Potassium Binding:
Essentials to know about the mode of action

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3 Things a cardiologist needs to know about potassium binders

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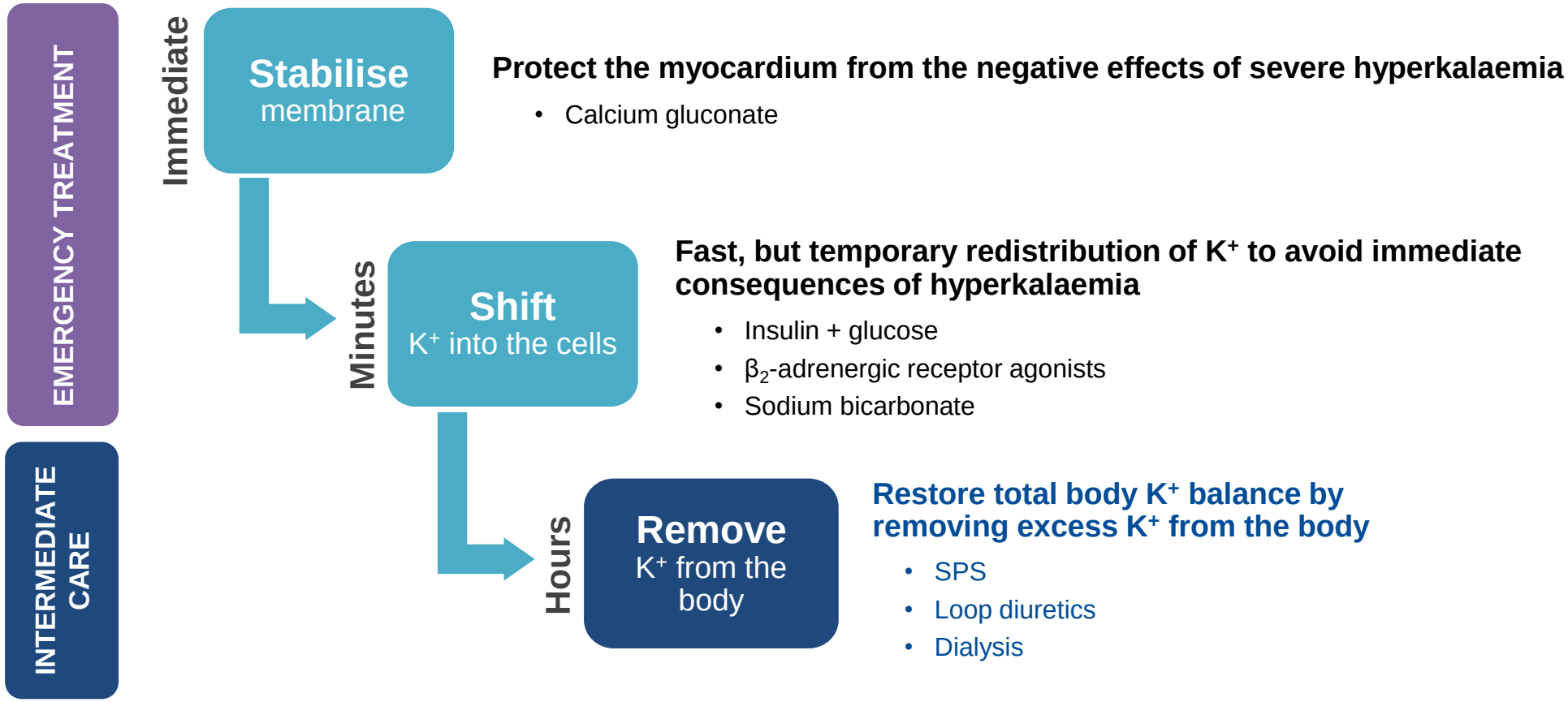
Disclosures

- None

Hyperkalaemia in the acute (inpatient) setting



Protect the myocardium from the negative effects of severe hyperkalaemia

- Calcium gluconate

Fast, but temporary redistribution of K^+ to avoid immediate consequences of hyperkalaemia

- Insulin + glucose
- β_2-adrenergic receptor agonists
- Sodium bicarbonate

Restore total body K^+ balance by removing excess K^+ from the body

- SPS
- Loop diuretics
- Dialysis

How to manage potassium levels on the long-term?

JD Dunn, et al. Am J Manag Care. 2015

Limitations of long-term hyperkalaemia management strategies

Strategy	Effect
RAASi reduction	• Worsens outcomes

Dietary restriction (50–75 mEq/day)	• Poor compliance
	  • Other diets
	  • K^+ is a common ingredient in many foods
	  • Restricts consumption of healthy foods (DASH diet)

Sodium Polystyrene Sulfonate (SPS)	• Limited data from clinical trials • Precaution related to Na • Serious GI AEs as colonic necrosis

Therapeutic options for long-term hyperkalaemia management

- Sodium Polystyrene Sulfonate (SPS)
- Sodium Zirconium Cyclosilicate (ZS-9)
- Patiromer

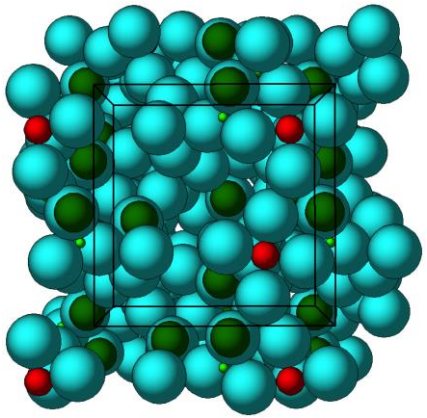
Sodium Polystyrene Sulfonate (SPS)

