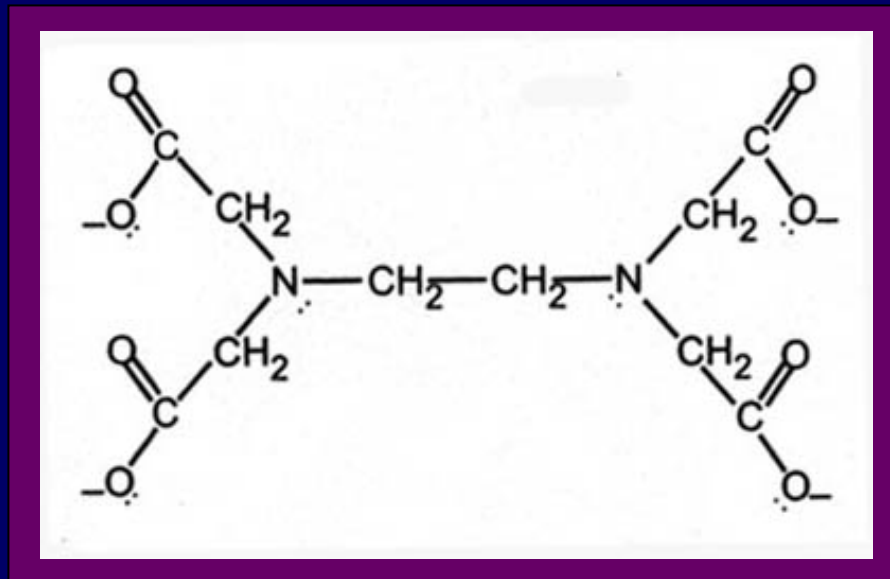
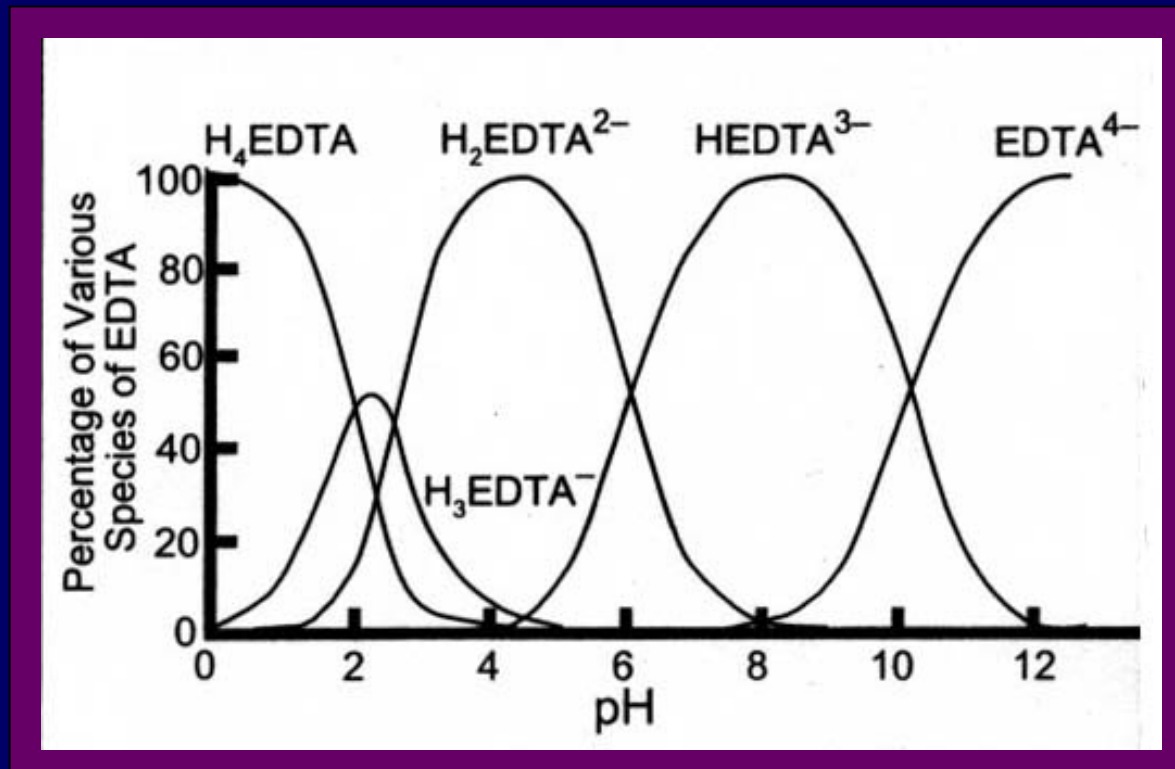

