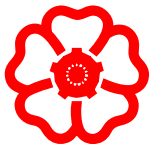


K I D N E Y

-

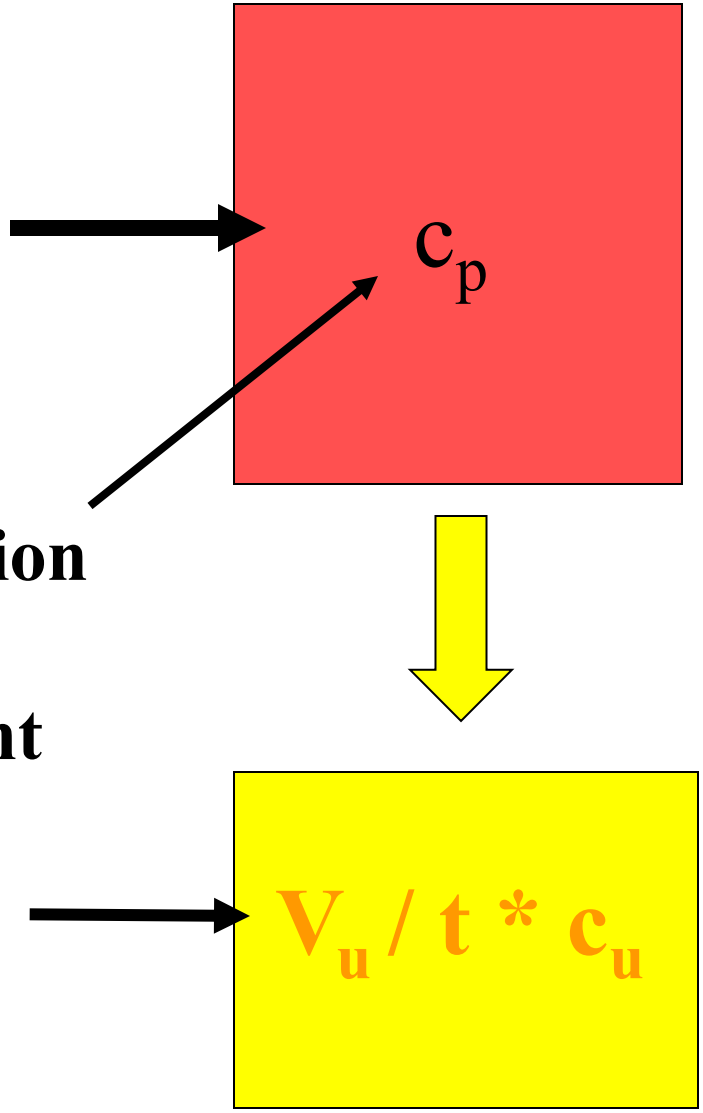
CLEARANCE

Clearance

is the proportion of substance amount excreted from the compartment (in a unit of time) to the concentration of a substance in the compartment.

Formally the clearance is considering the volume which is removed („cleared“) of a given substance in the time.

Clearance (2)


compartment
(plasmatic
space)
c_p
the concentration
of a substance
in compartment
the substance amount
excreted (in urine)
in given time
$V_u / t * c_u$

(3)

$$\text{Clearance} = \frac{V_u / t * c_u}{c_p} * 1000$$

$$= \frac{\text{ml / s} * \cancel{\text{mmol / l}}}{\cancel{\mu\text{mol / l}}} * \cancel{1000}$$

$$= \text{ml / s}$$

Clearance (4)

substance amount = volume * concentration

$$n = V * c$$

$$V_p * c_p = V_u * c_u$$

the substance amount in blood = the substance amount in urine

(creatinine – a substance without „threshold“)

Clearance (5)

$$V_p * c_p = V_u * c_u$$

the volume is here understood as the volume of plasma in a unit of time: V / t
(it is so called „volume speed“ in ml / s, too)

$$V_p / t * c_p = V_u / t * c_u$$

$$V_p / t = \frac{V_u / t * c_u}{c_p} * 1000$$

Clearance (6)

$$V_p / t = \frac{V_u / t * c_u}{c_p} * 1000$$

„the volume of plasma that is completely cleared of a substance in a unit of time“

$$GF = \frac{V_u / t * c_u}{c_p} * 1000$$

glomerular filtration rate

Clearance *(note)*

$$V_p / t = \frac{V_u / t * c_u}{c_p} * 1000$$

In the (especially older) literature is the relation used sometime with the different symbolic, however with the identical meaning:

$$\text{clearance} = \frac{U * V}{P} * 1000$$

Clearance (7)

GF = 1,33 – 2 ml / s (glomerular filtration, uncorrected)

V_u / t = the volume of definitive urine, excreted in a time unit (dimension: ml / s)
diuresis (ml / d) : 86.400 → ml / s

c_p = the concentration of creatinine in plasma (up to 115 μmol . l^{-1})

V_u * c_u = dU-creatinine = 9 – 16 mmol / d

(s = second, d = day
1 d = 86.400 s = 24 * 60 * 60)

Glomerular filtration rate

$$GF_{corrected} = GF_{uncorrected} * \frac{1{,}73}{\text{body surface}}$$

Glomerular filtration is recalculated to the standard body surface = 1,73 m^2.
Body surface of investigated person is read in the table according to the height and weight or it is calculated from this valuables.

