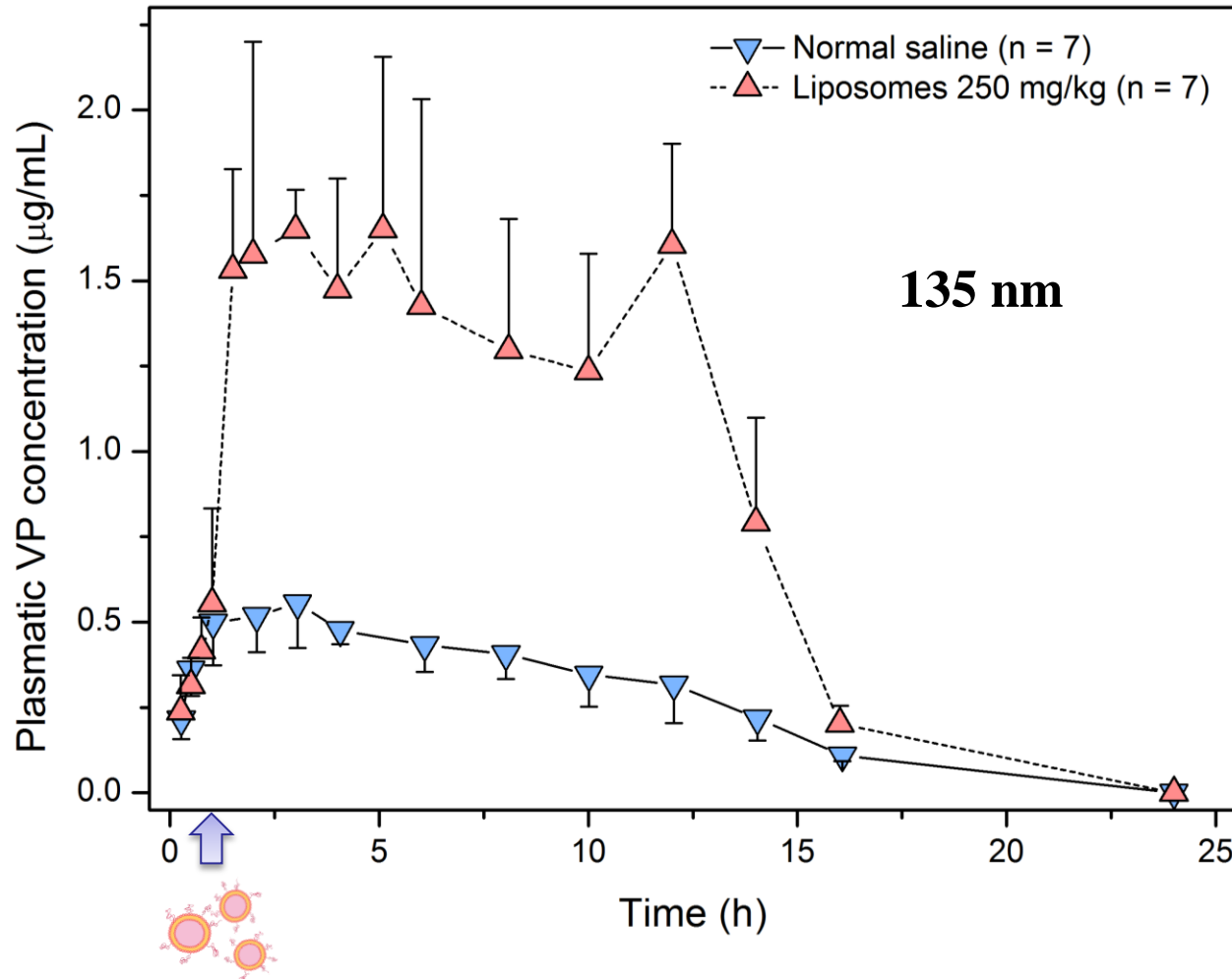


Uptake of drug and metabolite

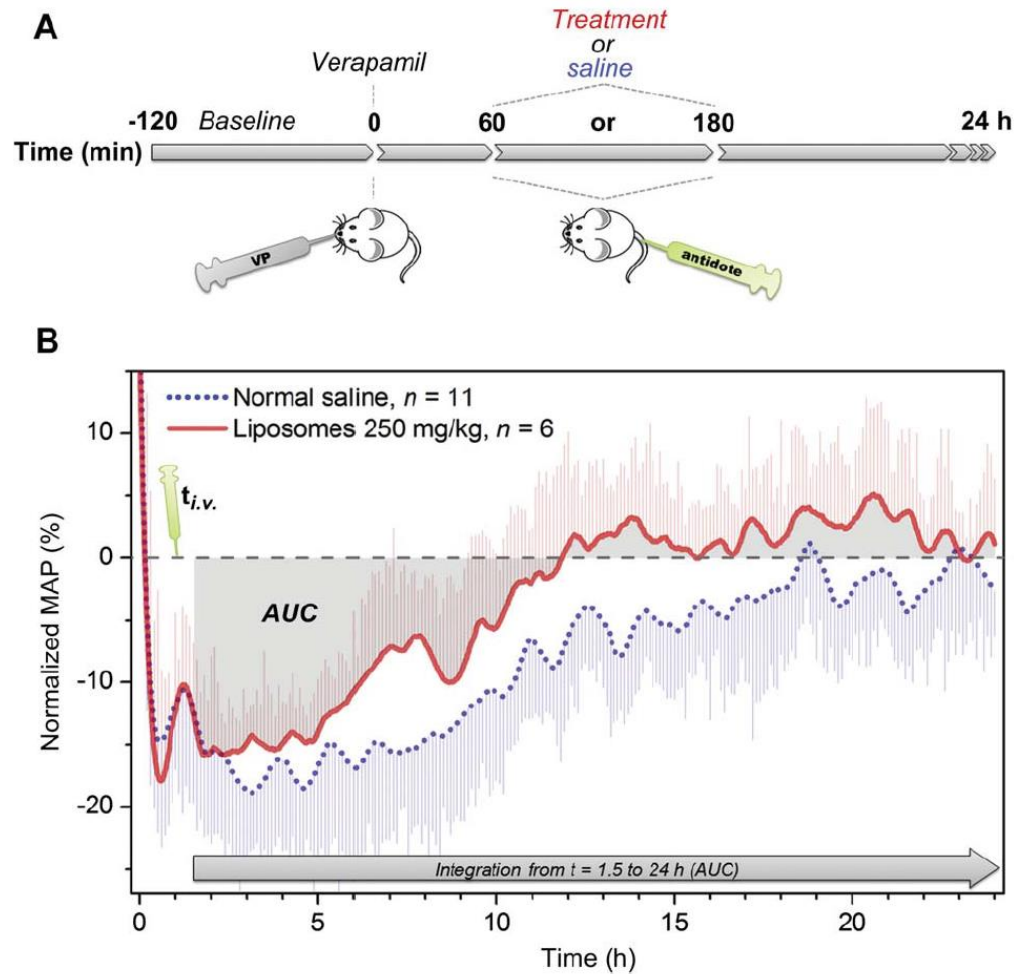


Pharmacokinetics of verapamil

Sprague-Dawley adult rats. Treatment (i.v.) 1 h after intoxication (VP 50 mg/kg, p.o.)