The Pharmacology of EDTA Chelation

Ethylene Diamine Tetraacetic Acid



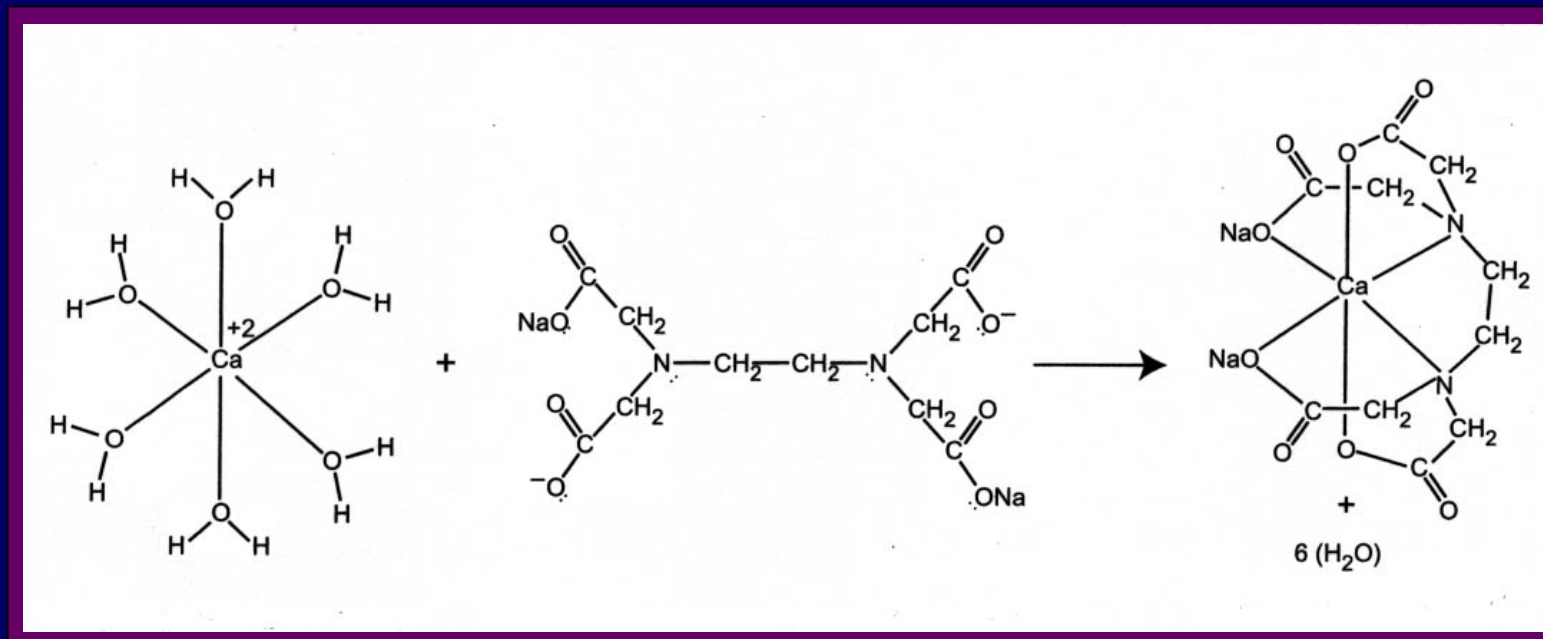
Amino Polycarboxylic Acid

Concentration of EDTA Species by pH



Bell CF. Metal Chelation. Principles and Applications. 1977.

Chelation of Ca^{++} by EDTA



EDTA Metal Complex Equilibrium Constants

METAL	VALUE (log)	METAL	VALUE (log)
Ba ²⁺	7.76	Sm ³⁺	17.14
Sr ²⁺	8.63	Eu ³⁺	17.35
Mg ²⁺	8.69	Gd ³⁺	17.37
Ca ²⁺	10.96	Tb ³⁺	17.93
V ²⁺	12.70	Y ³⁺	18.09
Mn ²⁺	14.04	Dy ³⁺	18.30
Fe ²⁺	14.33	Ni ²⁺	18.62
La ³⁺	15.50	Ho ³⁺	18.74
Ce ³⁺	15.98	Cu ²⁺	18.80
Al ³⁺	16.13	Er ³⁺	18.85
Co ²⁺	16.31	Tm ³⁺	19.32
Pr ³⁺	16.40	Yb ³⁺	19.51
Cd ²⁺	16.46	Lu ³⁺	19.83
Zn ²⁺	16.50	Hg ³⁺	21.80
Nd ³⁺	16.61	Fe ³⁺	25.10
		V ³⁺	25.90

Metals Consistently Removed by EDTA Chelation

Calcium

Cadmium

Zinc

Manganese

Copper

Vanadium

Iron

Lead

Perry HM Jr, Perry EF. J Clin Invest 1959.

