Osnove farmakologije: Režimi odmerjanja zdravil

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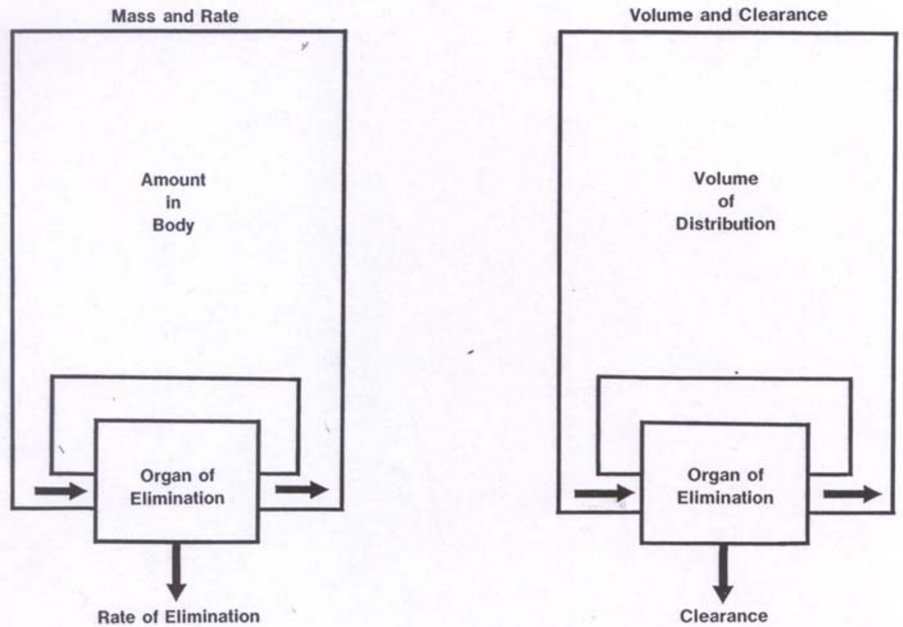


$$\text{Fractional Rate of Elimination} = \frac{\text{Rate of Elimination}}{\text{Amount in Body}} = \frac{\text{Clearance}}{\text{Volume of Distribution}}$$

The fractional rate of elimination of a drug can be thought of either as the fraction of the total amount in the body that is eliminated per unit time (left), or as the fraction of the total volume from which the drug is cleared per unit time (right).

Izločanje učinkovin

Izraženo s

- hitrostjo in maso, $dX/dt = k_e U$
- očistkom in volumnom, $Cl = k_e V$

- Hitrost eliminacije je količina učinkovine ki se eliminira iz telesa na enoto časa (mg/h) preko določenega organa, U je količina v telesu

- Očistek je volumen tekočine, iz katerega se izloči učinkovina na enoto časa (L/h) preko določenega organa, V je volumen telesa

Izločanje učinkovin

- $dX/dt = k_e\, U$, $U = V\, C$
- $Cl = k_e V$

U je količina v telesu (plazmi)
C je koncentracija v telesu (plazmi)

- $dX/dt = k_e\, V\, C$
- $dX/dt = Cl\, C$

Izločanje učinkovin

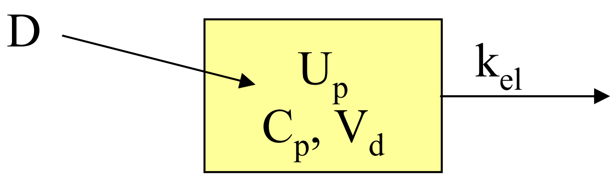
- $dX/dt = k_e U$, izločanje splošno

- $dU_E/dt = k_e U_P$, izločanje z urinom, blatom, znojem, izdihanim zrakom, skozi kožo, presnovo....

- $dU_{EU}/dt = k_{eu} U_P$, izločanje z urinom
  dU_{EU}/dt, hitrost izločanja v urin

- $dU_P/dt = - \; k_e U_P$
  dU_P/dt, hitrost izločanja iz plazme z urinom, blatom, znojem, izdihanim zrakom, skozi kožo, presnovo....