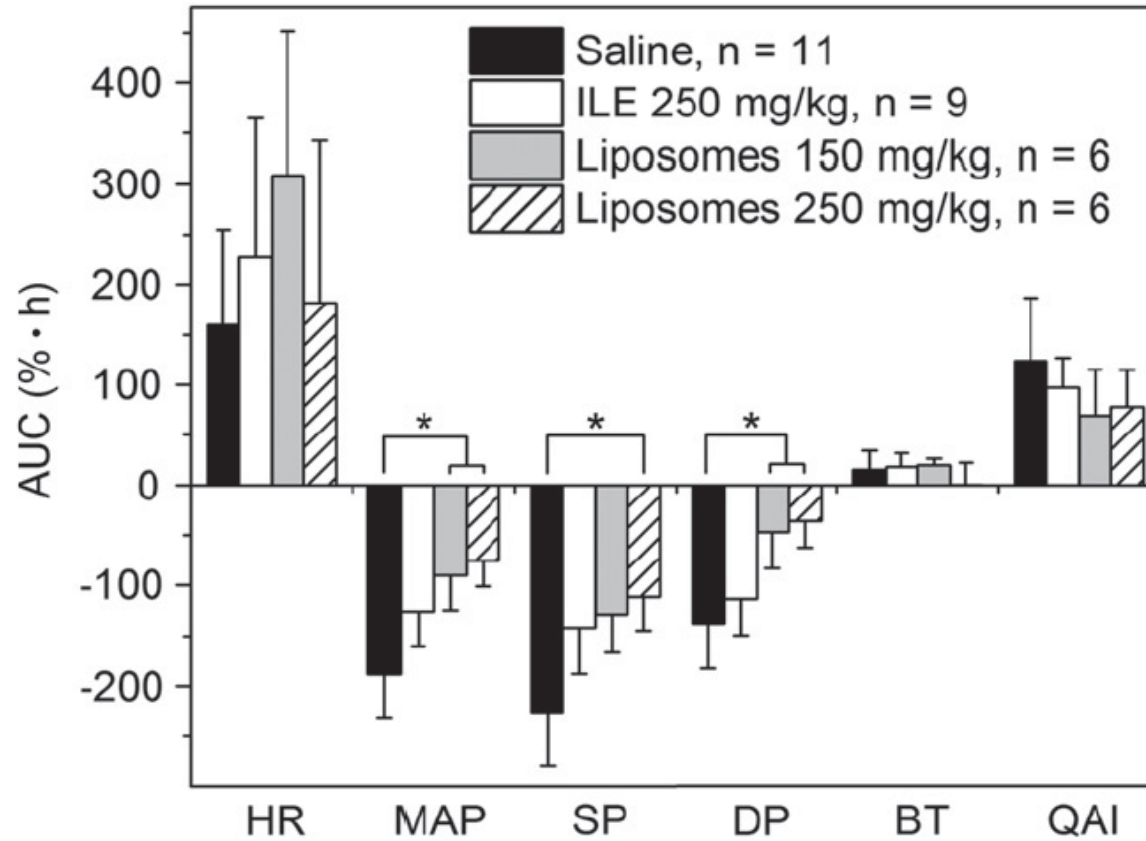


Treatment of verapamil intoxication



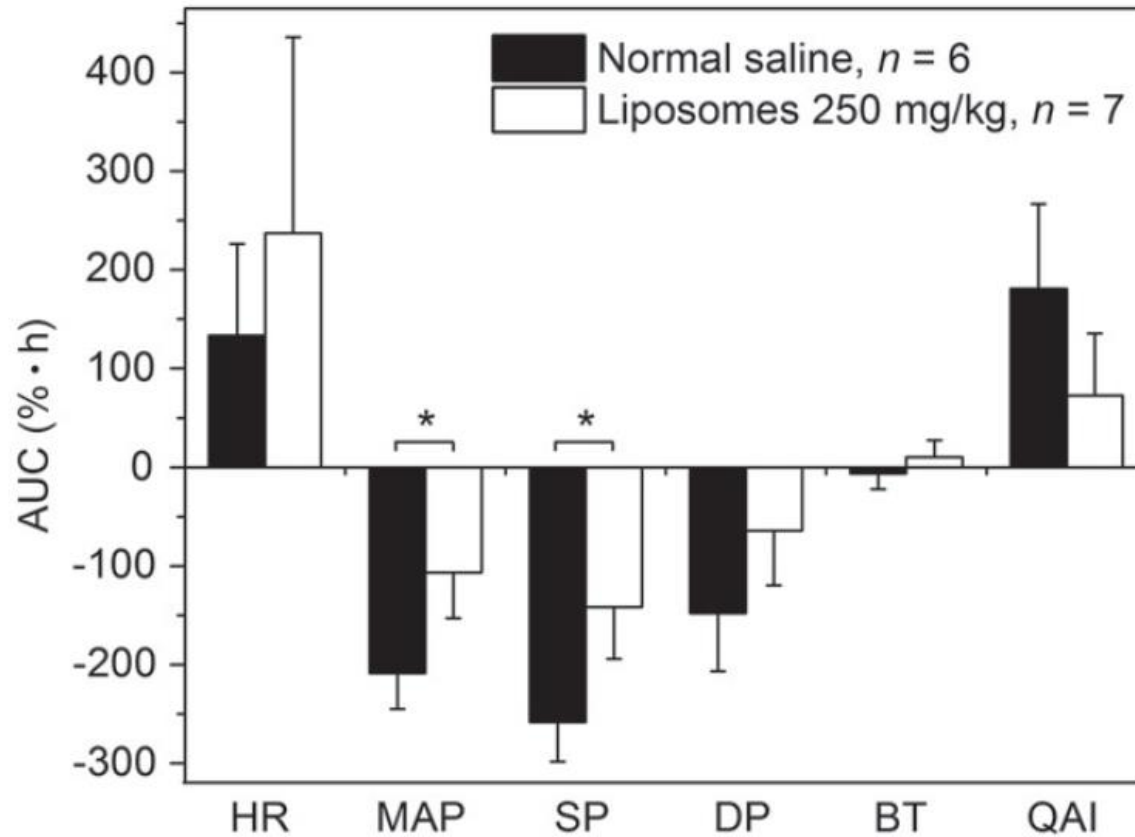
Treatment of verapamil intoxication

Verapamil 50 mg/kg p.o.

