Renal handling of substances

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II. Water reabsorption

- Osmosis
- Aquaporins
- Aquaporin-1, 2, 5, 9- present in the kidney.

PT-

- Passively reabsorbed (67%).

LOH –

✓ Descending thin segment : Passively reabsorbed (15%)

✓ Ascending thin segment : Impermeable

✓ Thick ascending limb : Impermeable

DT & CD - (8–17%)

✓ Distal convoluted tubule : Impermeable

✓ Connecting tubule (CNT) : Impermeable

✓ Cortical CD : Reabsorbed (ADH)

✓ Outer & inner medullary CD : Reabsorbed (ADH)

Obligatory reabsorption. (MUST)

- About 85% of filtered water is always reabsorbed, irrespective of body water balance.
- This reabsorption occurs by osmosis in response to a transtubular osmotic gradient
- 67% of obligatory reabsorption occurs in PT and 15−18% of obligatory in descending thin segment of LOH.

Facultative reabsorption. (OPTIONAL)

- Remaining 15−18% of water may or may not be absorbed depending upon body water balance.
- Occurs in CD (under control of ADH)

III. RENAL HANDLING OF POTASSIUM

Functions of K+

1. Maintenance of intracellular osmotic pressure
2. Optimal activity of enzyme pyruvate kinase (of glycolysis)
3. Proper synthesis of DNA and proteins by ribosomes
4. Optimal cell growth
5. Transmission of nerve impulse
6. Generation of cell memb. potential & muscle contraction
7. Extracellular K+ influences cardiac muscle activity
8. Regulation of acid-base & water balance in cells.

Glomerular filtration

- Filtration occurs freely

Tubular reabsorption & secretion

- PT -67% reabsorption
- LOH- 20%
- Early DT-10%
- CD - either reabsorb or secrete K+.
- Role of reabsorption or secretion by DT & CD depends on hormones.

1.Reabsorption of K+ by PT

1. 7% - by passively in proportion to H2O reabsorption (solvent drug)
2. 60% -Paracellular transport

a) Concentration gradient created between paracellular space & tubules fluid by active K+ uptake via Na+–K+–ATPase located in lateral cell membrane

b) Diffusion of K+ along concentration gradient occurs from tubular lumen into lateral intercellular spaces.

luminal fluid equilibrates with low K+ conc. in intercellular space.

c) Exit from basolateral membrane

i. Conductive K+ channel

ii. K+–Cl– co-transporter

iii. Na+–K+–ATPase pump

- K+ that exits from basolateral membrane is immediately absorbed in peritubular capillaries.

