Calcium

	II. a	
4	^{20}Ca 40,08	

↓

1 g Ca ≈ 25 mmol Ca

Calcium in the body : the whole calcium 1,0 – 1,3 kg

- **body fluids** 1 %
  - **ECF** 0,1 %
    - **blood plasma** 375 mg, 2,5 mmol / l
    - **IST**
  - **ICF** 0,99 %
- **bones** 99 %

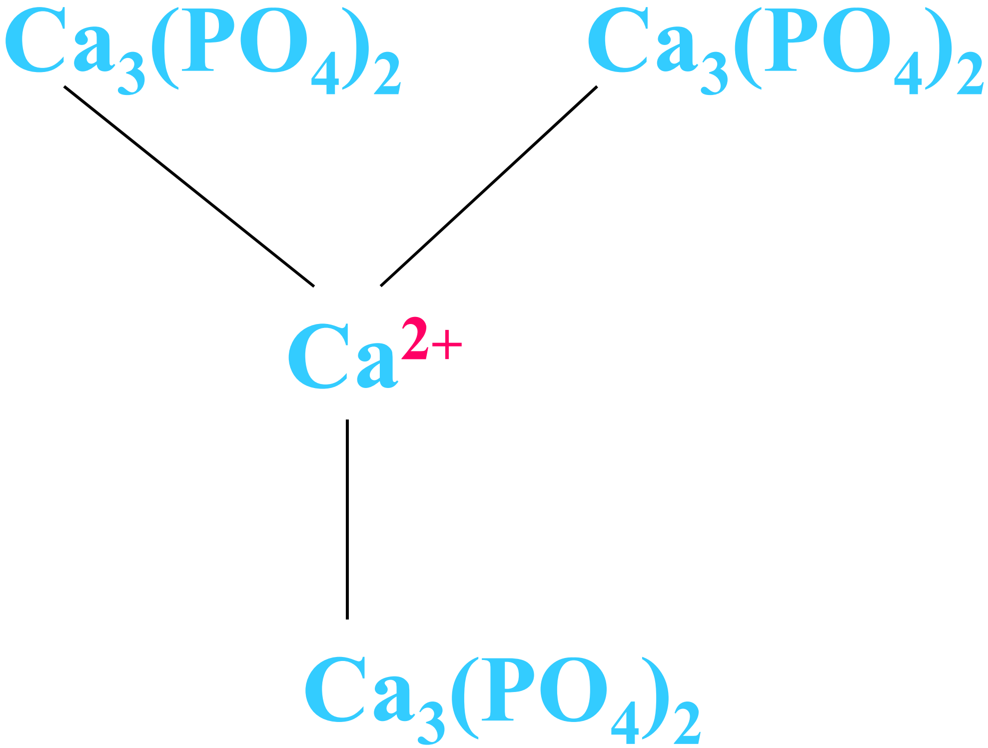
blood plasma →

50 % free, ionized Ca (1,25 mmol / l)
32 % Ca binding to albumin (0,8 mmol / l)
8 % Ca binding to globulins (0,2 mmol / l)
10 % Ca in complexes with anions (0,25 mmol / l)

→ **hydrogencarbonates, lactate, phosphate, …**

Only free ionized calcium is physiologically effective !!

Apatit/e :



$Ca_{10}P_6O_{24}^{2+}$

Carbonatapatite, hydroxyapatite :

$Ca_3(PO_4)_2$ $Ca_3(PO_4)_2$

Ca^{2+}

$Ca_3(PO_4)_2$

CO_3^{2-}

$2\ OH^-$

↓

hydroxyapatite is the main structural component of bone
≈ 65 % of bone weight

Fluoroapatit/e :

$Ca_3(PO_4)_2$ $Ca_3(PO_4)_2$

Ca^{2+} $2\ F^-$

$Ca_3(PO_4)_2$

(dentin/e)

Insoluble calcium salts :

$CaCO_3$ - $Ca(HCO_3)_2$ is „soluble“ it exists in water solution only !