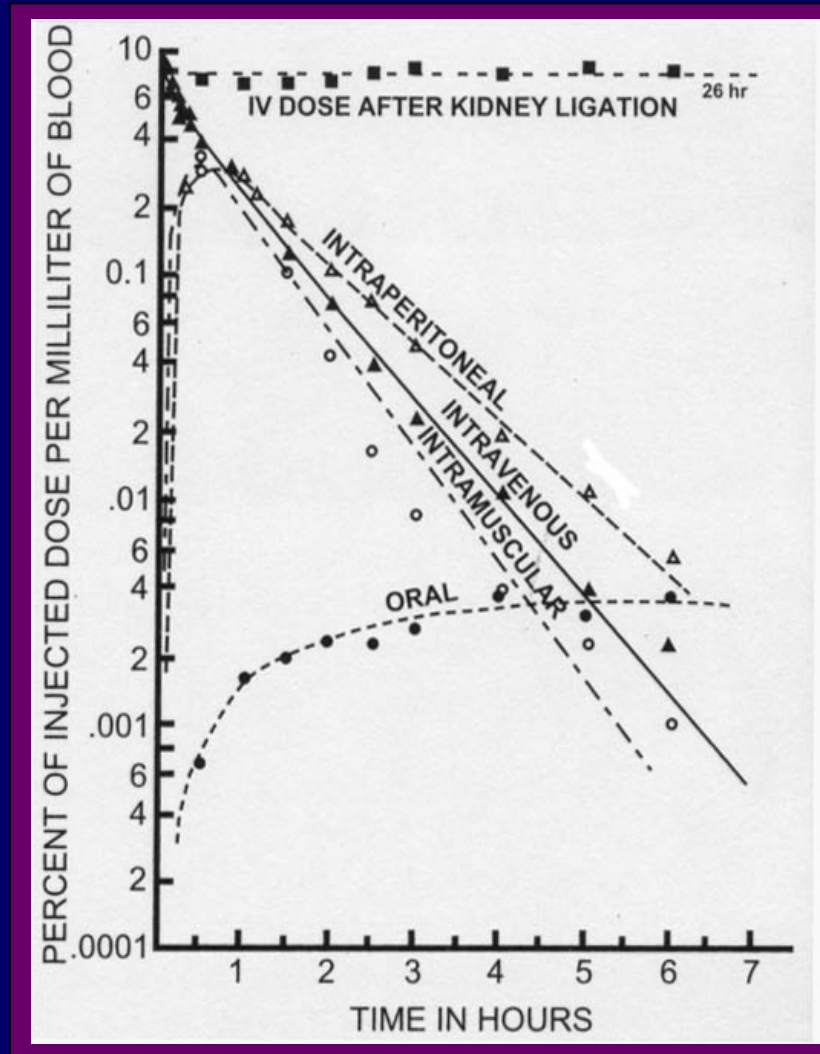
Chelation of Ca^{++} by EDTA

- **45-72% efficiency chelating Ca^{++}**
- **28% excess Ca^{++} excreted during infusion**
- **60% excess Ca^{++} excreted 6 hrs post infusion**
- **12% excess Ca^{++} excreted 6-12 hrs post infusion**
- **Serum ionized Ca^{++} reduced**
- **Up to 3.2 mg/dL Ca^{++} bound during infusion**

Response to EDTA-induced Hypocalcemia

- Protein bound Ca^{++} ionized
- Soft tissue Ca^{++} ionized
- PTH secretion induced
- Calcitriol (Vitamin D3) synthesis induced
- Bone resorption stimulated
- Osteoclast differentiation stimulated
- Osteoblast differentiation suppressed

Absorption of Disodium EDTA



Foreman H, et al. J Biol Chem 1953.

Pharmacodynamics of EDTA

- **Poorly absorbed PO – 5-10% dose**
- **Oral dose absorbed in colon**
- **Does not cross the skin**
- **Does not cross the blood brain barrier well**
- **Volume distribution ~ECF**
- **No significant metabolism**
- **Rapid renal excretion - 98% within 24 hrs**

EDTA General Toxicity

- **Safe drug**
- **LD₅₀ 500 - 7000 mg/Kg species dependent**
- **Tetany, seizures, and death**
- **IP LT₅₀ 78 days (CI 35-170 days) in cats**
- **IV LT₅₀ 18.5 days (CI 12-28 days) in dogs**
- **Toxicity consistently exaggerated by critics**

EDTA Renal Toxicity

- **Most important clinical adverse effect**
- **Proximal convoluted tubules**
 - Loss of epithelial cells**
 - Dilated, vacuolated cells**
- **Distal convoluted tubules**
 - Desquamated epithelial cells**
 - Eosinophilic casts**
- **16 day ED₅₀ 203 mg/Kg (CI 131-314 mg/Kg)**
in rats (62.5 mg/Kg x 16 days not toxic)
- **Clinical issue in Pts with abnormal CrCl**

EDTA Reported Toxicities

- **“Vitamin B” & Trace Metal Deficiencies**
- **Local pain, phlebitis, & thrombophlebitis**
- **Hypotension**
- **Gastrointestinal Sx - nausea, abdominal pain**
- **Glycosuria, hypoglycemia, glucose control**
- **Cerebral embolism & stroke**
- **Clotting parameters**
- **Cardiac effects**
- **Miscellaneous effects**

**“The only difference between
a poison and a medicinal,
is the dose.”**

Paracelsus