The importance of correction on the body surface

- **the direct proportion:**

body surface → surface of the kidney → number of nephrons → function capacity of kidney

Tubular reabsorption of water :

$$R_{H_2O} = \frac{GF - V_u / t}{GF}$$

$$R_{H_2O} = 1 - \frac{V_u / t}{GF}$$

$$R_{H_2O} = 0{,}988 - 0{,}997$$

$$= 98{,}8 - 99{,}7\ \%$$

(The uncorrected value of GF is used in the calculation)

The calculation of creatinine clearance, summary (1):

a/ the volume of urine excreted per 1 s:

V/t = diuresis (ml) : 86.400 → (ml/s)

b/ glomerular filtration rate (uncorrected):

$$GFR = \frac{U * V/t}{P} * 1000 \rightarrow (1{,}33 - 2 \text{ ml/s})$$

(U → mmol/L)
(V/t → ml/s)
(P → μmol/L)

c/ glomerular filtration rate corrected to the standard surface:

$$GFR_{corr} = GFR * \frac{1{,}73}{surface} \rightarrow (ml/s)$$

The calculation of creatinine clearance, summary (2):

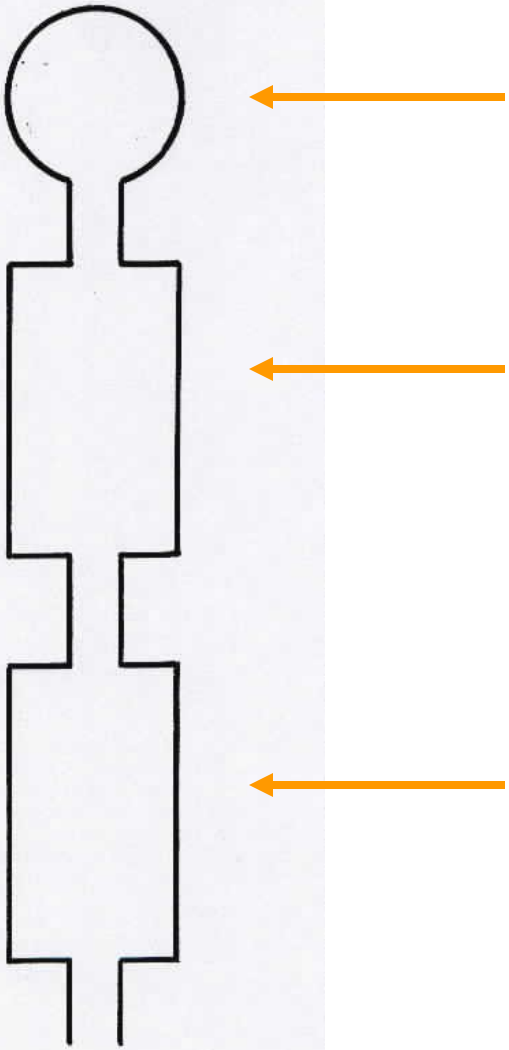
d/ tubular reabsorption:

$$R = \frac{GFR - V/t}{GFR} = 1 - \frac{V/t}{GFR} \qquad (R_{H2O} = 0.988 - 0.997)$$

e/ urine excretion of creatinine:

U * diuresis → (9 – 16 mmol/d) (diuresis → L)

Glomerular filtration and tubular secretion of different substances:

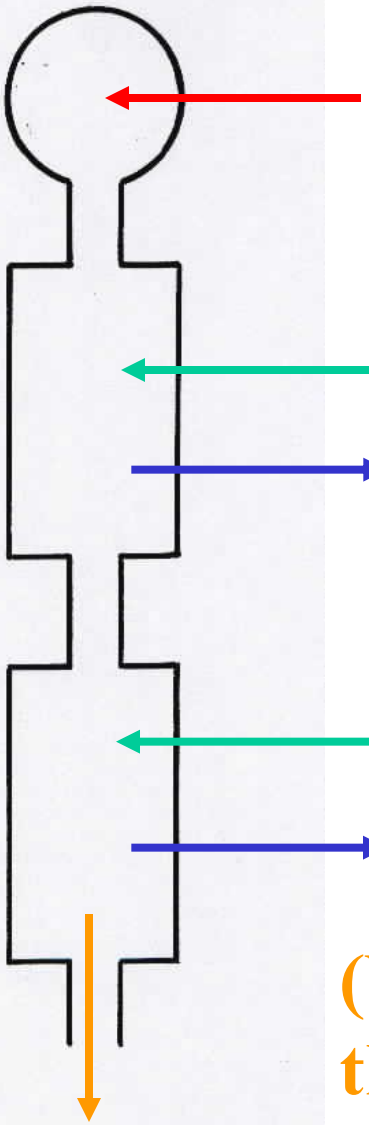


glomerulus

proximal tubule

distal tubule

The excretion of a substance by kidney:



$(GF * c_P)$
the substance amount, filtrated in 1 s

tubular secretion (T_S)

tubular reabsorption (T_R)

