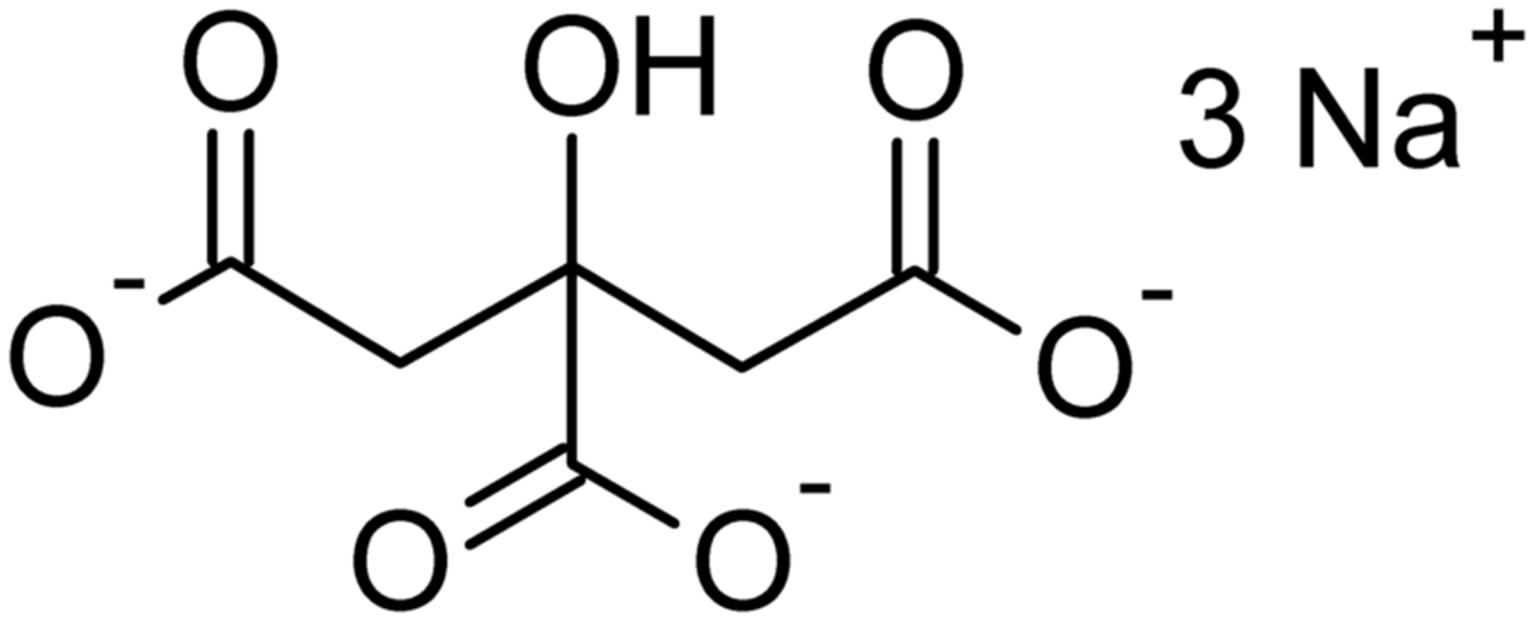
Citrate Dialysate Anticoagulation and Adequacy