$Ca(COO)_2$

$CaSO_4$ (only slightly soluble – it produces the permanent hardness of water)

$Ca_3(PO_4)_2$

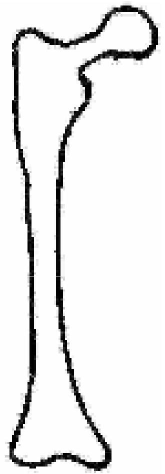
$CaHPO_4$ - $Ca(H_2PO_4)_2$ is soluble

Occurrence and movement of calcium in the body :

Daily intake approximately
25 - 30 mmol

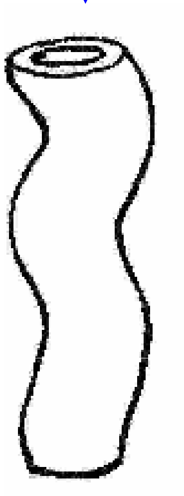
(phosphate, oxalate, phytate)

Mineral deposit
25 mol Ca
(rapidly exchangeable 100 mmol)



remodeling of bone
7,5 mmol / d

rapid exchange
500 mmol / d



absorption
up to 15 mmol / d

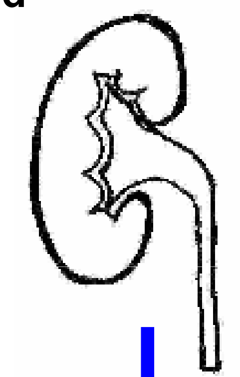
secretion
up to 7 mmol / d

ECF
2,5 mmol / l
total 35 mmol only

ICF
signal function
0,1 µmol / l

filtration
240 mmol / d

tubular resorption
230 mmol / d



Excretion fraction max. 5 %
PTH decreases it,
calcitonin and high supply of Na^+ increases it

17 – 25 mmol /d

5 – 6 mmol /d

Calcium homeostasis :

1/ parathyrin (PTH, parathyroid hormone)

2 / calcitonin (thyreocalcitonin)

3 / calcitriol

4 / (osteocalcin)

Parathyrin (PTH) (1) :

prepro-PTH	115 AA	
pro-PTH	90 AA	
PTH	84 AA	$t_{1/2} \approx 3 - 5$ min

N-terminal sequence (28 AA) $\rightarrow$ biological activity

hypocalcemia $\rightarrow$ incr. of PTH

hypercalcemia,
calcitriol $\rightarrow$ decr. of PTH

incr. = increase/d
decr. = decrease/d

Parathyrin (PTH) (2):

membrane receptor (bone, kidney)

↓

adenylatcyclase

↓

incr. intracellular **cAMP**

↓

incr. intracellular calcium

↓

phosphorylation of protein by kinases

↓

activation of enzymes/proteins with end biological effect of hormone

Sensor for calcemia :

receptor $\rightarrow$ G_q – protein $\rightarrow$

incr. in P-Ca^{2+} has hier *inhibition* influence
(the difference from other cells !!)

sensor in parathyroid gland

Effect of PTH :

1/ bone: → osteoclast → bone resorption → incr. calcemia

2/ kidney:
- incr. resorption of Ca^{2+} → incr. calcemia, decr. calciuria
- decr. resorption of HPO_4^{2-} → incr. phosphate-uria
- incr. 1α-hydroxylation of calcidiol (prox. tubulus) → calcitriol → incr. gut resorption

3/ gut: incr. intestinal resorption (calcitriol) → incr. calcemia

Calcitonin :

(thyreocalcitonin, 32 AA)

- antagonist of PTH, effect stimulated by estrogens
- limited signification for regulation, protection against violent incr. of calcemia
- calcemia is in control of the calcitonin secretion (sensor similar to parathyroid gland)
- decr. bone resorption, incr. new production of matrix (treatment of osteoporosis)
- decr. reabsorption of Ca and phosphate in the kidney tubule → incr. exkretion of Ca and phosphate
- it is species-specific (salmon calcitonin has 50 % of AA identical with the human one)
- analgesic effect in bone pain

Calciols :

7-dehydrocholesterol (liver)

↓

calciol (skin UV)

↓

calcidiol (liver 25α-OH) → the main metabolite of calciol in plasma

(< 10 µmol / l, season differences,
$t_{1/2} \approx$ 20-30 d,
bonding to D-binding protein)

↓

calcitriol (kidney 1α-OH)

inhibition: incr. calcitriol
incr. calcitonin
excess in intake of Ca

stimulation: PTH at hypocalcemii
somatotropin

Calcitriol :

1/ enterocyte: incr. resorption of Ca into ECF – mechanismus:

- change of conformation of cytosol **calmodulin**
  → more effective bonding of Ca^{2+} →
  → easier Ca^{2+} crossing of the membrane

- **calbindin** (= CaBP = calcium binding protein)
  induction of its synthesis → possibility of Ca transport in the cell

- **Ca^{2+}-ATPase**, → induction of its synthesis
  → draw Ca from enterocyte to ECF