2.Reabsorption of K+ by LOH

- 20% - thick ascending limb along with Na+ reabsorption

1. $Na^+ – K^+ – 2Cl^-$ active transport

2. Paracellular passive reabsorption occurs as a function of voltage gradient across the thick ascending limb.

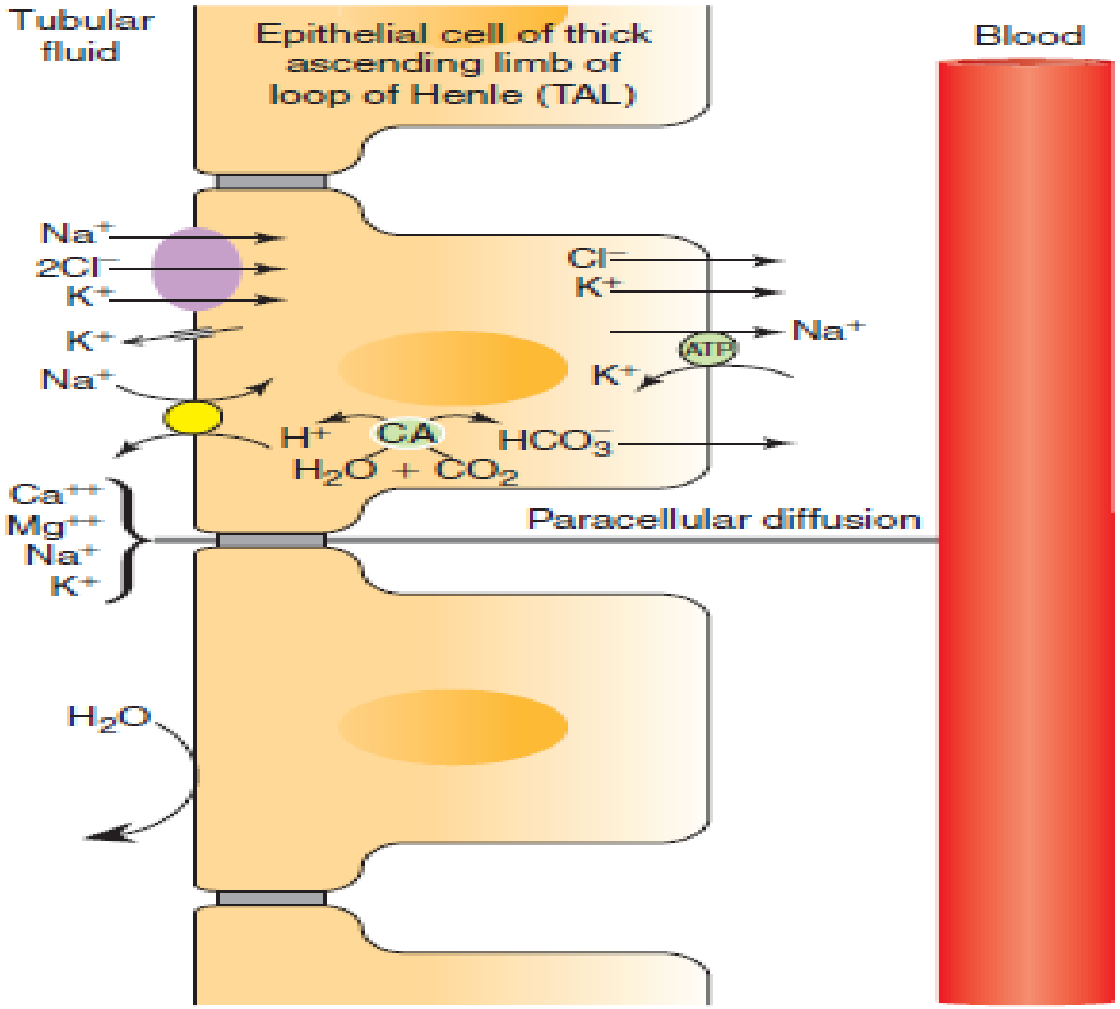


Fig. 6.2-9 The active (transcellular) and passive (paracellular) transport mechanism operating across the tubular cells in thick ascending limb (TAL) of loop of Henle.

Reabsorption & secretion of K+ by DT & CD

Early DT

- Normally, K+ is secreted.
- During K+ depletion, K+ is reabsorbed.

Late DT & CD

- Reabsorb or secrete K+, depending upon dietary intake

- Reabsorption of K+ - when dietary intake is very low

- K+ excretion low 1% of the filtered load because kidneys conserve as much K+ as possible.

Secretion of K+

- Principal cells are involved in K+ secretion.
- Depending upon dietary K+ intake, aldosterone levels, acid−base status and urine flow rate.