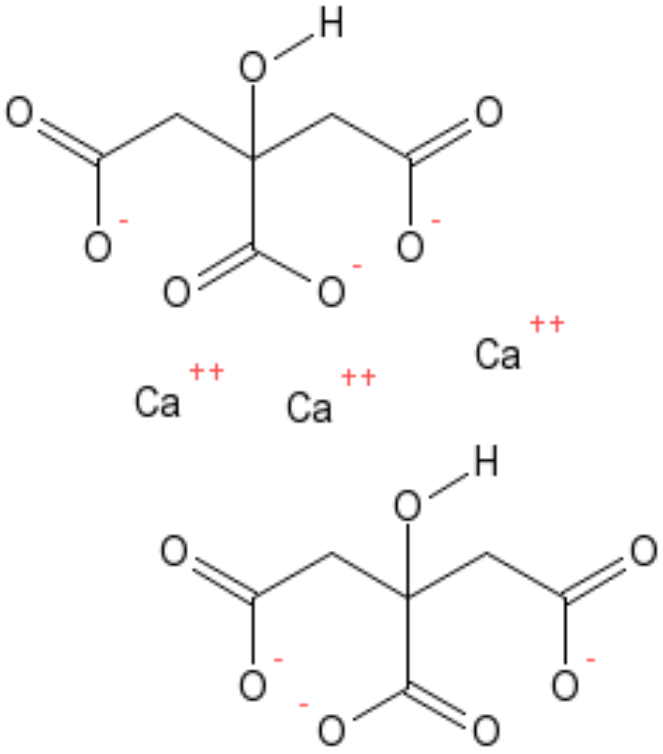
SKC In-service Sept 2015

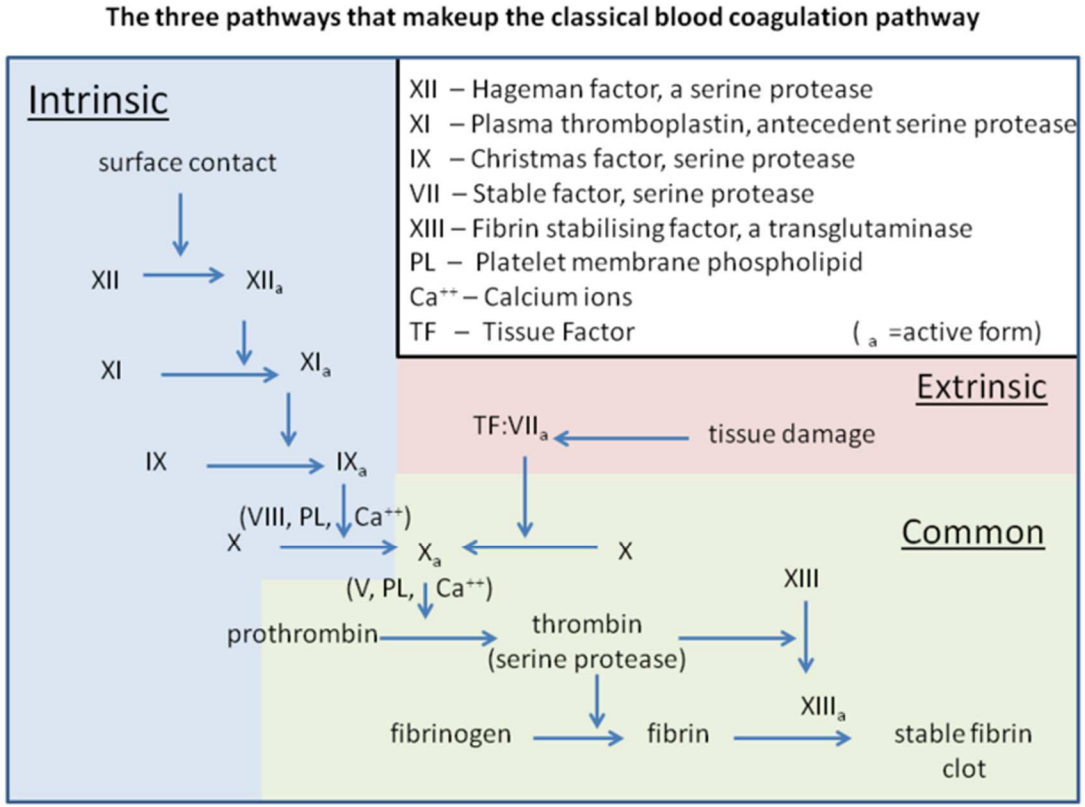