T_S

T_R

$$V_U/t * c_U = GF * c_P + T_S - T_R$$

$(V_U/t * c_U)$
the substance amount excreted into the urine in 1 s

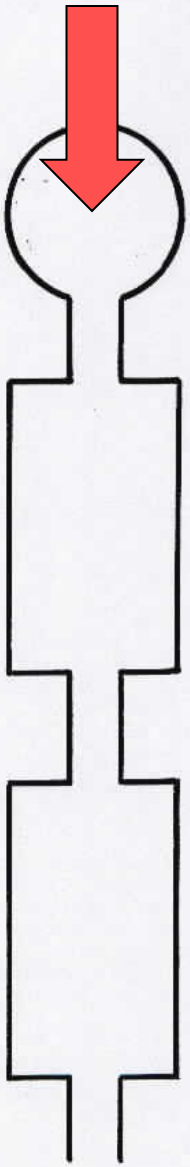
Fractional excretion

$FE_{Na^+} = 0{,}01 \quad (= 1\ \%)$

$FE_{K^+} = 0{,}11 \quad (= 11\ \%)$

$FE_{H_2O} \leq 0{,}02 \quad (\leq 2\ \%)$

compare: $R_{H_2O} = 0{,}988 - 0{,}997$

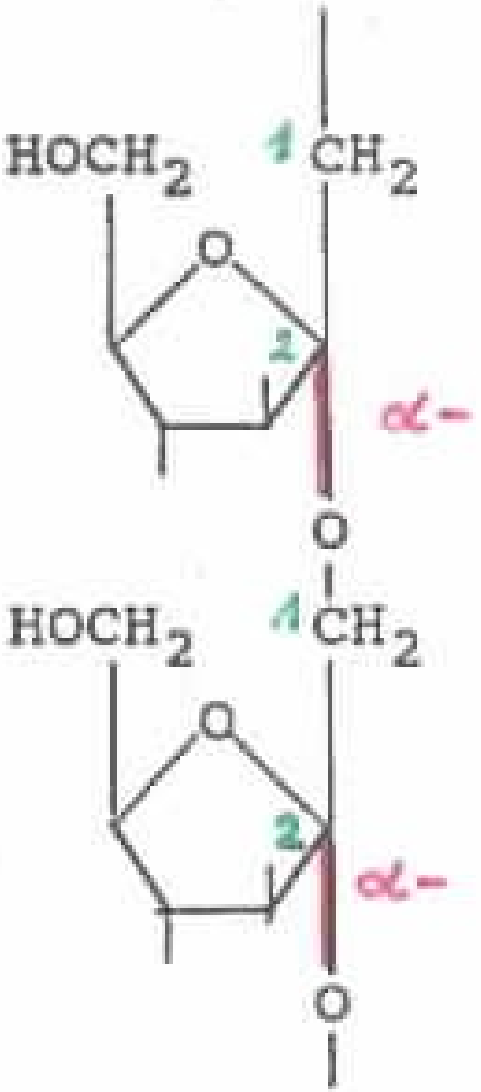


Inulin:

Excreated exclusively by glomerular filtration. It is the exact measure of glomerular filtration (GF).
As a substance foreign to human body it must be infused intravenously. The sampling is possible till the steady concentration of inulin in plasma is reached.
Determinations were used for scientific research.

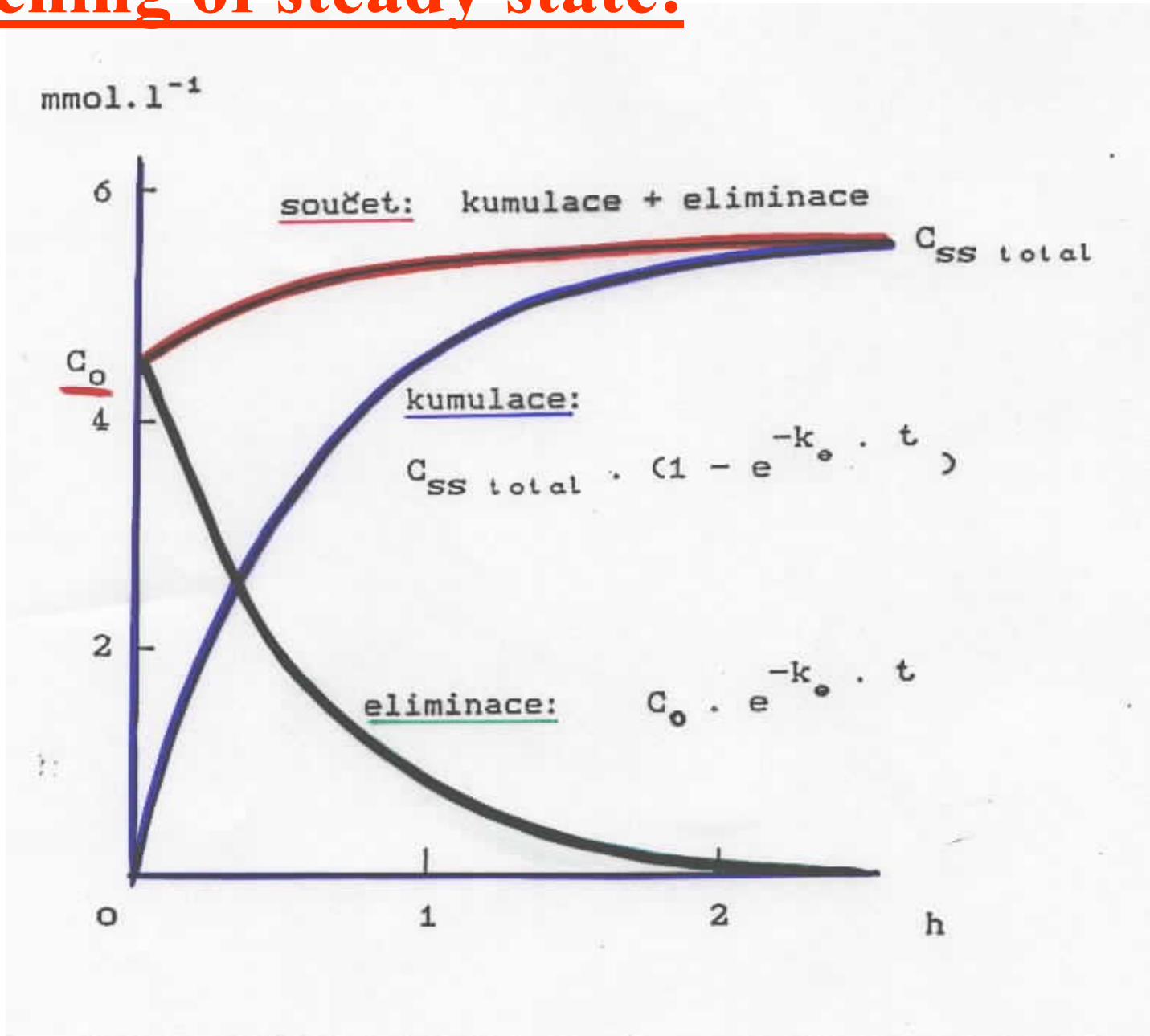
- **inulin:** $M_{r\ INULIN} \cong 5.200$, bolus dose 50 mg · kg^{-1}
  → infusion …. $P_{INULIN} \cong 200 – 300$ mg · l^{-1}
- **synthetic polyfructan** → lower M_r , identical conditions, soluble even in cold water