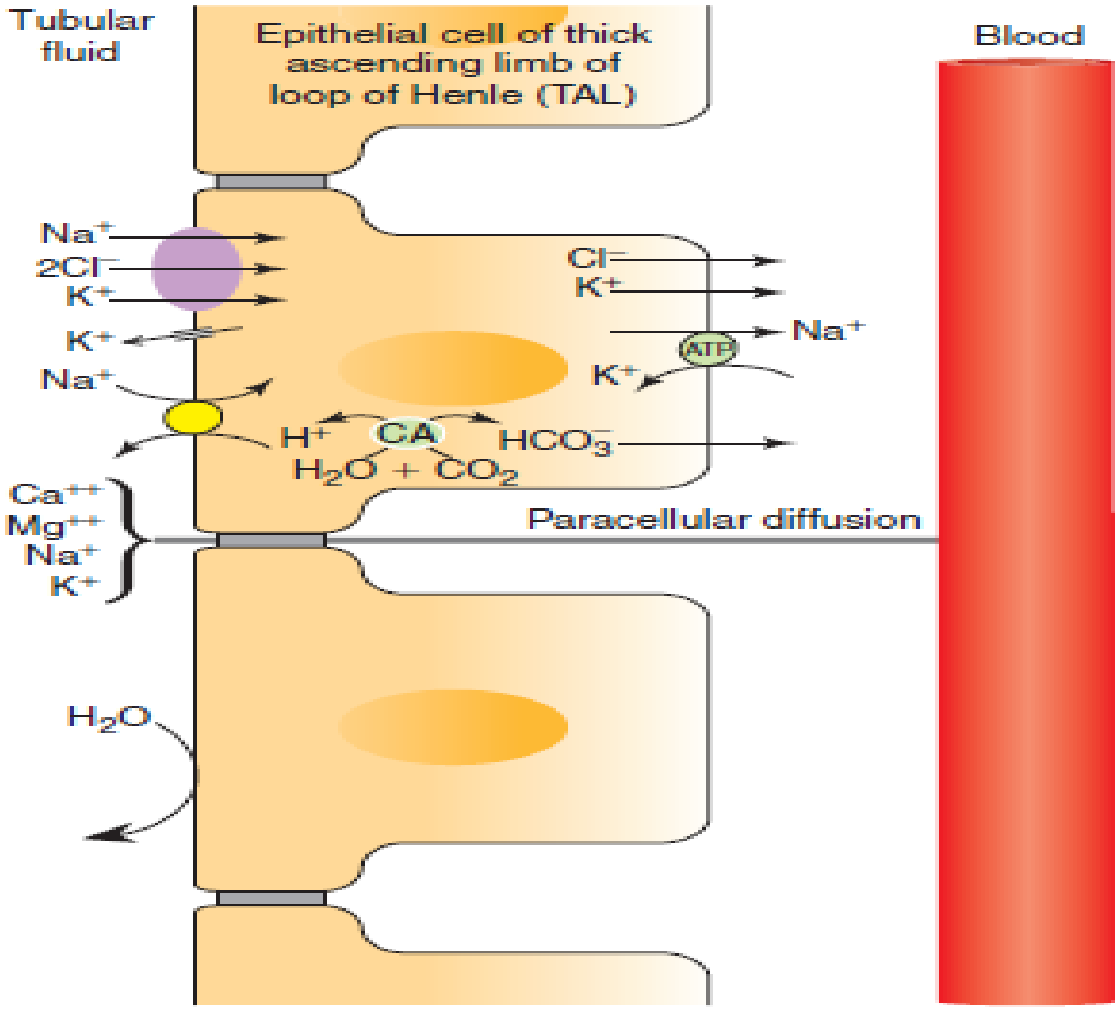
Mechanism of K+ secretion

1. At basolateral membrane,

- K+ is actively transported into cell by Na+−K+−ATPase.
- Mechanism maintains high intracellular K+ concentration.

2. At apical membrane

- K+ passively secreted into lumen via K+ channels, down its electrical & chemical gradient.



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Regulation of K+ tubular secretion

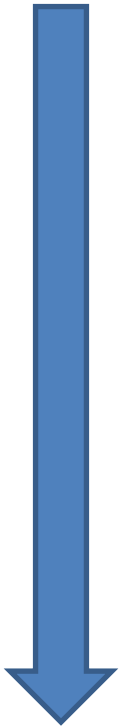
1. Plasma K+ level

- Hyperkalaemia -High K+ diet or rhabdomyolysis stimulates K+ secretion within minutes.
- Hypokalaemia- low K+ diet or diarrhoea, decreases K+ secretion

2. Aldosterone.

- Hyperkalaemia & angiotensin II - Aldosterone secretion increased
- Hypokalaemia & ANP- Aldosterone secretion is decreased

Chronic rise in aldosterone level



Increases K+ secretion by principal cells

Mechanisms

1. By increasing Na+–K+–ATPase activity.

leads to increased pumping of Na+ out of cell at basolateral membrane &

Increased Na+ entry into cells across luminal membrane.

2. By making transepithelial potential difference (TEPD) more lumen negative.

3. By increasing permeability of apical membrane to K+

3. Glucocorticoids

- Indirectly work
- Increase K+ excretion by increasing GFR which increases tubular flow which increases K+ secretion.

4. ADH

- Increases Na+ & water reabsorption

➢ ADH-induced increased Na+ uptake across luminal membrane creates an electrochemical gradient which increases K+ secretion into lumen

- Decreases tubular flow which in turn decreases K+ secretion

- Inhibitory effect + stimulatory effect = maintained constant level despite wide fluctuations in water excretion.