Enkratna intravenska injekcija



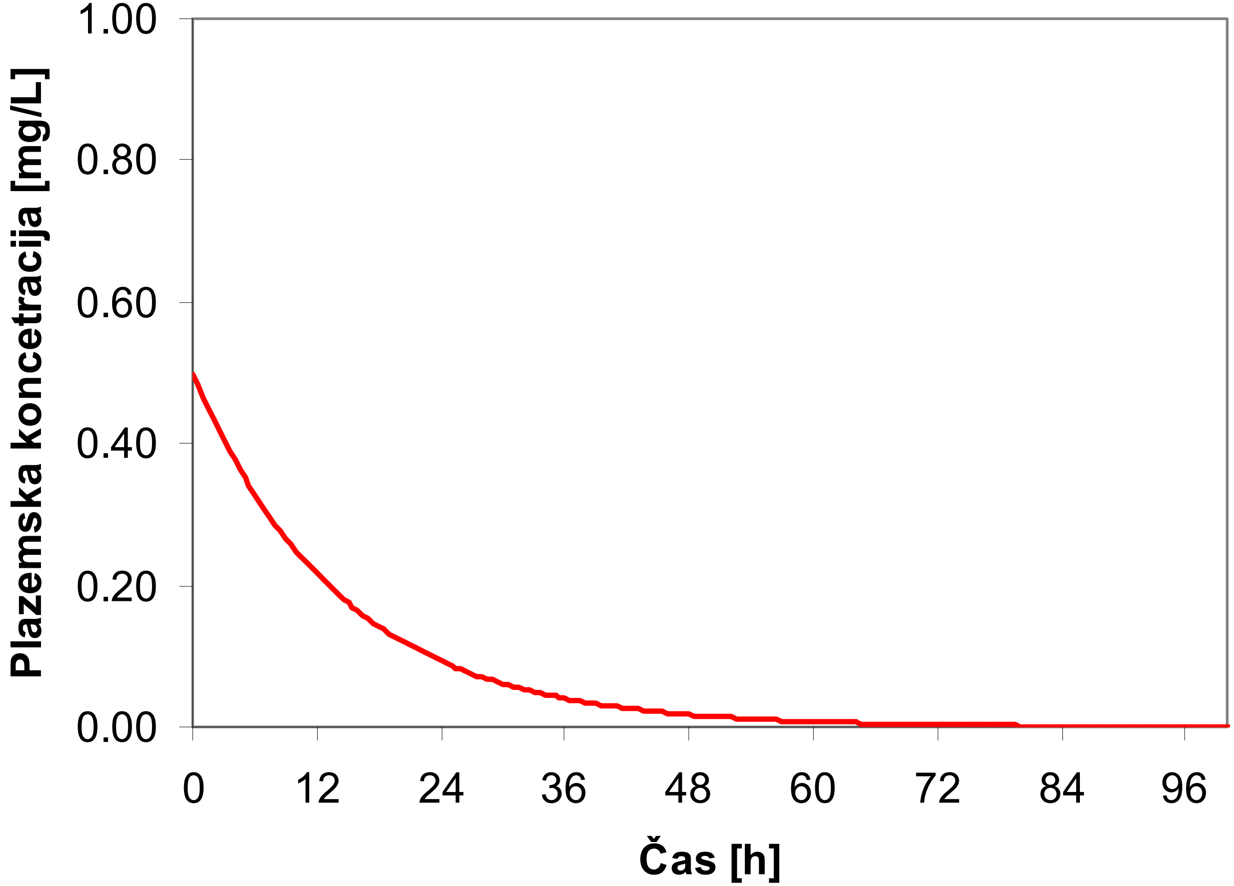
$$\frac{dU_p}{dt} = -k_{el} \cdot U_p$$

$$C_p = \frac{D}{V_d} \cdot e^{-kel \cdot t}$$

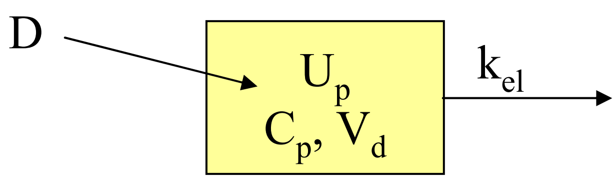
D… začetna in vzdrževalna doza
k_{el}… eliminacijska konstanta $[h^{1-}]$
V_d… volumen distribucije
τ… dozirni interval