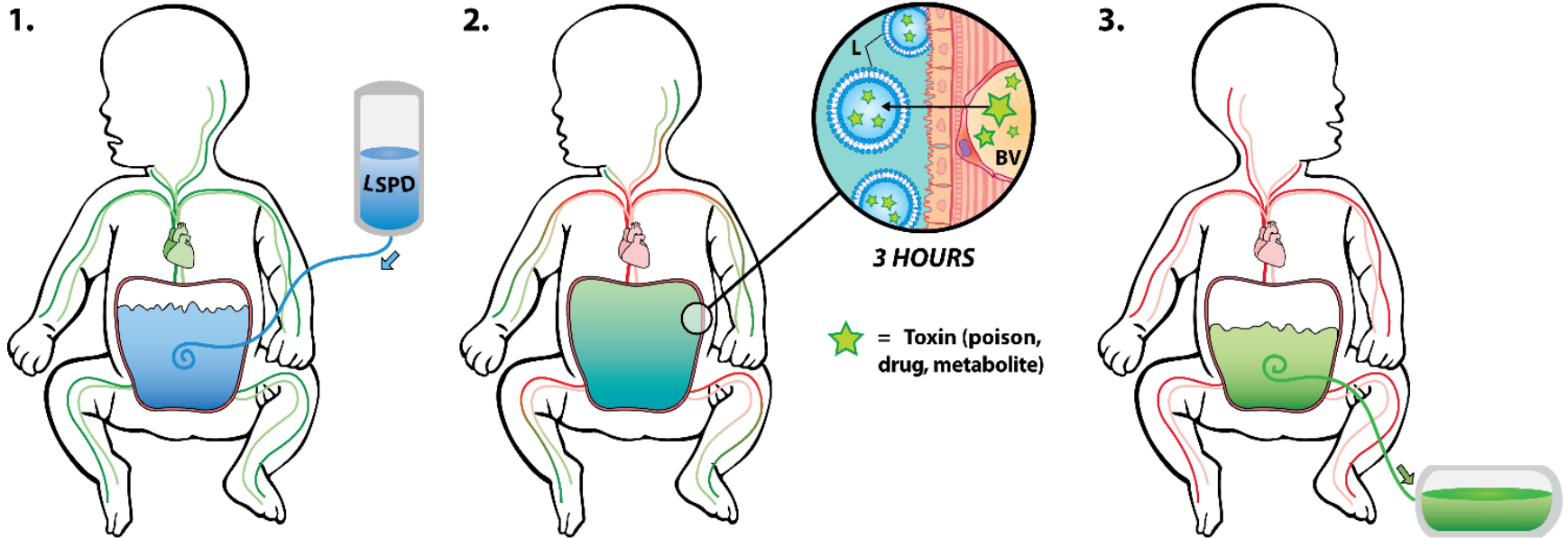


Detoxifying capacity - 3 h post oral dosing

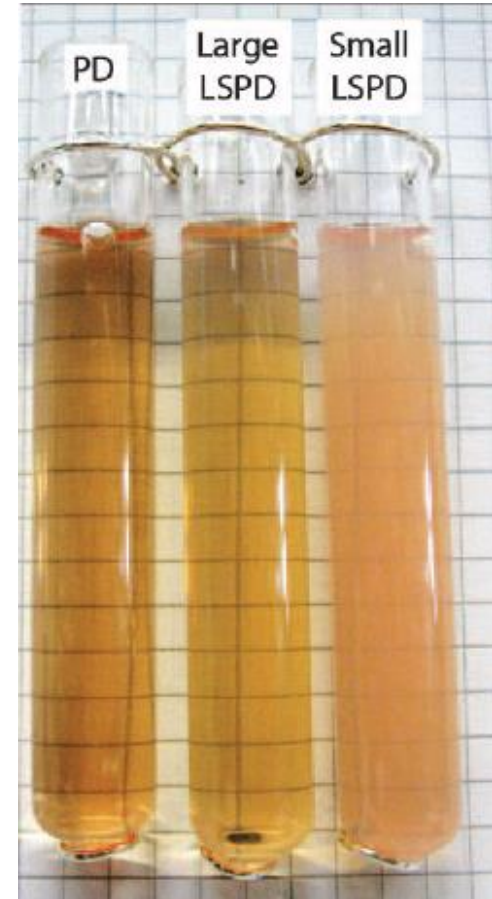
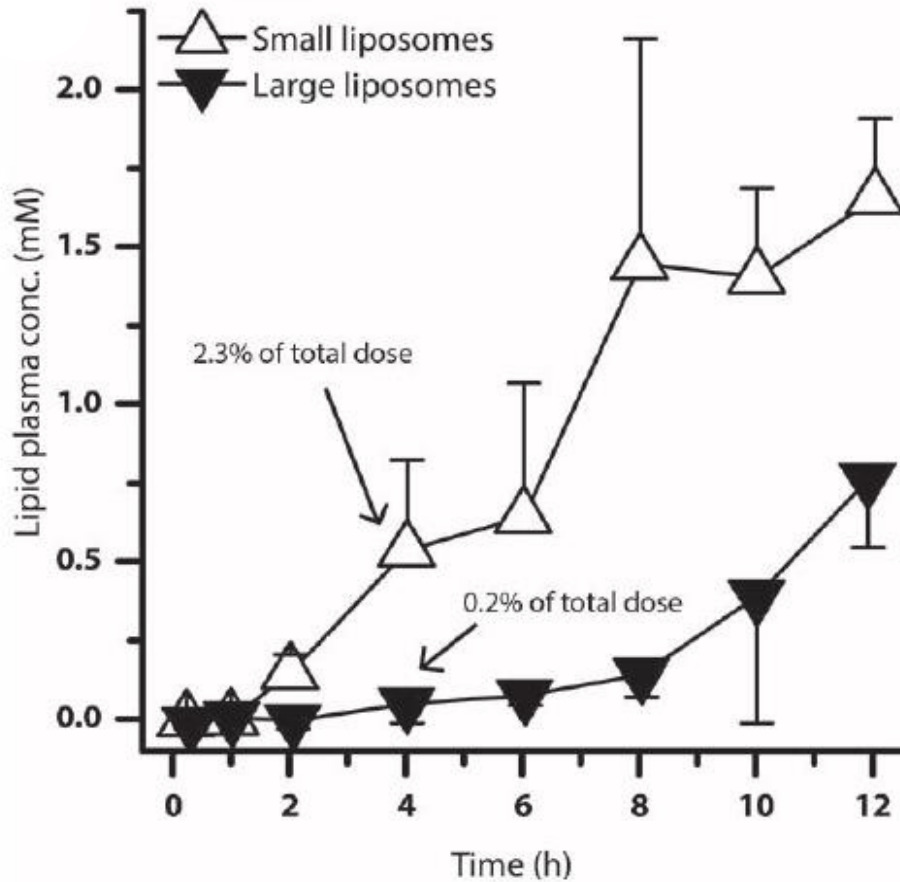
Verapamil 50 mg/kg p.o.