Citrate



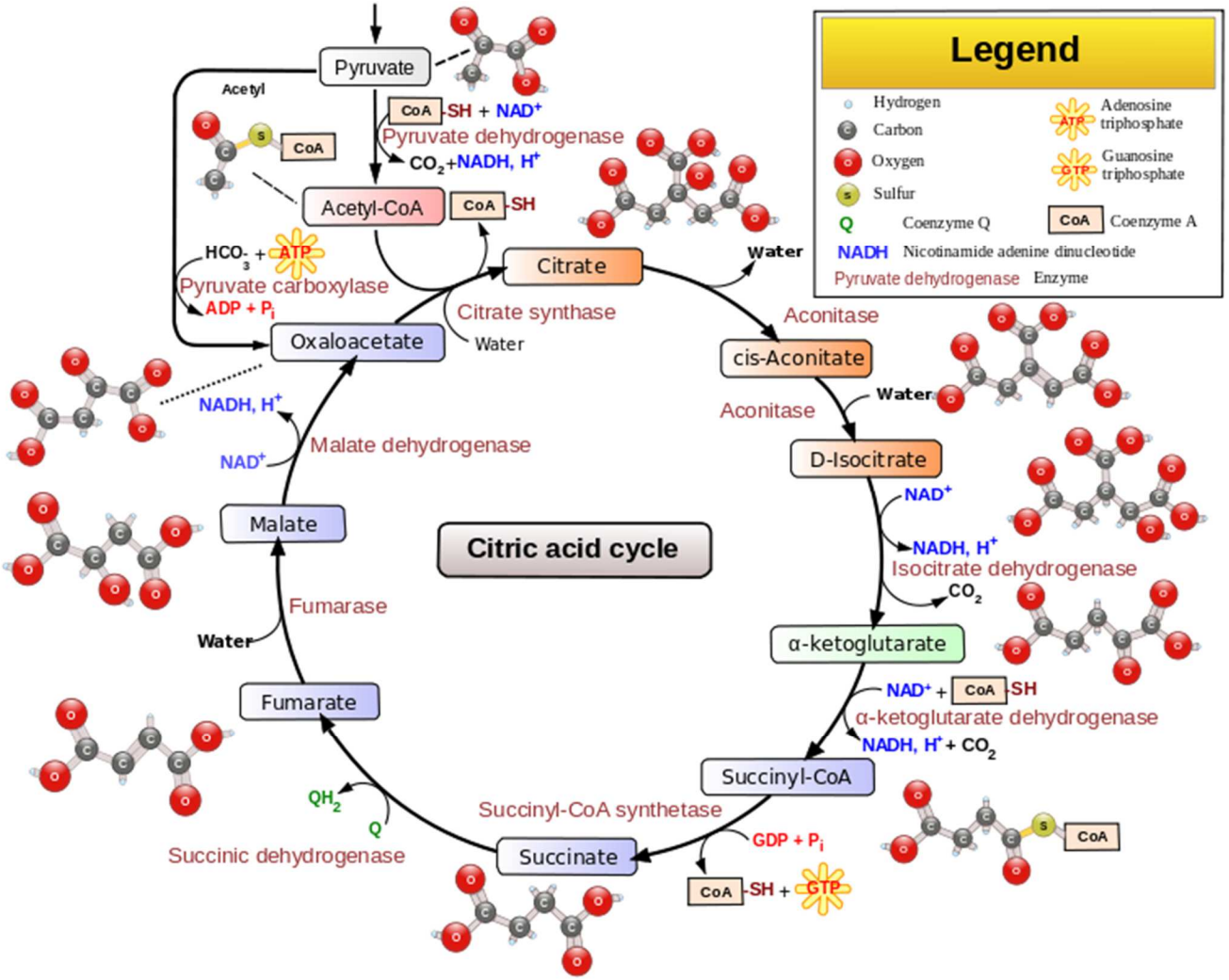
Trisodium citrate salt, solid at room temperature