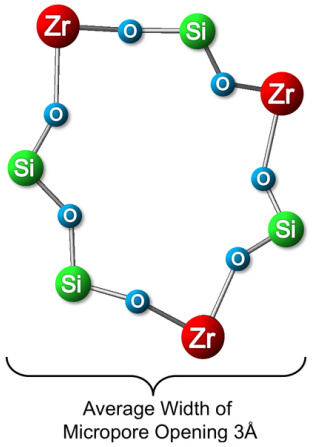
Pharmacology	• Non-specific, sodium-based cation-exchange resin
	• Swells in a solvent
	  • Allows exchange between potassium and reactive group (sodium)
	  • Not exclusively selective for potassium (calcium or magnesium)
	• Faecal elimination

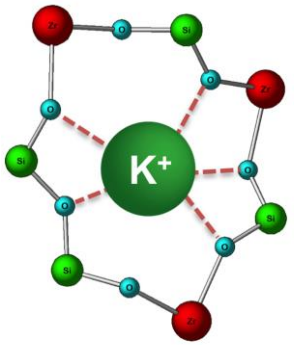
Pharmacokinetics & pharmacodynamics	• Not absorbed into the system • In vitro: 3.1 mEq per gram SPS • In vivo: 1 mEq per gram SPS (competition)
Dosing	• 15g: 1 to 4 dd (oral powder) • 30 to 50 g: 1 to 4 dd (enema)
Adverse events and clinical monitoring	• GI disturbances (irritation, vomiting, nausea, constipation, diarrhoea) • Hypokalaemia, hypomagnesaemia, sodium loading • Intestinal necrosis
Drug-drug interactions	• Antacids, laxatives, digoxin, sorbitol, lithium, and thyroxine
Clinical efficacy	• 1 – 2 hours • -0.82 tot -1.14 mEq/L (10 hours; dose dependent)

Sodium Zirconium Cyclosilicate (SZC/ZS-9)

Pharmacology	• Inorganic non-absorbable sodium-potassium cation exchange compound • Selectively traps potassium ions moving through the GI tract • Micropores have diameters specific for potassium (i.e. no capture of sodium, calcium, or magnesium)
Pharmacokinetics & pharmacodynamics	• Not systemically absorbed → eliminated in the faeces
Dosing	• 5g or 10g, 3 dd
Adverse events and clinical monitoring	• No serious AEs • GI disturbances (diarrhoea and constipation) • Hypokalaemia • Long-term safety and efficacy remains undetermined: No data for administering drug > 4 weeks
Drug-drug interactions	• No clinically meaningful interactions identified yet
Clinical efficacy	• Onset: 1 hour • 4-week -0.8 to -1.2 mEq/L







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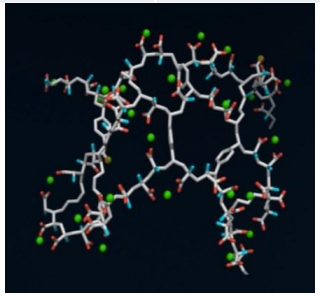
F. Stavros et al. PLOS ONE 2014

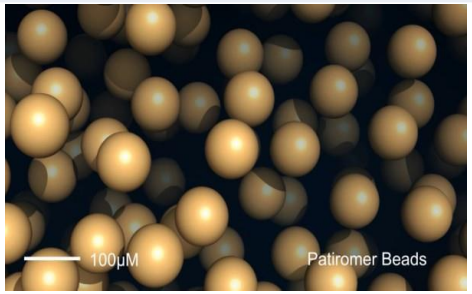
Patiromer

Pharmacology	• Non-absorbable, calcium-based, potassium-specific organic spherical polymer
	  • High-capacity polymer exchanging calcium for potassium
	  • Primary site of action: Distal colon (highest concentration of free potassium) → Enhances faecal excretion

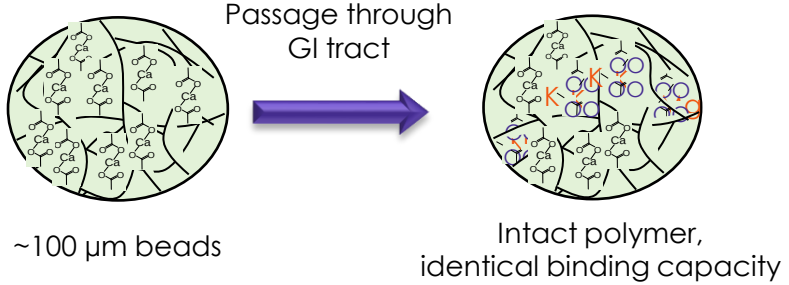
Pharmacokinetics & pharmacodynamics	• Tasteless/odourless powder that should be mixed • Free of sodium • Not metabolized or absorbed systemically • Dose-dependent
Dosing	• 8.4g, 16.8g, 25.2g (sachets)
Adverse events and clinical monitoring	• No serious AEs • GI disturbances • Hypomagnesaemia • Hypokalaemia
Drug-drug interactions	• Binding to several (cardiovascular) drugs • 3 hours apart from other oral drugs
Clinical efficacy	• Onset: 7 hours • 48 hours: -0.75 mEq/L ---- 4 weeks: -1.01 mEq/L Clinical studies will be discussed in another lecture



High-capacity polymer



Uniform, spherical patiromer beads



Li L, et al. J Cardiovasc Pharmacol Ther. 2016

Differences

- SPS: Limited selectivity for potassium
  - Adverse events
  - No data in clinical trials
- SZC/ZS-9: Fastest onset of action
  - Sodium
- Patiromer: Calcium instead of sodium
  - Desirable in heart failure or cirrhosis
  - Dosing once a day

- Trial data for patiromer and SCZ/ZS-9 will be discussed in another lecture

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