Peritoneal dialysis

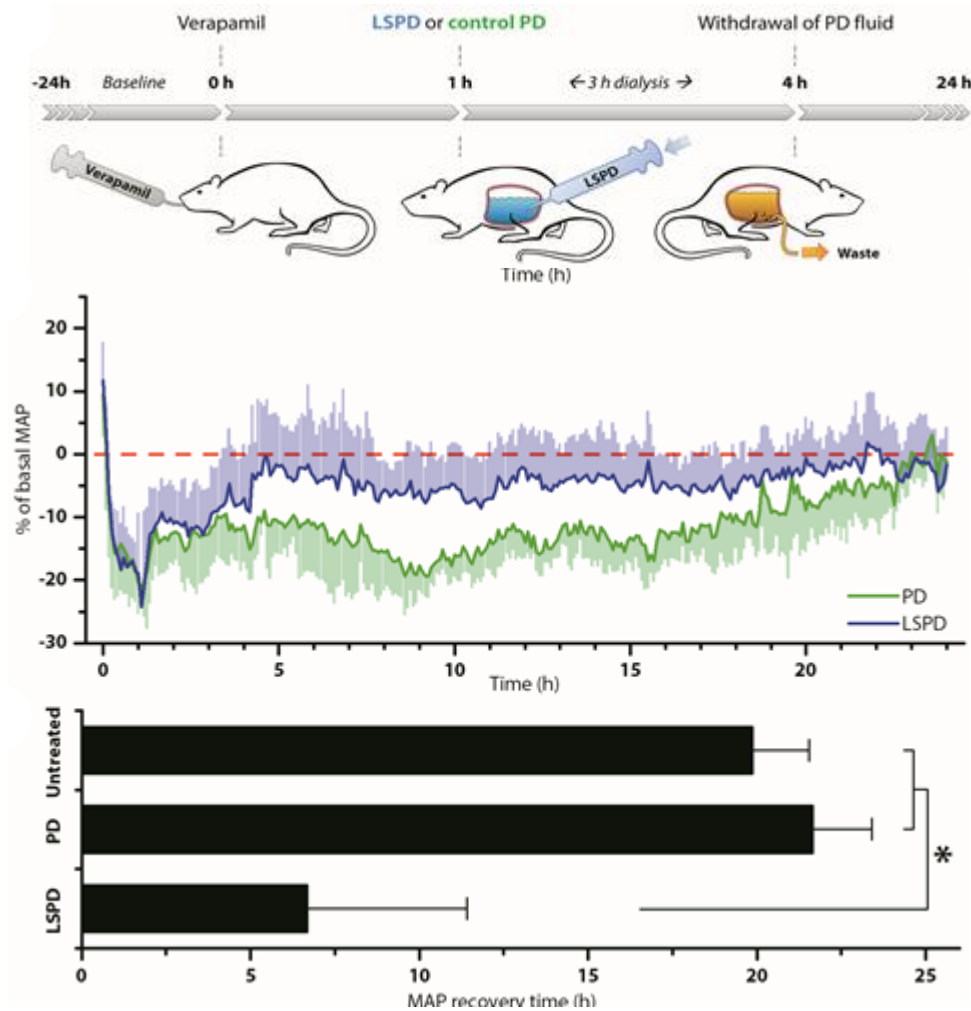


Peritoneal dialysis with liposomes

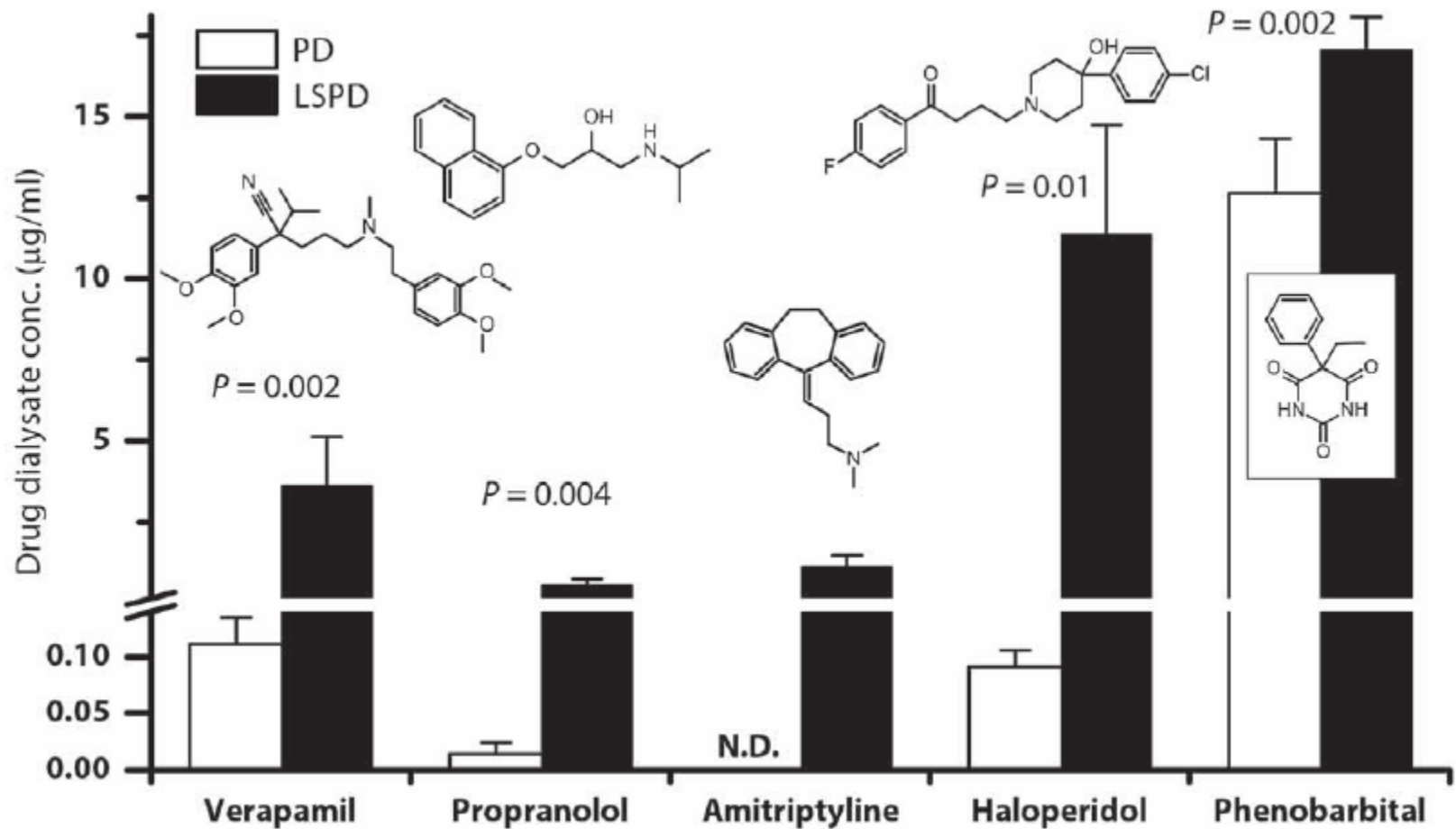