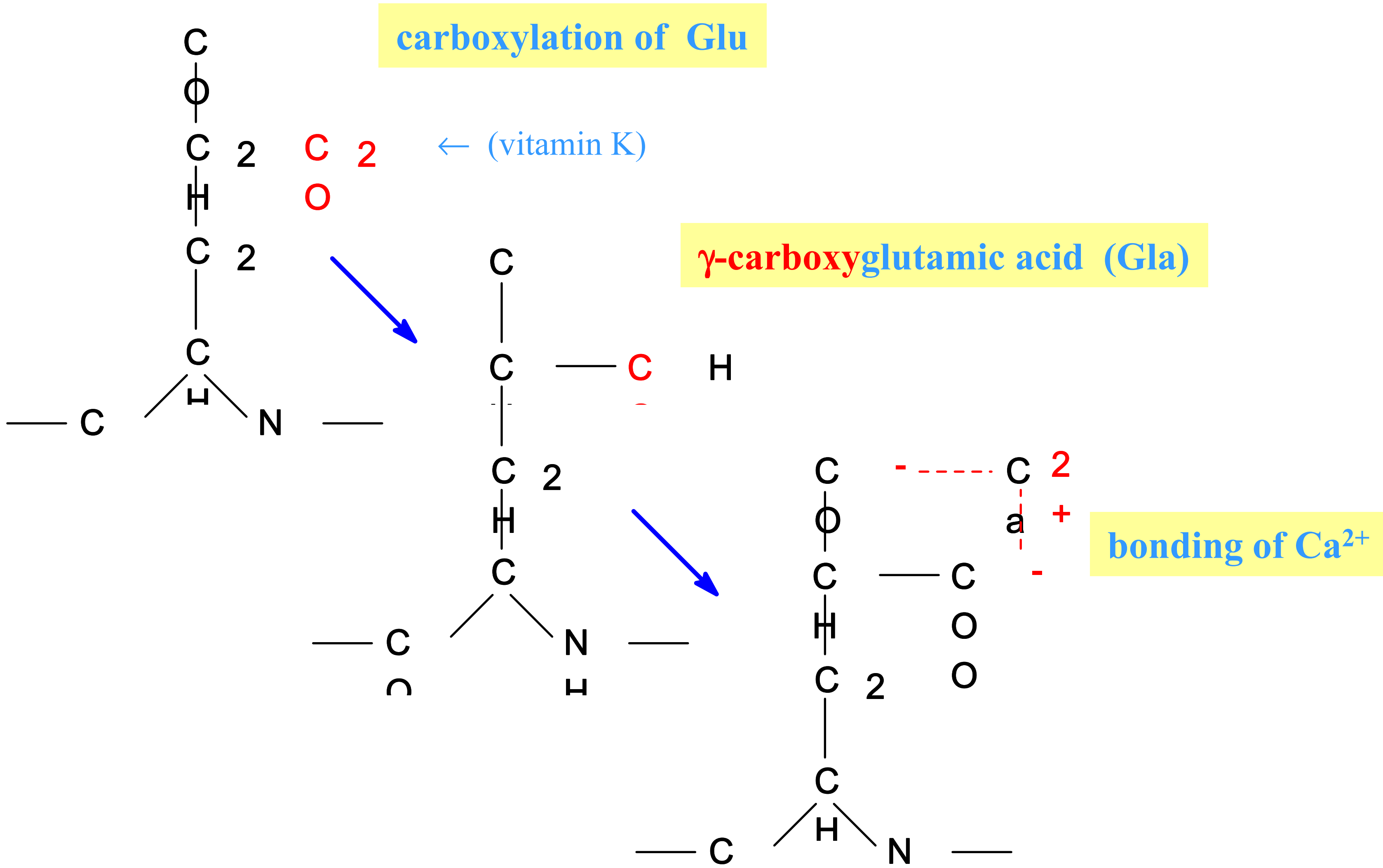
2/ bone: regulation of resorption and new formation of bone tissue = the opposite actions, the mechanismus not understandable

Osteocalcin (1) :

= BGP = bone Gla protein 49 AA $t_{1/2} \approx 4 - 5$ min

- contents 3 carboxyglutamate (Gla) for the bond of Ca^{2+} see next
- regulates the deposit of bone mineral
- marker of bone remodeling (osteoblast activity in forming of organic matrix)

Osteocalcin (2) :



Calcium (1) :

- in the Czech Republic suffers from osteoporosis every 3rd woman and every 5th man

- needed calcium ≈ 1 g / d (≈ 25 mmol / d)
  older man + woman in menopause ≈ 1,5 g Ca / d

- ½ g Ca ≈ ½ l milk
  ≈ 65 g solid cheese
  ≈ ¼ l white yogurt

Calcium (2) :