$$t_{1/2} = \frac{\ln 2}{k_{el}}$$

D (mg)	V_D (L)	k_{el} (h^{-1})	$t_{1/2}$ (h)
50	100	0.07	10



Večkratna intravenska injekcija



$$\frac{dU_p}{dt} = -k_{el} \cdot U_p$$

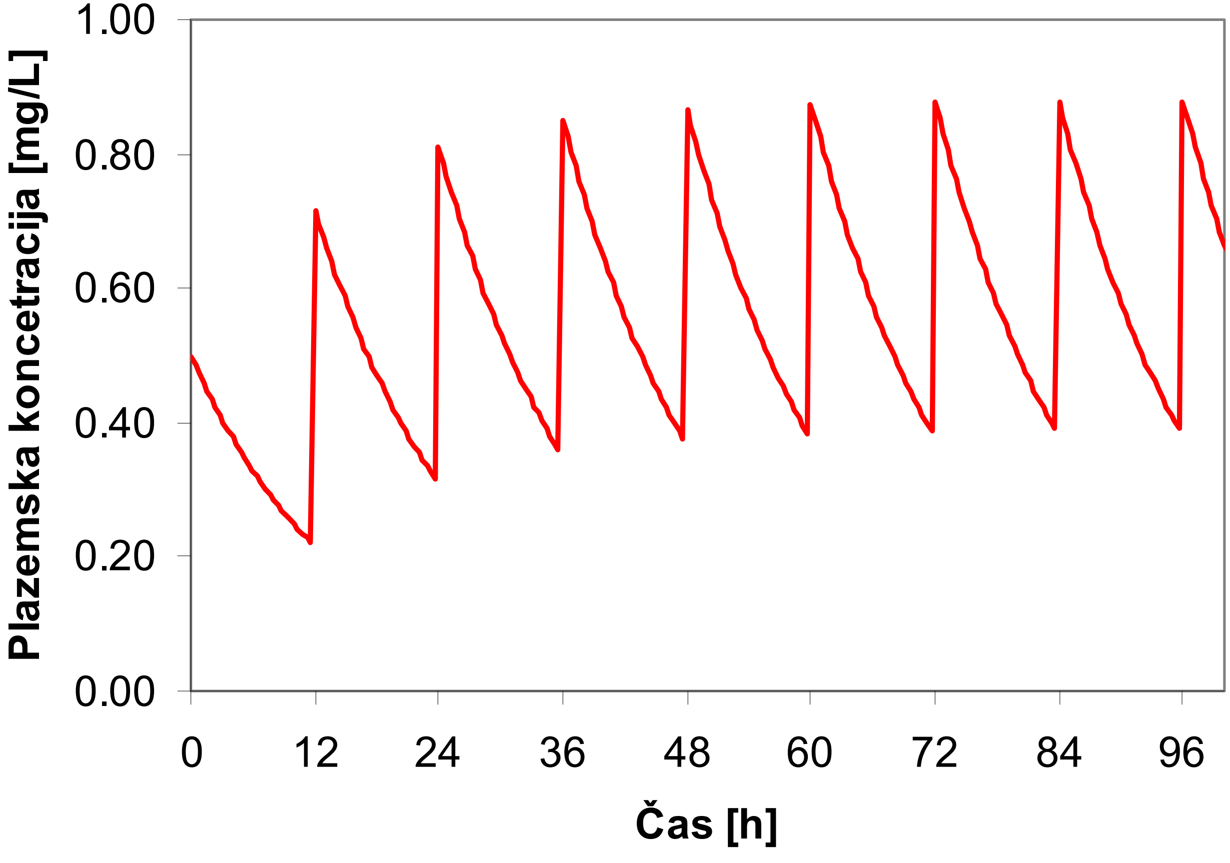
$$C_pss = \frac{D}{V_d} \cdot \frac{1}{1 - e^{-kel \cdot \tau}} \cdot e^{-kel \cdot t}; 0 < t < \tau$$

$$C_pss^{\max} = \frac{D}{V_d} \cdot \frac{1}{1 - e^{-kel \cdot \tau}}$$

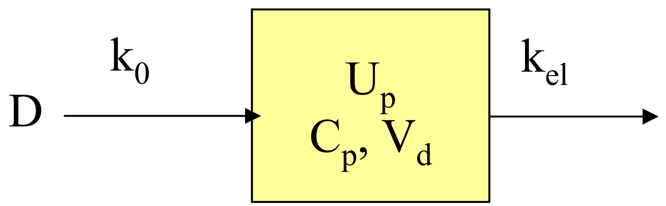
$$C_pss^{\min} = \frac{D}{V_d} \cdot \frac{1}{1 - e^{-kel \cdot \tau}} \cdot e^{-kel \cdot \tau}$$