Drug detoxification

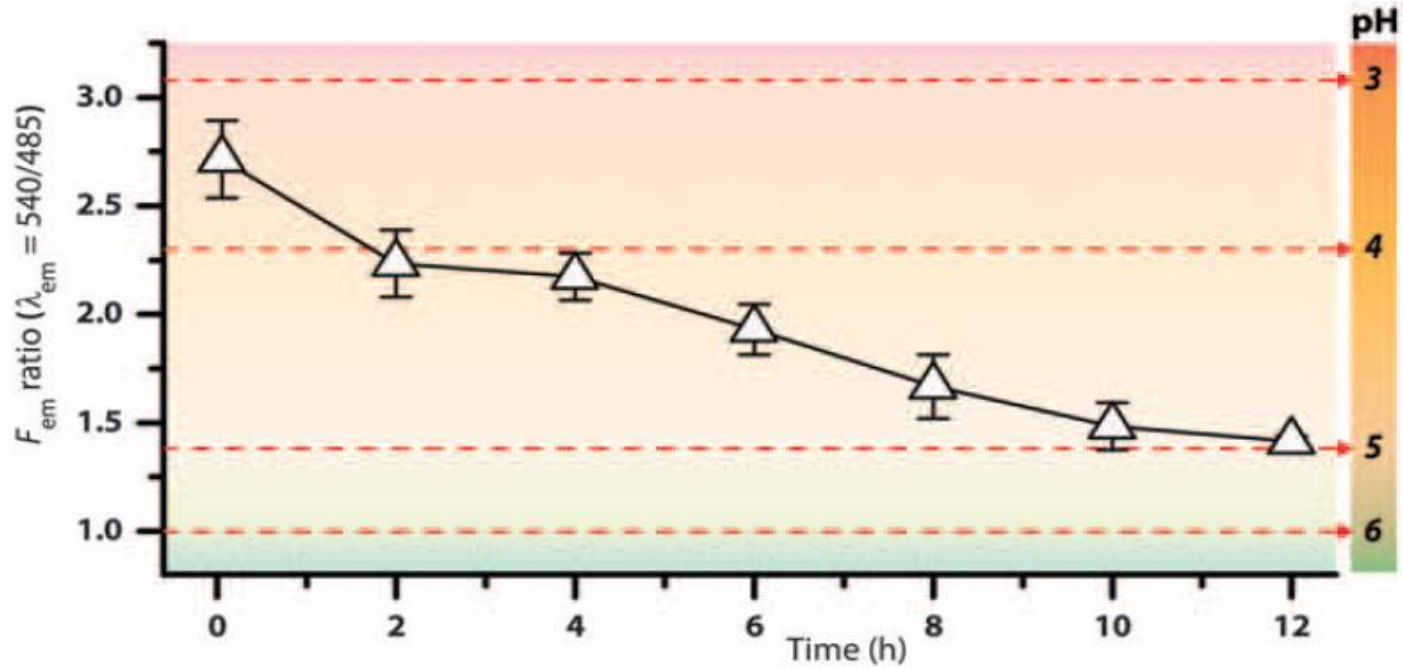
850 nm



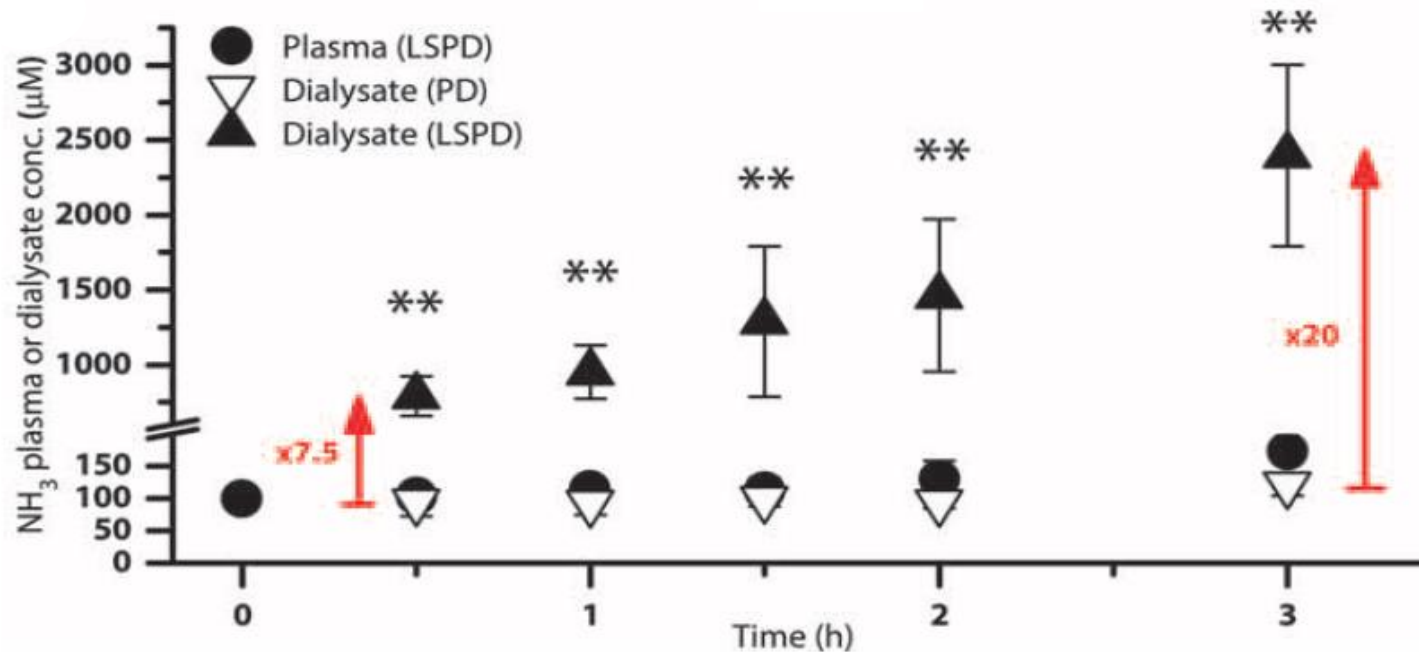
Versatility