How it works


H
O
O
O
O
O
O
O
O
Ca ++
Ca ++
Ca ++
H
O
O
O
O
O
O
O

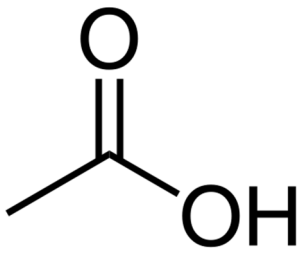

The three pathways that makeup the classical blood coagulation pathway
Intrinsic
surface contact
XII
XII$_a$
XI
XI$_a$
IX
IX$_a$
(VIII, PL, Ca^{++})
X
X$_a$
X
(V, PL, Ca^{++})
prothrombin
thrombin
(serine protease)
XIII
XIII$_a$
fibrinogen
fibrin
stable fibrin
clot
XII – Hageman factor, a serine protease
XI – Plasma thromboplastin, antecedent serine protease
IX – Christmas factor, serine protease
VII – Stable factor, serine protease
XIII – Fibrin stabilising factor, a transglutaminase
PL – Platelet membrane phospholipid
Ca^{++} – Calcium ions
TF – Tissue Factor
($_a$ =active form)
Extrinsic
TF:VII$_a$
tissue damage
Common

What happens to citrate in the body?



$$CO_2 + H_2O \rightleftarrows H_2CO_3 \rightleftarrows HCO_3^- + H^+$$

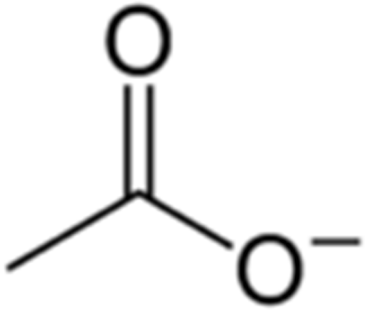
Acetate



Acetic Acid
Liquid at room temperature

(Naturalyte 4mEq/L)