$$\overline{C_pss} = \frac{D}{V_d \cdot k_{el} \cdot \tau}$$

D (mg)	V_D (L)	k_{el} (h^{-1})	$t_{1/2}$ (h)	τ
50	100	0.07	10	12 h



Enkratna intravenska infuzija



$$\frac{dU_p}{dt} = k_0 - k_{el} \cdot U_p$$

$$k_0 = \frac{D}{T}$$

T… čas infuzije

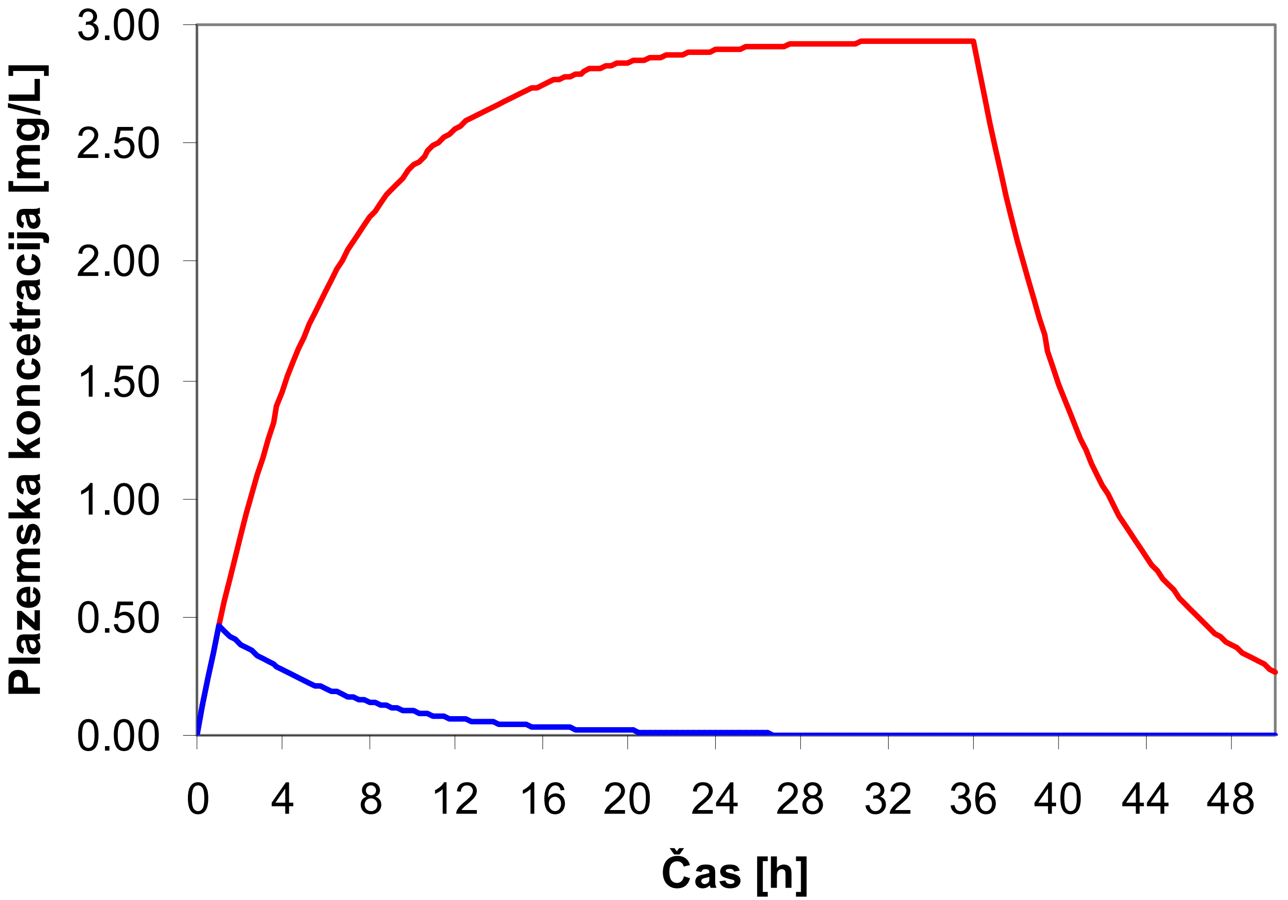
$$C_p = \frac{k_0}{V_d \cdot k_{el}} \cdot \left(1 - e^{-kel \cdot t}\right)$$

$$C_p ss = \frac{k_0}{V_d \cdot k_{el}}$$

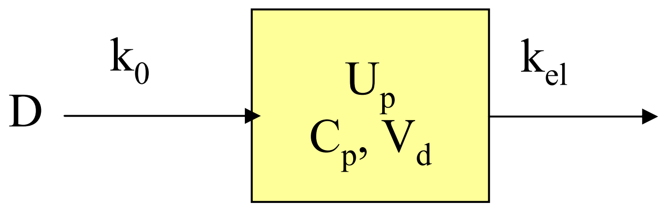
$$C_p^{\ post} = \frac{k_0}{V_d \cdot k_{el}} \cdot \left(1 - e^{-kel \cdot T}\right) \cdot e^{-kel \cdot (t-T)}$$

$$C_p ss^{\ post} = \frac{k_0}{V_d \cdot k_{el}} \cdot e^{-kel \cdot (t-T)}$$

	k_0 (mg/h)	V_D (L)	k_{el} (h^{-1})	T (h)	$t_{1/2}$ (h)
A	50	100	0.18	24	4
B	50	100	0.18	1	4