Stability of transmembrane pH-gradient



Uptake of ammonia



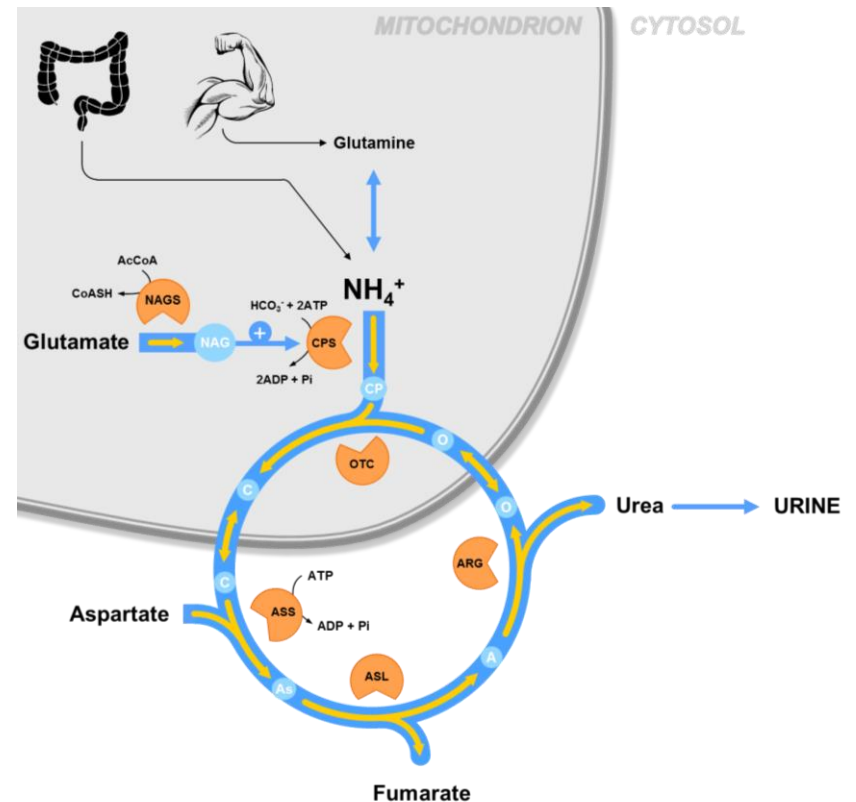
Hyperammonemia – congenital disorders