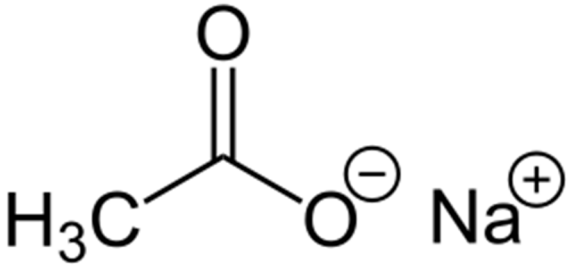
+ HCO3- =



Acetate

+ CO2

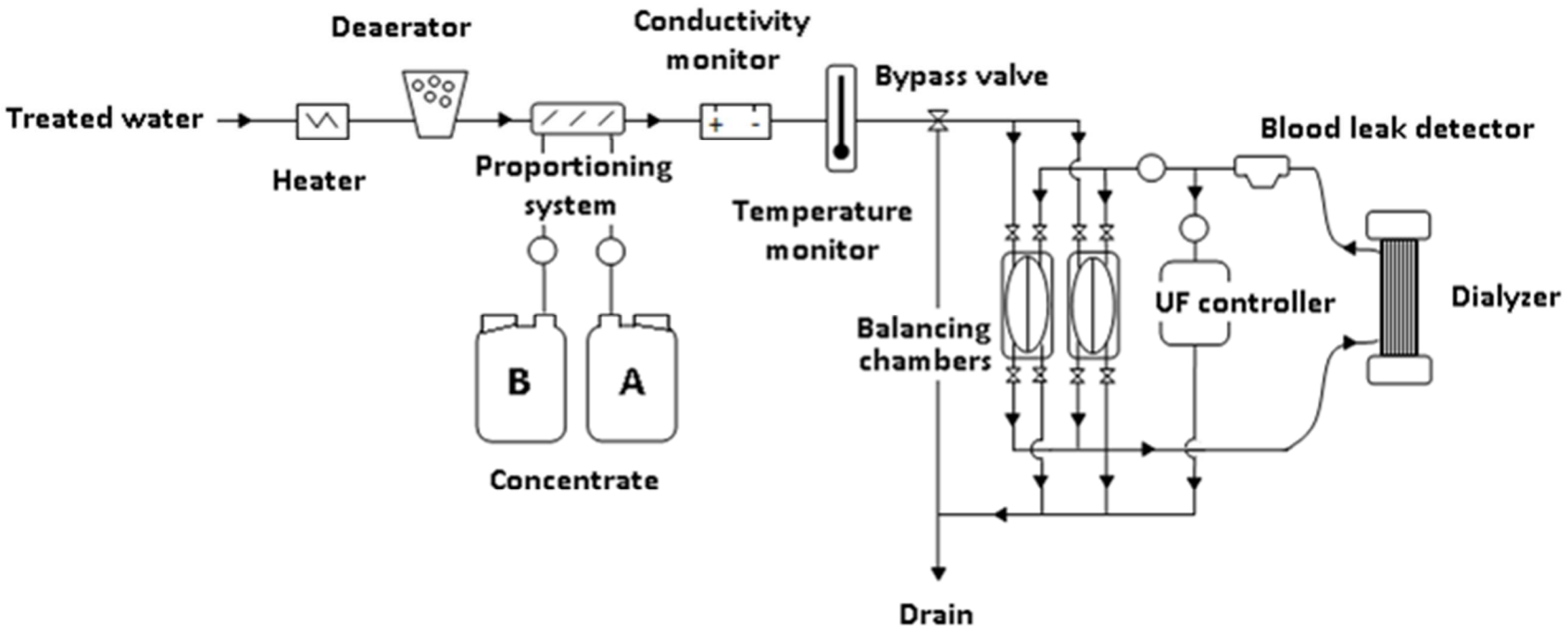
H20



Salt: Sodium acetate trihydrate

(Granuflo 8mEq/L)

Proportioning



Acetic acid or citric acid necessary to acidify dialysate to maintain a physiologic pH

Acetate

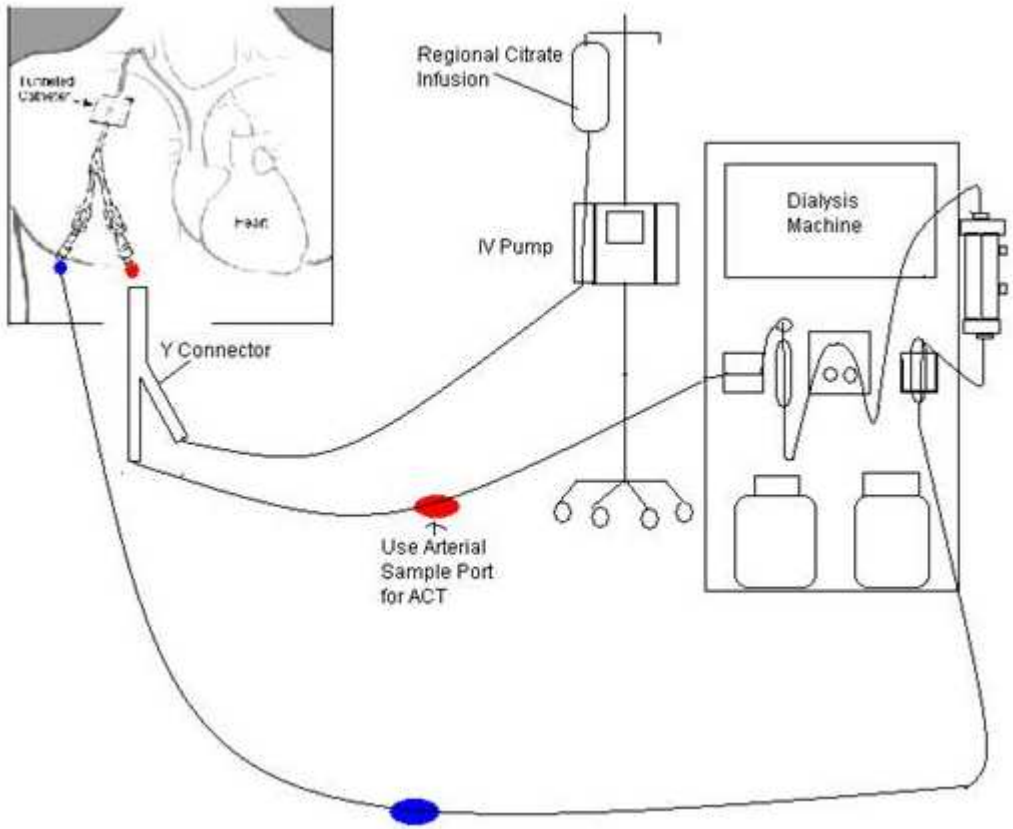
- Normal plasma level < 100 µmol/L
- Post dialysis levels 100-500 µmol/L
- Single acetate bath post dialysis level 2-10 mmol/L
  - Nausea, hypotension, alteration in mentation, hypoxia, fatigue, increased inflammation
- Dependent upon metabolism in liver, and to lesser extent muscle
- Older more comorbid population (liver disease, malnourished, low muscle mass) may be less able to metabolize acetate and more prone to adverse reaction, especially with newer dialysis Rx (high flux, higher flows, etc)