Večkratna intravenska infuzija



$$\frac{dU_p}{dt} = k_0 - k_{el} \cdot U_p$$

$$k_0 = \frac{D}{T}$$

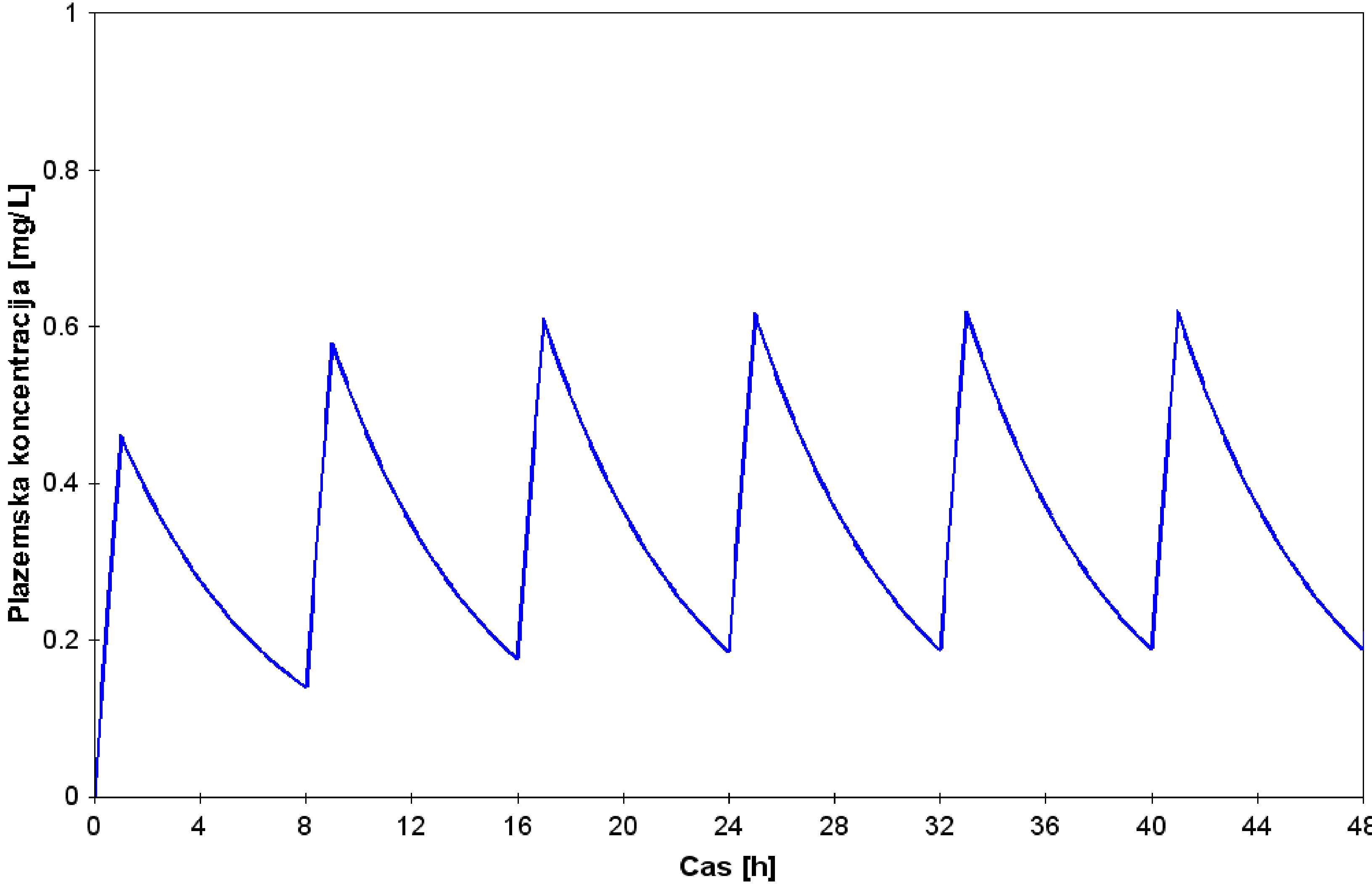
T… čas infuzije

$$C_{pSS} = \frac{k_0}{V_d \cdot k_{el}} \cdot \left(1 - e^{-kel \cdot T}\right) \cdot \frac{1}{1 - e^{-kel \cdot \tau}} \cdot e^{-kel \cdot (t - T)}; \ T < t < \tau$$

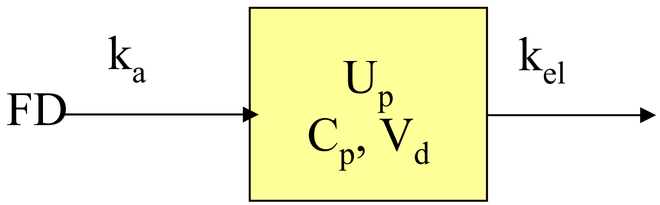
$$C_{pSS}^{\max} = \frac{k_0}{V_d \cdot k_{el}} \cdot \left(1 - e^{-kel \cdot T}\right) \cdot \frac{1}{1 - e^{-kel \cdot \tau}}$$

$$C_{pSS}^{\min} = \frac{k_0}{V_d \cdot k_{el}} \cdot \left(1 - e^{-kel \cdot T}\right) \cdot \frac{1}{1 - e^{-kel \cdot \tau}} \cdot e^{-kel \cdot (\tau - T)}$$

k_0 (mg/h)	V_D (L)	k_{el} (h^{-1})	T (h)	$t_{1/2}$ (h)	τ
50	100	0.18	1	4	8 h



Enkratna ekstravaskularna aplikacija
(peroralna, intramuskularna)



$$\frac{dU_p}{dt} = F \cdot k_a \cdot U_{gi} - k_{el} \cdot U_p$$

$$C_p = \frac{F \cdot D}{V_d} \cdot \left(\frac{k_a}{k_a - k_{el}} \right) \cdot \left(e^{-kel \cdot t} - e^{-ka \cdot t} \right)$$