➤ Main cause: urea cycle disorder

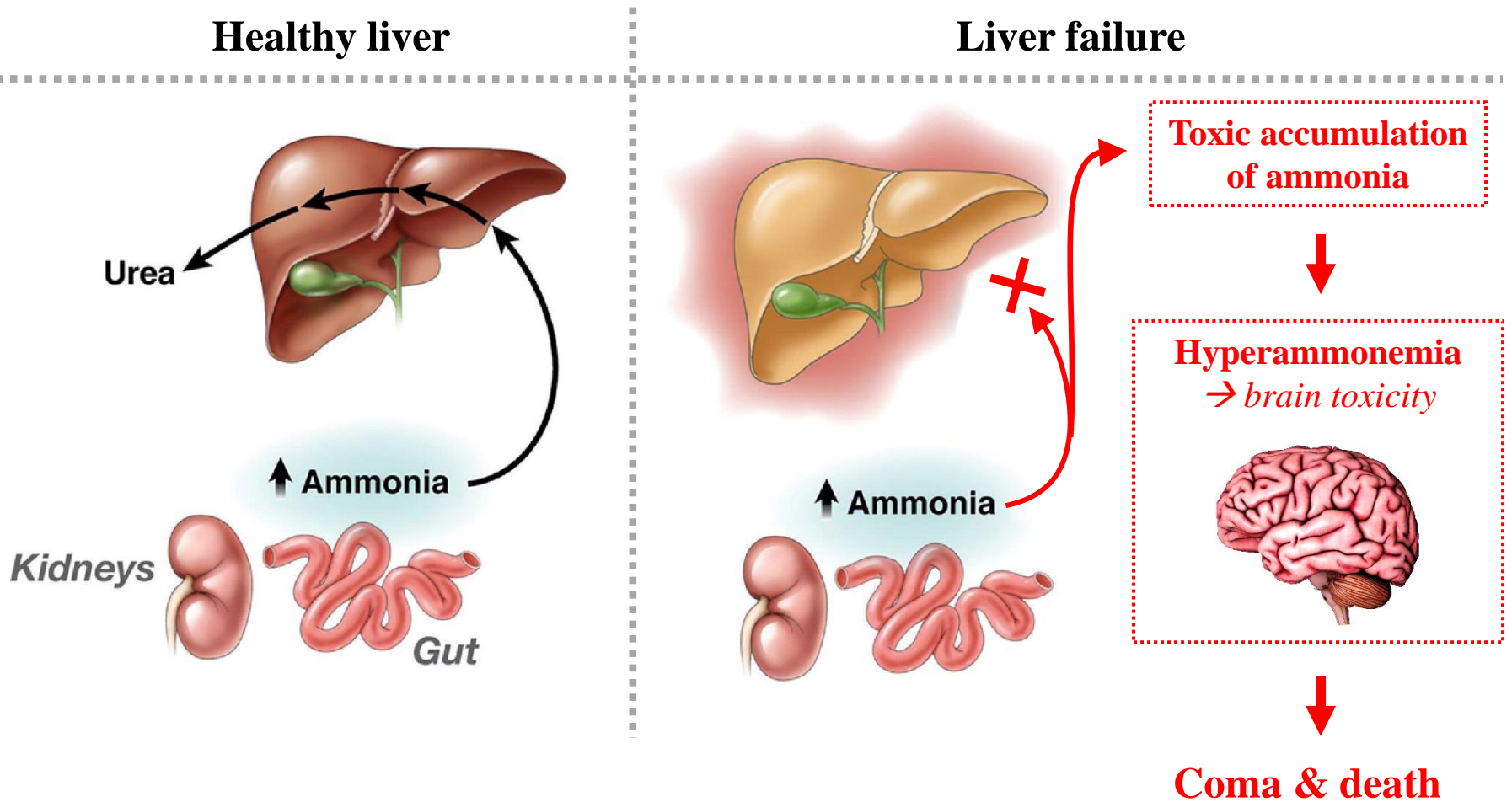
- Congenital enzyme deficiency
- ~1:12'000 live births