5. Flow of tubular fluid.

- Increase flow –

Increases K+ secretion rapidly,

- Decrease flow –

Decreases secretion of K+ by DT & CD

6. Acid–base balance

K+ secretion affect by DT & CD

Acute acidosis reduces K+ secretion by

1. By decreasing Na+–K+–ATPase activity across basolateral membrane

   It reduces intracellular K+ Conc.

- Reduces electrochemical driving force for K+ exit across apical membrane.

2. By reducing permeability of apical membrane

- It decreases K+ secretion & tends to increase intracellular K+ Conc.

Net result = K+ constant

Acute alkalosis : opposite effects

3.RENAL HANDLING OF GLUCOSE

1. PT

- Active transport mechanism

1. Carrier mediated Na+–glucose co-transport.

- **Apical membrane –**

➢ Carrier protein - in early PT -SGLT-2 & late PT - SGLT-1

➢ (SGLT = sodium-dependent glucose transporter)

- **Basolateral surface**

➢ Carrier is driven by Na+ concentration gradient

2. Facilitated diffusion

- Moves glucose out of cell via basolateral membrane.
- Carrier protein in early PT - GLUT-2 & late PT - GLUT-1

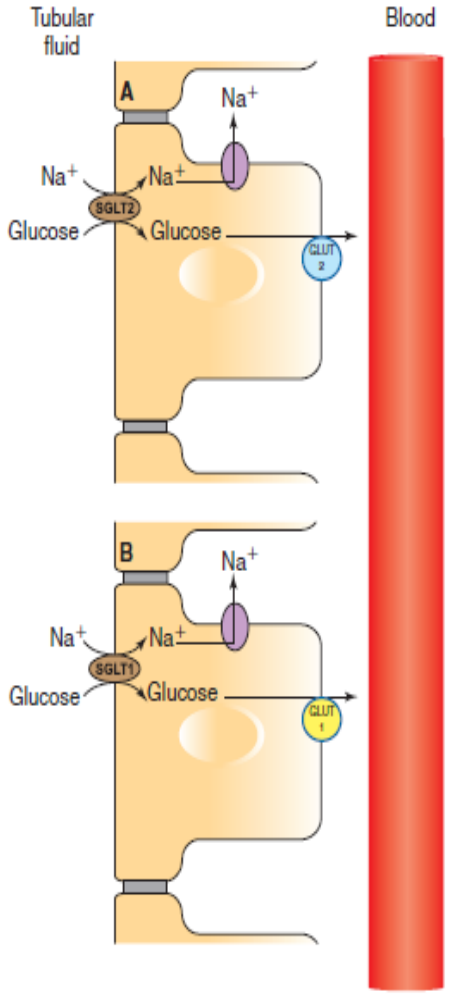


Fig. 6.2-14 Mechanism of glucose reabsorption in: A, early proximal tubule and B, late proximal tubule.