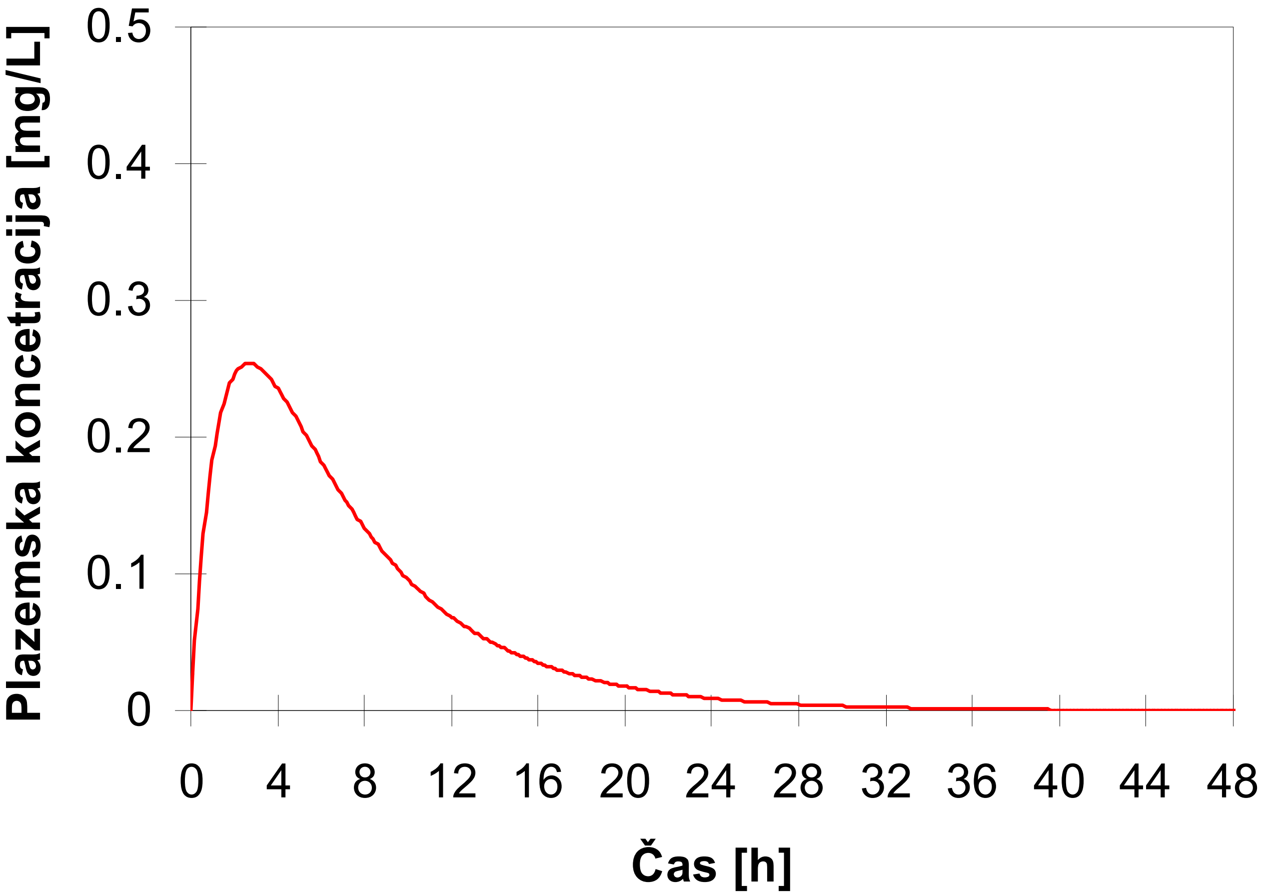
$$AUC_{0 \to \infty} = \frac{F \cdot D}{V_d \cdot k_{el}}$$

$$\overline{C_p ss} = \frac{F \cdot D}{V_d \cdot k_{el} \cdot \tau}$$

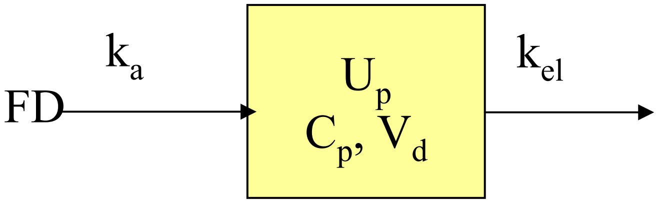
$$AUC_{0 \to \tau} = \frac{F \cdot D}{V_d \cdot k_{el}}$$