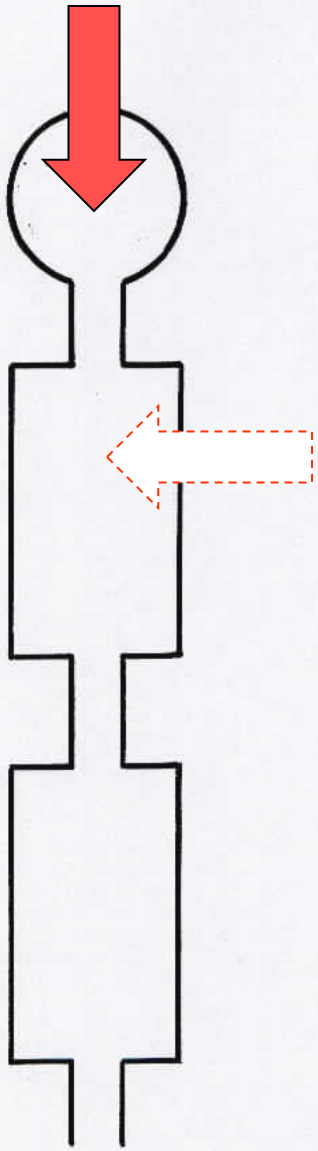
Oman pravý



inulin

The reaching of steady state:





Creatinine:

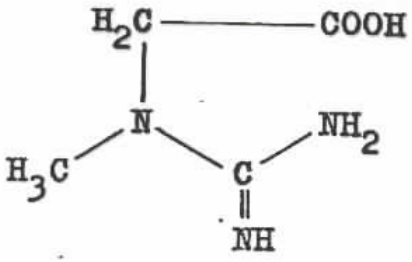
It is excreted mainly by glomerular filtration, but from small part by secretion in proximal tubule too. Therefore the creatinine clearance has the higher value in comparison with the inulin clearance (mentioned is 2,33 vs. 2,00 ml/s).

It is used for routine determinations of glomerular filtration rate.

Gradually it is replaced with the determination of cystatin C.

Creatinine (anhydride of creatine) is considerably more soluble

Kreatin $C_4H_9N_3O_2$ $M_r = 131,13$

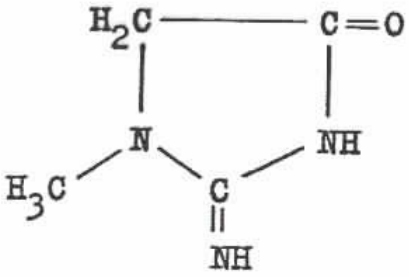


3-methyl-guanidino.octová kys.

Rozpustnost v 1 kg vody (18°C): 13,5 g

Slabě zásaditá látka.

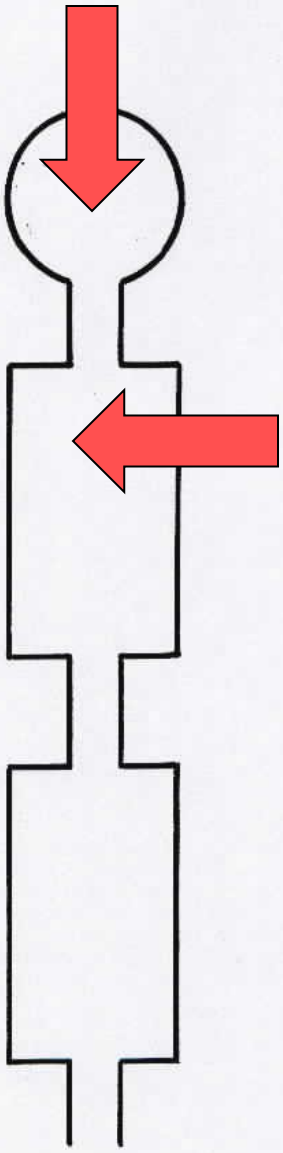
Kreatinin $C_4H_7N_3O$ $M_r = 113,12$



anhydrid kys. 3-methyl-guanidino-octové

Rozpustnost v 1 kg vody (16°C): 87 g

Silně zásaditá látka.