Characteristics

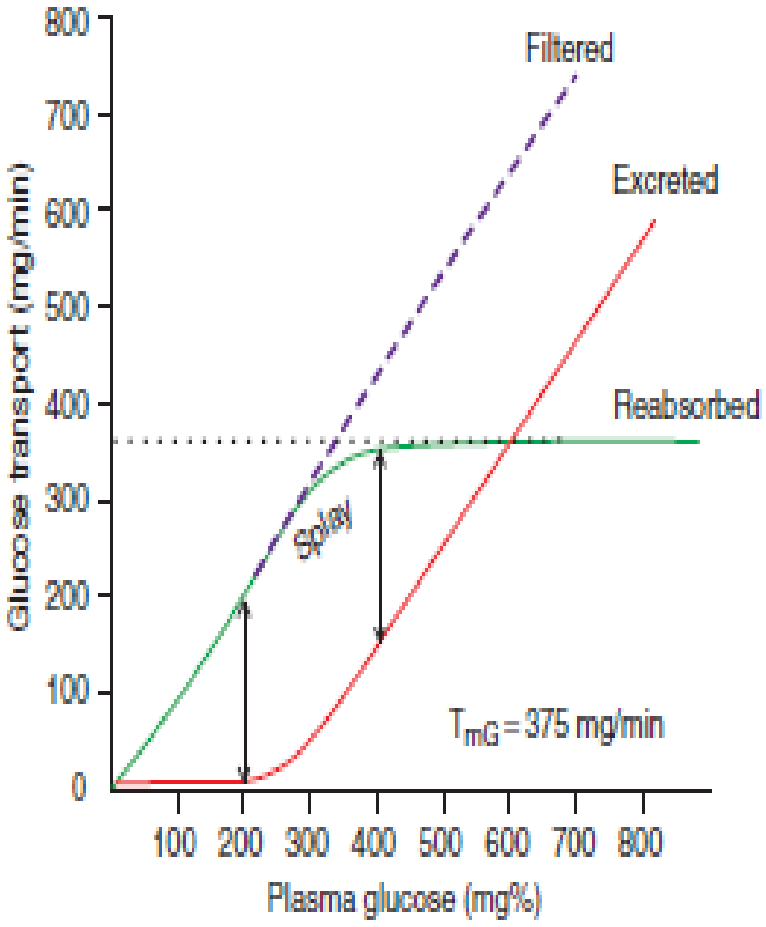


Fig. 6.2-15 Glucose titration curve (for details see text).

Filtered load increases with plasma glucose conc.

Renal threshold

- Plasma glucose conc. At which glucose first appears in urine (glycosuria =180–200 mg/dL)
- At plasma levels below renal threshold

Transport maximum (Tm)

- Plasma conc. at which carriers are fully saturated.
- Beyond plasma glucose conc. Of 350 mg/dL (TmG) reabsorption rate does not increase. i.e. becomes constant and is independent of PG.
- As TmG is reached, urinary excretion rate increases linearly with increase in plasma glucose conc.

Splay

- Region of glucose curve between threshold & TmG, i.e. between PG 180 & 350 mg/dL.

- It represents excretion of glucose in urine before TmG is fully achieved.

- In region of splay,

1. Reabsorption curve - rounded

- Though reabsorption rate is increasing with increase in PG, but reabsorption is less than filtration.

2. Excretion curve - rounded

- Though urinary excretion is increasing with increase in PG, but there is no linear relation.

- Causes of splay are:

1. Heterogenicity in glomerular size, proximal tubular length & number of carrier proteins for glucose reabsorption.
2. Variability in TmG of nephron.

variability in number of glucose carrier, transport rate of carriers & binding affinity of Na+ glucose carriers.

4.RENAL HANDLING OF PROTEINS,PEPTIDES & A.A

Normal

- 100-150 mg
- In that 15 mg - albumin
- Rest –LMWP(25 mg of LMWP -Tamm−Horsfall proteins derived from cells of TAL, rest derived from plasma)

Proteinuria - More than 150 mg/day in urine

Types:

a. **Glomerular proteinuria**
b. **Tubular proteinuria -** e.g. in tubulointerstitial disorders & Fanconi's syndrome,
c. **Overflow proteinuria -**

When in body LMWP increased, LMWP filtered > reabsorptive capacity of tubules. e.g. in multiple myeloma (Bence−Jones protein appear in the plasma)

d. **Nephrogenic proteinuria -**

Damage to PT cells, tubular enzymes are released in urine e.g. N-acetyl β-glucosaminidase (NAG) & γ-glutamyl transferase (γ-GT)

5.RENAL HANDLING OF UREA

Glomerular filtration

- Freely filtered
- Varies with protein intake.

Tubular transport

- PT reabsorb 5% urea passively.
- PST,descending & ascending thin segment (ATS) - receive urea by diffusion (secretion)

Thick ascending limb, DCT, CNT, CCD & OMCD are all impermeable to urea.