- in childhood and during adolescence we utilize ≈ 50 % from given Ca
- in adulthood we utilize ≈ 20 - 25 % from given Ca !!
- Ca is absorbed at most
  - from medium-fat dairy products
  - from some vegetable (cauliflower, Brussel sprout, chicory, broccoli)
  - from sour dairy products (sour milk, yogurt, ….)

    more Ca is absorbed from the acidic products than from milk alone !!
  - from marginal sources: poppy seed, walnut, sardines

Calcium (3) :

- **unsuitable sources of calcium**
  - spinach - high content of oxalates
    → formation of insoluble $Ca(COO)_2$
  - processed cheese - fortified with large amount of phosphates
    → formation of insoluble $Ca_3(PO_4)_2$ a $CaHPO_4$
  - Coca Cola comprises considerable amount of phosphoric acid !!
  - foliar vegetable with high content of Mg
    (magnesium should be taken one half less than calcium)

The solution „ACD – R 110“ (preparation of conserved blood, „citrate blood“) 1

Natrii citras dihydricus	
($Na_3C_6H_5O_7 \cdot 2\ H_2O$)	**1,4 g**
Acidum citricum monohydricum	
($C_6H_8O_7 \cdot H_2O$)	**0,5**
Glucosum	
($C_6H_{12}O_6$)	**2,5**
Aqua pro injectione	**ad 100,0**

pH of the solution $\approx$ 5,1 $\pm$ 0,1

100 ml of the solution + 350 to 450 ml of blood

The solution „ACD – R 110“ (preparation of conserved blood, „citrate blood“) 2

blood (400 ml) + ACD slution (100 ml) → conserved blood (500 ml)

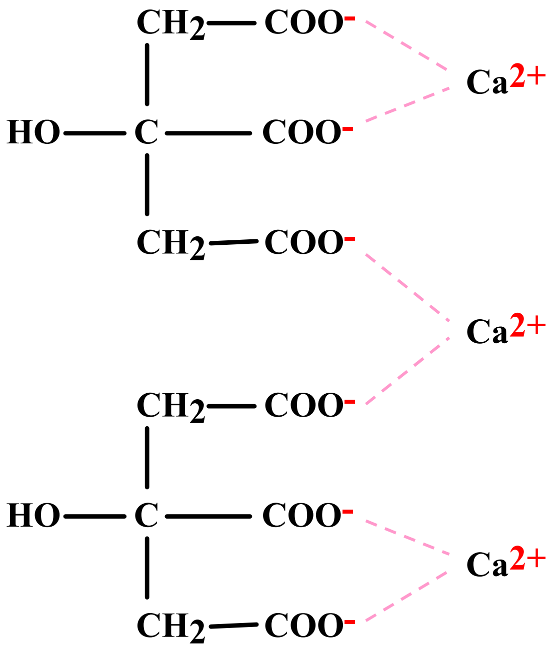
1,4 g of citrate (M_r = 294,10) / 500 ml → 2,8 g / l
2,8 / 294,10 = 9,52 mmol / l

0,5 g of citric acid (M_r = 210,14) / 500 ml → **1 g / l**
1 / 210,14 = 4,75 mmol / l

total citric anion: **14,28 mmol / l**

The solution „ACD – R 110“ (preparation of conserved blood, „citrate blood“) 3

1 conserved blood (500 ml) → ≈ 7,14 mmol of citrate anion



$3\ Ca^{2+} + 2\ citrate^{3-} \rightarrow$

$\rightarrow\ Ca_3(citrate)_2$

$Ca_3(citrate)_2$ = calcii citras
= calcium citrate
is **UNDISSOCIATED** salt,
soluble in water

= the exception: undissociated salts are insoluble !!

On this exceptional solubility of undissociated salt is based almost the whole blood transfusion service !!

In the conserved blood must not be present any undissociated and concurrently insoluble salt, it is precipitate (e.g. calcium oxalate) !
The citrate anion is added in greate abundance (see next), so it bonds (removes) safely from the solution all calcium ions, needed for blood clotting.

The solution „ACD – R 110" **(preparation conserved blood, „citrate blood")** **4**

$3\ Ca^{2+} + 2\ citrate^{3-} \rightarrow Ca_3(citrate)_2$

$1{,}5\ Ca^{2+} + 1\ citrate^{3-}$

1 mmol of citrate binds cca 1,5 mmol of *free* Ca

7,14 mmol of citrate (in 500 ml of conserved blood)
are able to bind 10,7 mmol of (*free*) Ca
it is (*theoretically*) Ca from more than 4 l of blood !!

P-[tCa] ≈ 2,5 mmol / l

At big volumes of transfused blood we should think about origin of possible hypocalcemia !
(→ administration of calcii gluconas from the 2nd transfusion ?)

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