D (mg)	F	Vd (L)	k_a (h^{-1})	k_{el} (h^{-1})
50	0.8	100	0.72	0.18

T_{max}	C_{max}	$t_{1/2\ ka}$ (h)	$t_{1/2\ kel}$ (h)
2.7	0.25	1	4



Večkratna ekstravaskularna aplikacija



$$\frac{dU_p}{dt} = F \cdot k_a \cdot U_{gi} - k_{el} \cdot U_p$$

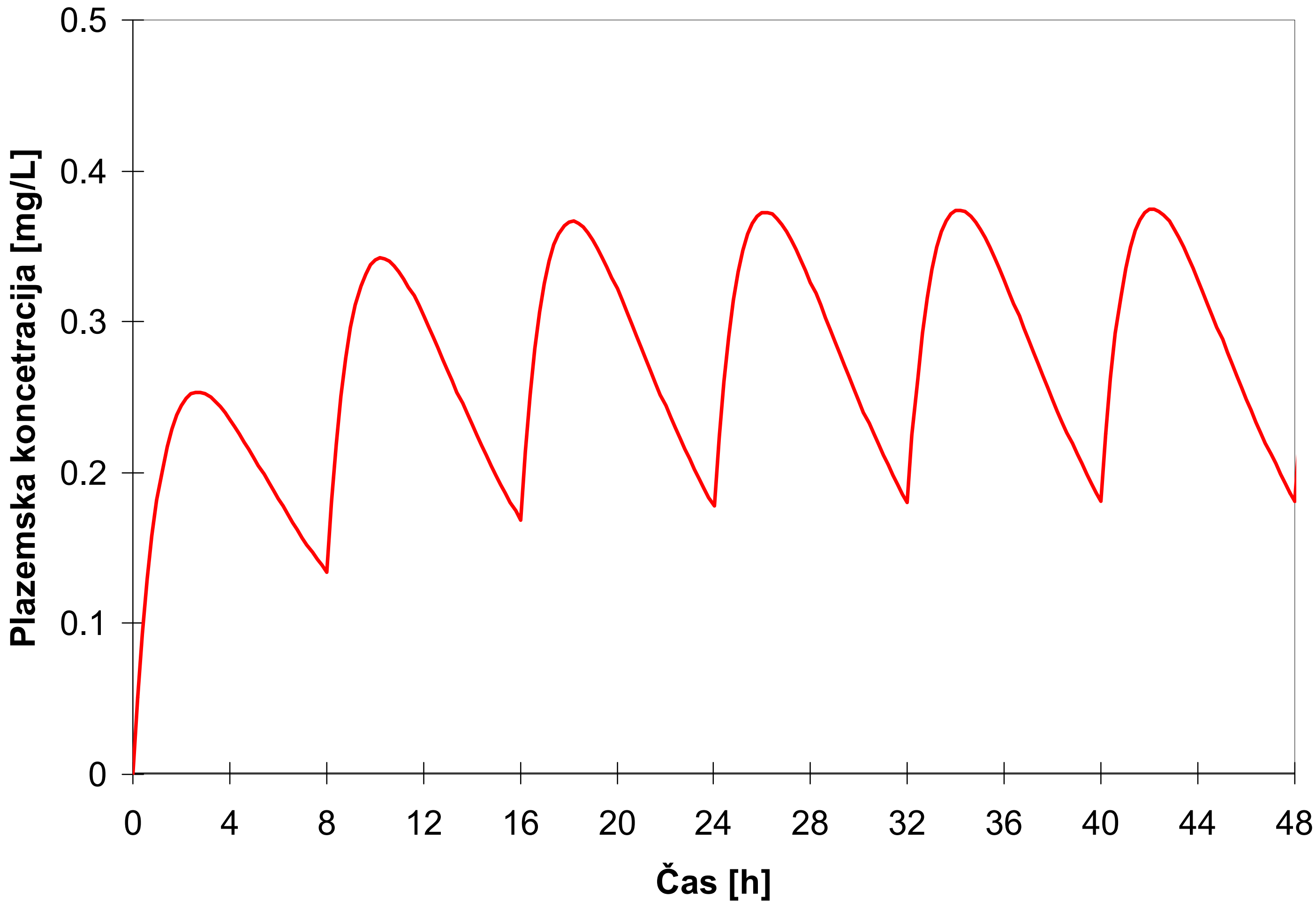
$$C_p ss = \frac{F \cdot D}{V_d} \cdot \left(\frac{k_a}{k_a - k_{el}} \right) \cdot \left[\left(\frac{1}{1 - e^{-kel \cdot \tau}} \right) \cdot e^{-kel \cdot t} - \left(\frac{1}{1 - e^{-ka \cdot \tau}} \right) \cdot e^{-ka \cdot t} \right]$$

$$C_p ss^{\max} = \frac{F \cdot D}{V_d} \cdot \left(\frac{1}{1 - e^{-kel \cdot \tau}} \right) \cdot \left[\left(\frac{k_a \cdot \left(1 - e^{-kel \cdot \tau}\right)}{k_{el} \cdot \left(1 - e^{-ka \cdot \tau}\right)} \right) \right]^{-kel / (ka - kel)}$$

$$C_p ss^{\min} = \frac{F \cdot D}{V_d} \cdot \left(\frac{k_a}{k_a - k_{el}} \right) \cdot \left[\left(\frac{e^{-kel \cdot \tau}}{1 - e^{-kel \cdot \tau}} \right) - \left(\frac{e^{-ka \cdot \tau}}{1 - e^{-ka \cdot \tau}} \right) \cdot e^{-ka \cdot t} \right]$$

$$tss^{\max} = \frac{1}{k_a - k_{el}} \cdot \ln \left[\frac{k_a \cdot \left(1 - e^{-kel \cdot \tau}\right)}{k_{el} \cdot \left(1 - e^{-ka \cdot \tau}\right)} \right]$$