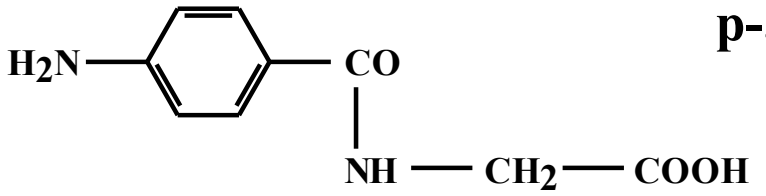


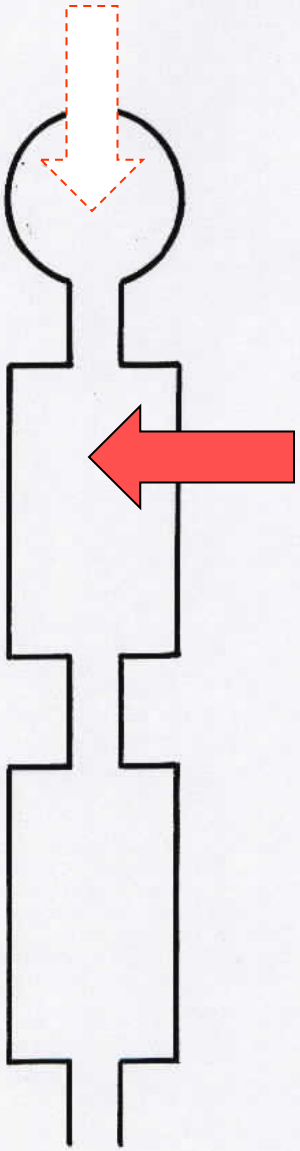
p-aminohippuric acid:

It is excreted both by glomerular filtration (GF) and by tubular secretion (T_S) (in the proximal tubule).

Its clearance (the sum GF + T_S) had given the blood amount, which pass through the kidney in the time unit.

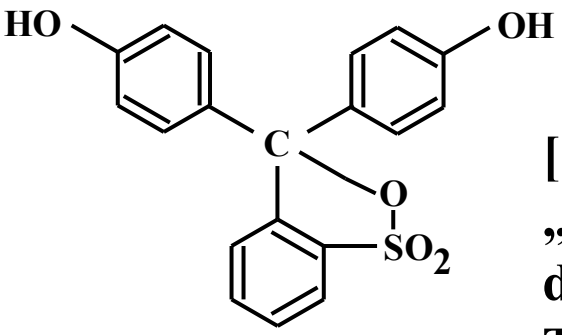
(p-amino.benzoyl.glycine, p-amino.hippuric acid, PAH)





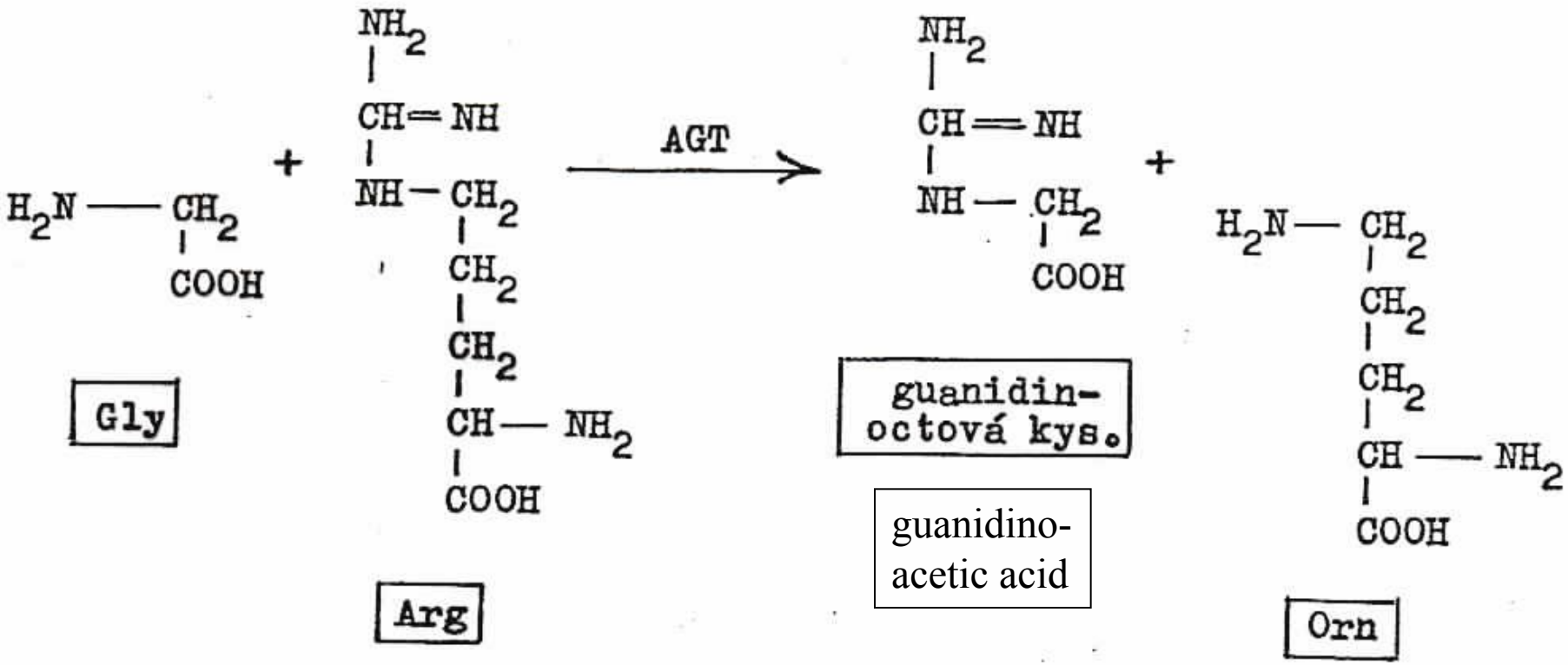
Phenolsulfophtalein:

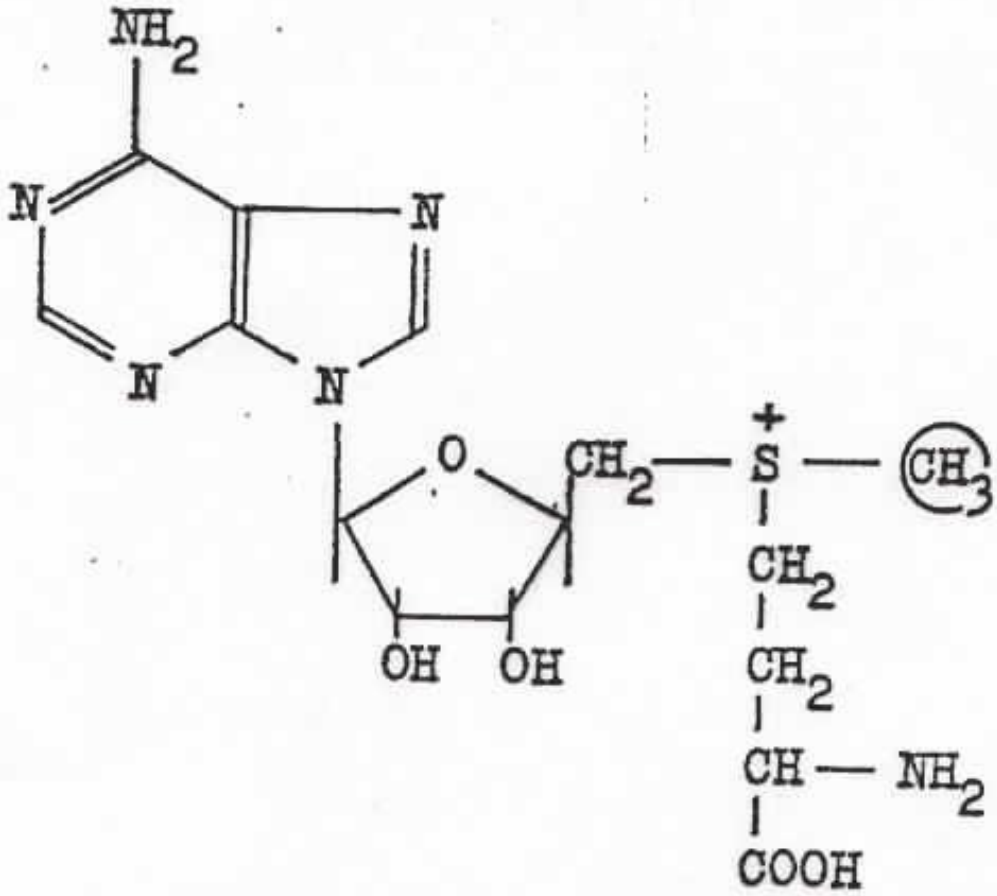
It is excreted mainly by tubular secretion (from 95 %). It is approximate indicator of secretion in the proximal tubule (T_S) , resp. rate of blood flow through the proximal tubule.



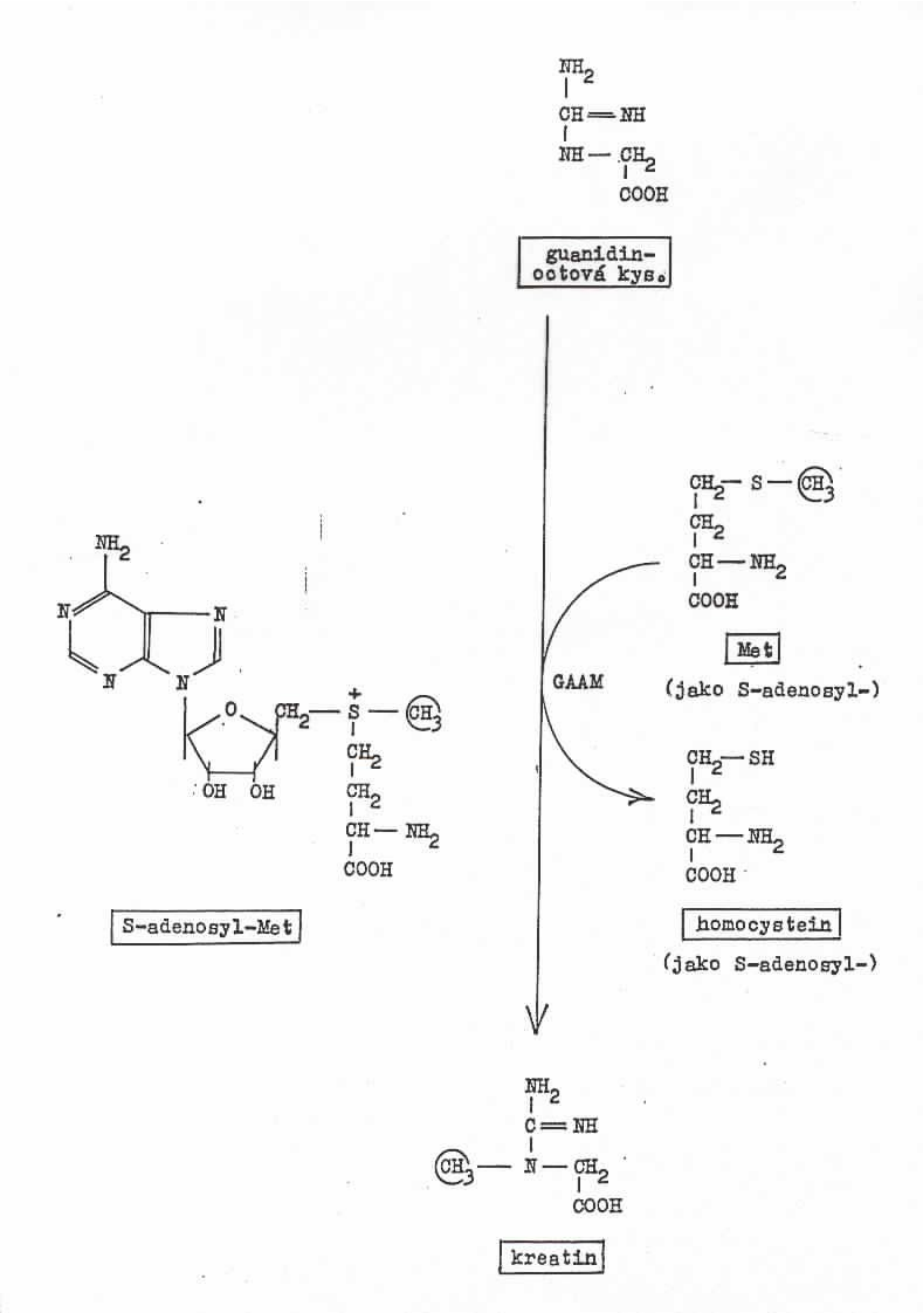
[Phenol.sulfo.phtalein (= FSF, PSP, „phenol red“) is a tri.phenyl.methane dye – an acid-base indicator. The undissociated form is drawn, the form is present in strong acidic environment.]