Citrate

- Regional anticoagulation -> 1mmol/L in serum
- Half life 30-60 min, liver cleared, kinetics similar in normal patients and ESRD patients
- Serum level increases to 0.17 mmol/L (with 2.4mEq/L or 0.8mmol/L) and back to normal in 1 hour post dialysis
- Estimate 0.5-0.8 mmol/L concentration in dialysis circuit which provides light anticoagulation
- Expect a 50% reduction in clearance with liver failure
- One molecule of citrate generates 3 HCO3-

Regional Citrate

- Requires close monitoring so is typically reserved for inpatient settings



When would a patient need citrate dialysate?

- History of Heparin Induced Thrombocytopenia (HIT)
- Severe clotting problems
- Bleeding risk factors or active bleeding
- Acetate reactions

Citrasate

- Studies have suggested the following in regards to citrasate:
  - Improved urea kinetics
  - Reduction in heparin dose
  - Reduction in systemic inflammation
  - Improvement in patient well-being
  - Use is safe both in chronic dialysis and inpatient dialysis
- Data is observational and subject to bias, RCTs available to inform our decisions are limited
- Potential problems with Citrasate:
  - Hypocalcemia
  - Hypomagnesemia (?Torsades / SCD)
  - Alteration in A bath will require close monitoring of dialysate proportioning / final electrolyte concentrations
  - ? Cost

Why is anticoagulation required for Hemodialysis?

- Classically the uremic condition is thought to predispose patients to bleeding disorders or platelet dysfunction. This concern does not apply to well dialyzed patients.

- ESRD patients are at higher risk of clotting problems related to underlying systemic inflammation and endothelial injury which can activate the clotting cascade

What happens if I do not anticoagulate?

- Overt clotting of circuit
  - Usually clotting occurs at the dialyzer or venous drip chamber filter
  - Potential for significant blood loss (circuit volume ~300mL; 1 Unit PRBC ~250mL)
  - Lost treatment time / clearance with new setup of clotted circuit
- Insidious clotting of circuit
  - Clotting can occur during treatment that is not obvious or detectable
  - Activation of clotting cascade and inflammatory factors
  - Loss of dialyzer fiber bundle volume / surface area leading to loss of clearance

Anticoagulation and Adequacy

- Subacute loss of fiber bundle volume can decrease membrane surface area leading to a reduction in clearance
- Inability to reach URR or spKt/V targets