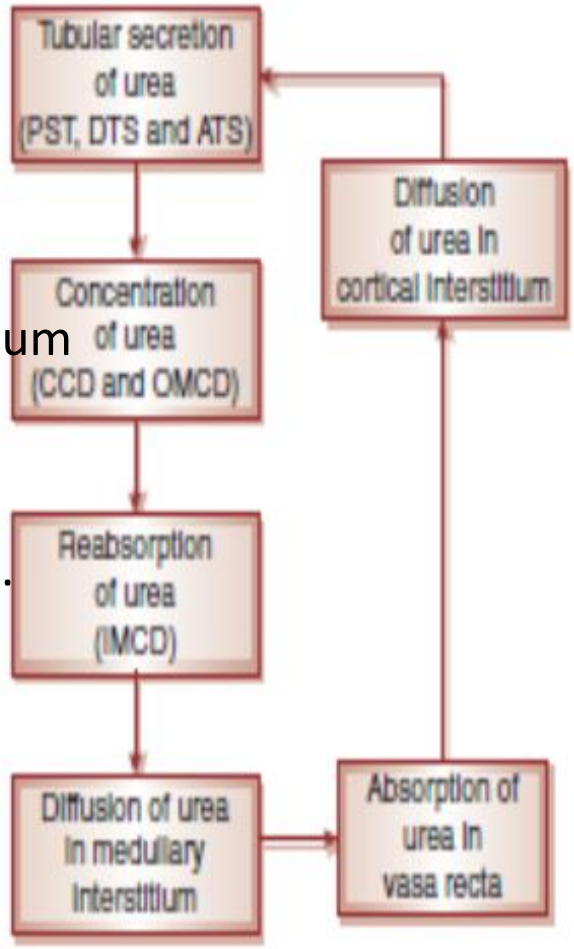
IMCD - reabsorbs large amount of urea by specialized urea transport protein (UT-A)

- In kidneys (UT-A1−UT-A4) , in RBC -UT-B
- This protein is stimulated by ADH, which increases urea permeability of the IMCD.

Urea recycling

1. Concentration of urea in CCD & OMCD
2. Rapid ,massive reabsorption of urea by IMCD
3. Carriage of urea by vasa recta to cortex interstitium
4. Tubular secretion of urea fromrenal cortical interstitium occurs into PST of cortical nephrons.

- Important role in countercurrent system



6.RENAL HANDLING OF URIC ACID

Glomerular filtration –

- Freely filtered

Tubular transport

- Early PT - reabsorbs 95%
- Mid PT- secrete 50%
- Late PT - reabsorbs 40% ,
  post-secretory reabsorption

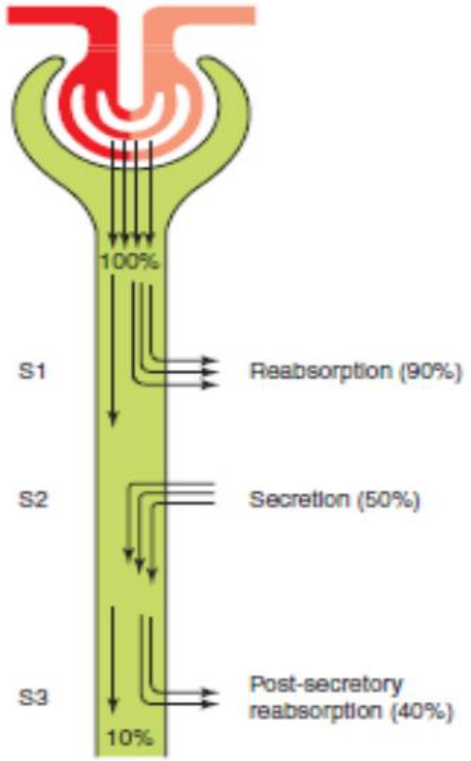


Fig. 6.2-17 Tubular transport of uric acid: reabsorption, secretion and post-secretory reabsorption.

Mechanism of reabsorption

1. Passive reabsorption via paracellular pathway.
2. Secondary active transport
   Transcellular pathways (carrier protein - urate transport protein)

7.RENAL HANDLING OF PAH

PAH

- Exogenous weak organic acid
- Neither stored nor metabolized & is excreted virtually unchanged in urine.
- USE- PAH clearance used to measure renal plasma flow

- 10% of PAH is bound to plasma proteins, so it is cleared from plasma both by glomerular filtration & by tubular secretion

1. As with glucose, filtered load of PAH increases in direct proportion to plasma PAH conc.
2. Secretion of PAH - Tm limited process. antiporte

Table 6.2–4 Some organic anions and cations secreted by proximal tubule cells

Anions secreted by proximal tubule

Endogenous anion	**Drugs**
PAH	Acetazolamide
cAMP	Furosemide
Bile salts	Penicillin
Oxalate	Probenecid
Prostaglandins	Salicylate (aspirin)
Water	NSAIDs

Cations secreted by proximal tubule

Endogenous cation	**Drugs**
Creatinine	Atropine
Dopamine	Cimetidine
Epinephrine	Morphine
Norepinephrine	Quinine
	Procainamide
	Verapamil