➤ Symptoms

- Severe neurologic damages, **death**
- Mortality rate 60-85%



Hyperammonemia – liver failure



Industrial development

ETH – Spin-off

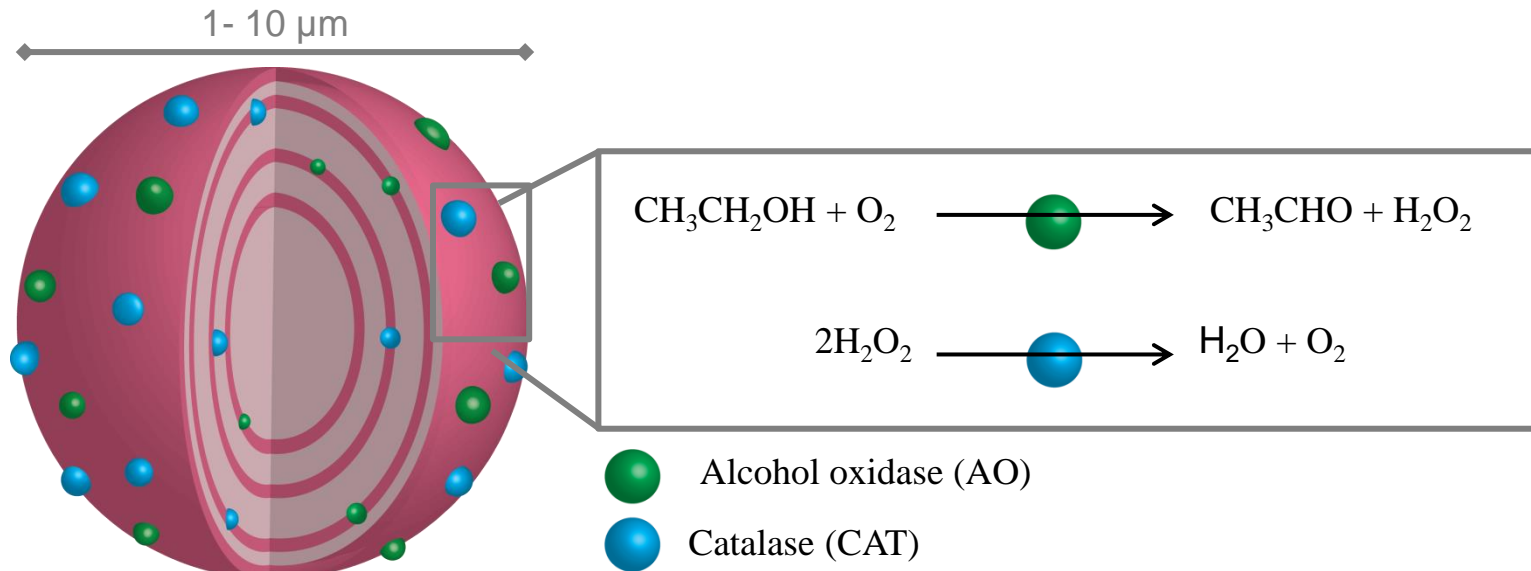
- Optimization of composition
- Manufacturing process – scale up
- Completion of preclinical studies
- Clinical studies (Acute on chronic)



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New developments

Treatment of alcohol overdose



Acknowledgements

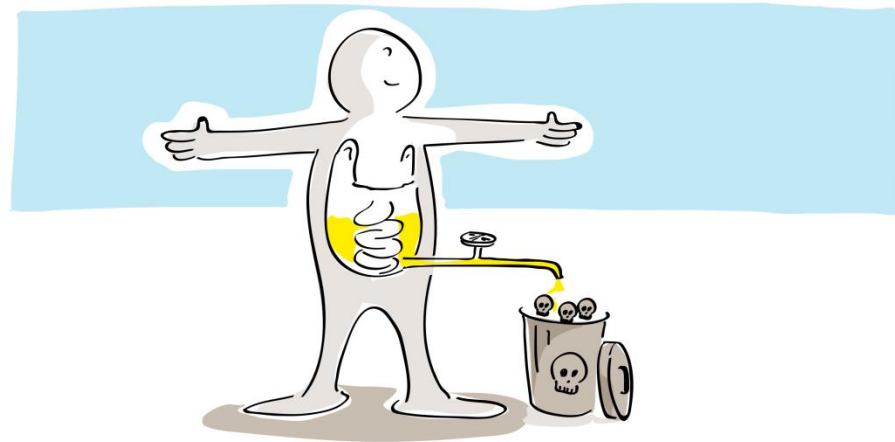
Prof. C. Rose (CHUM)
Prof. N. Bertrand (Laval University)
Dr. V. Forster (Versantis)



SCHWEIZERISCHER NATIONALFONDS
ZUR FÖRDERUNG DER WISSENSCHAFTLICHEN FORSCHUNG

KTI/CTI

DIE FÖRDERAGENTUR FÜR INNOVATION
L'AGENCE POUR LA PROMOTION DE L'INNOVATION
L'AGENZIA PER LA PROMOZIONE DELL'INNOVAZIONE
THE INNOVATION PROMOTION AGENCY



Declaration of conflict of interest: Prof. J.-C. Leroux has financial interests in Versantis AG