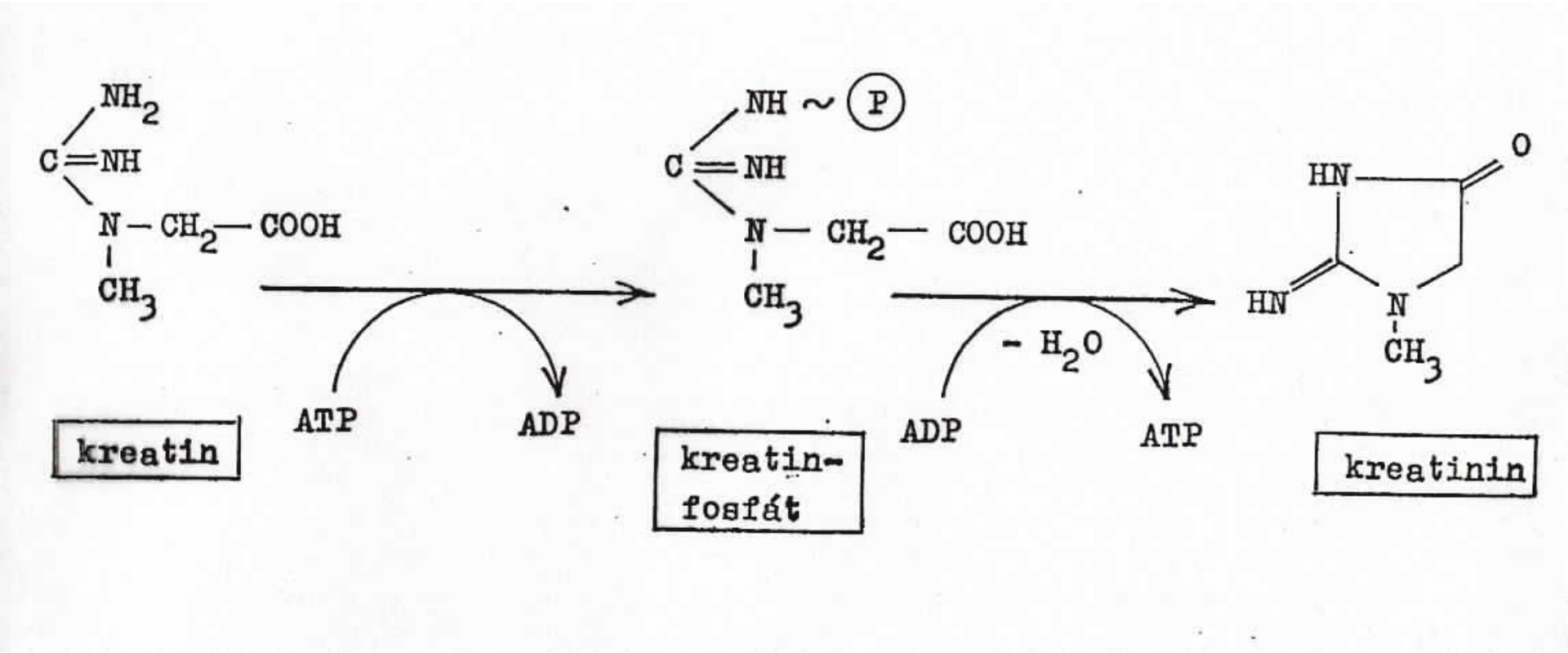
Biosyntéza kreatinu
Biosynthesis of creatine

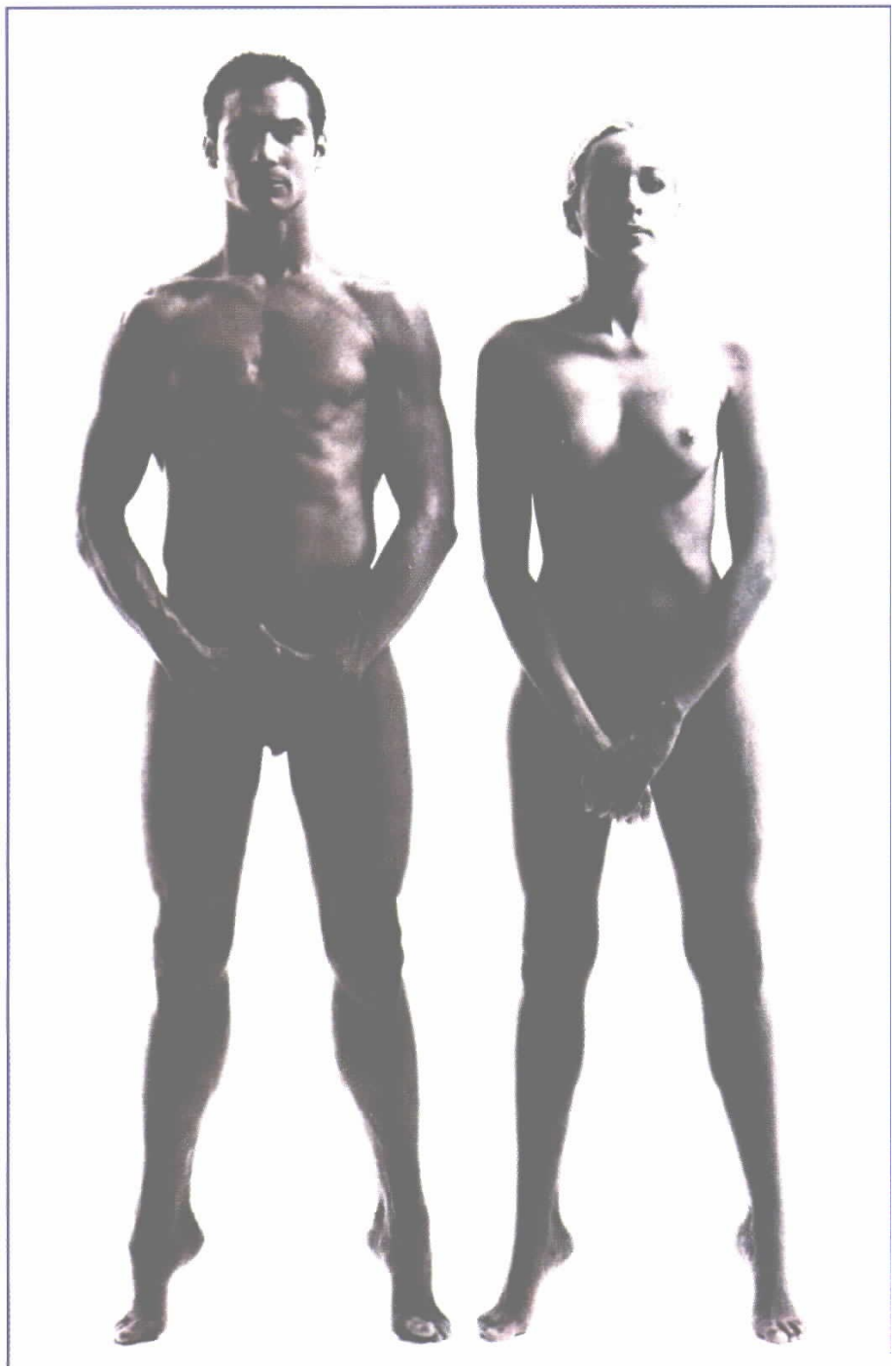




S-adenosyl-Met


guanidin-
octová kys.
Met
(jako S-adenosyl-)
GAAM
S-adenosyl-Met
homocystein
(jako S-adenosyl-)
kreatin


NH2
C=NH
N – CH2 – COOH
CH3
ATP
ADP
kreatin
NH ~ P
C=NH
N – CH2 – COOH
CH3
kreatin-
foszfát
- H2O
ADP
ATP
HN
O
HN
N
CH3
kreatinin



kreatininová clearance

kreatinin v séru: ....
(do 115) umol/l

kreatinin v moči: ....
mmol/l

diuréza: ..... ml/d

(v)..... ml/s

odpad kreatininu:.....
(9 - 16) mmol/d

filtrace (1,33-2) ml/s

- nekorigovaná: .....

- korigovaná: .....
(1,73 m2)

resorbce: .....
(0,988 - 0,997)

(větší podíl svalové hmoty u muže)

(the greater part of muscle substance in man)

Cystatin C, clearance (1) :

The creatinine clearance is replaced with the clearance of cystatine C. It is low-molecular protein, which has the function of inhibitor of cysteine proteinases in extracellular fluids (hence its name: Cys + statin).
Cystatin C is regularly released into blood circulation from the all nuclear cells. Its concentration in blood is constant (independent e.g. on inflammatory states).
[Cystatin C demostrates greater intraindividual variability, however the lower interindividual variability in comparison with creatinine. It allows earlier reveal of kidney damage.]
In the kidneys it is excreted only by glomerular filtration (the creatinine from small part by secretion in proximal tubule too !)
Immunochemical determination.

Cystatin C, clearance (2) :

The corrected clearance (= „relative glomerular filtration“) is now *in adults* („the convention 2005“) uniformly calculated from the relation:

$$GF\ (ml / s / 1{,}73\ m^2) = [84{,}69 * \text{cystatin C}\ (mg/l)^{-1{,}680}] / 60$$

In patients *up to 14 years of age* is the result multiplied by so called „prepubertal factor“ 1,384

The programes*) are at your disposal for backword recalculation of this corrected clearance (= „relative glomerular filtration“) to the uncorrected clearance (= „absolute glomerular filtration“) according to the weight and height of the given patient.
The reading is necessary to determine right dosage of drugs, which are excreted mainly by kidneys.

*) http://www.klinkem.lu.se/GFRcz.htm

The properties of substance for measurement of GF:

- free filtration (= the substance is not bonded on plasma proteins, free-passing through the glomerular filter)
- it has neither T_R nor T_S
- no metabolism
- no deposit in the kidneys
- no toxicity
- without influence on the GF
- determination of the substance in plasma and urine is accessible