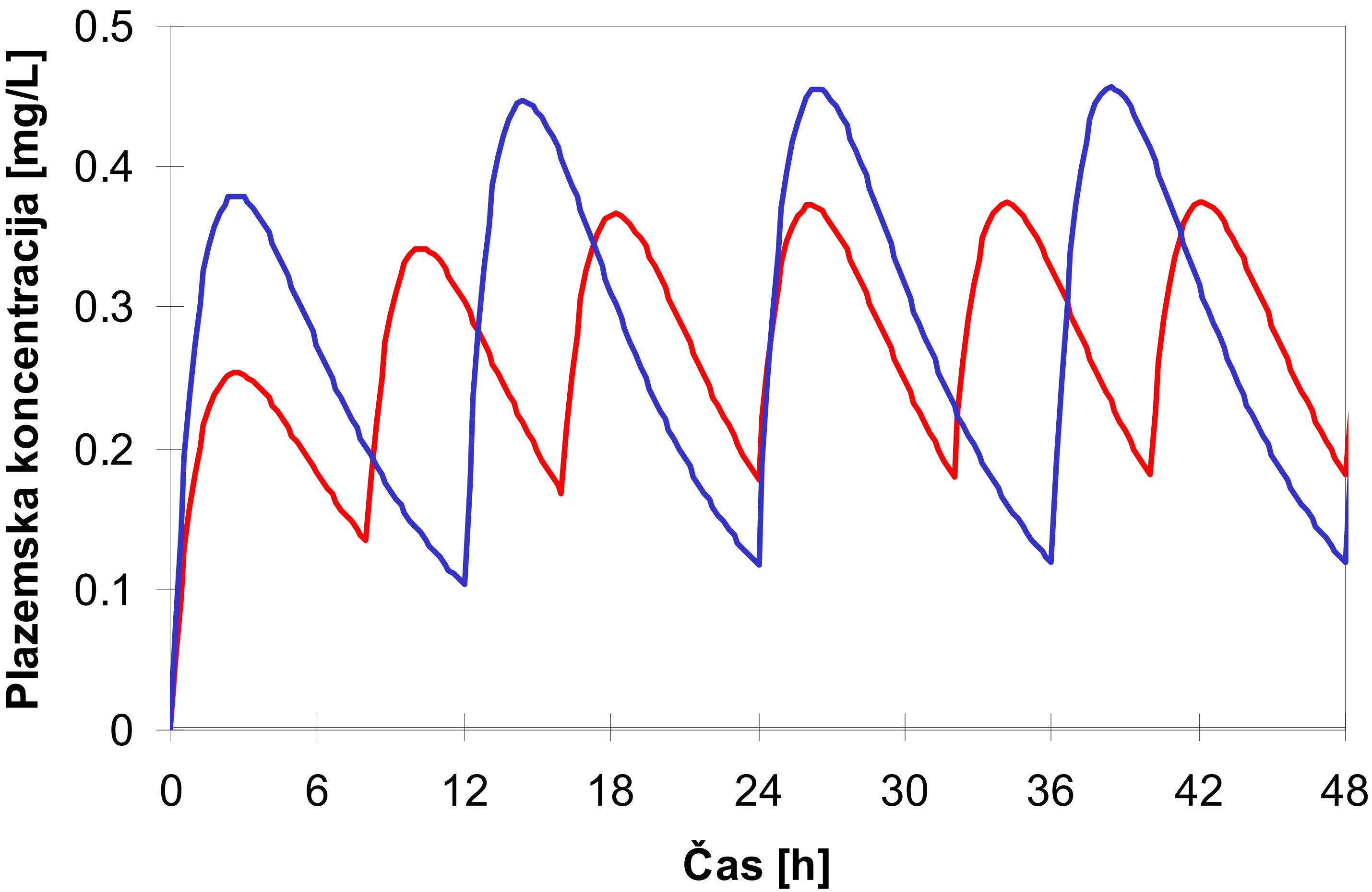
D (mg)	F	Vd (L)	k_a (h^{-1})	k_{el} (h^{-1})	τ	$t_{1/2\ ka}$ (h)	$t_{1/2\ kel}$ (h)
50	0.8	100	0.72	0.18	8 h	1	4



C_{SS}^{max} = 0.375 mg/L

C_{SS}^{min} = 0.181 mg/L

Aplikacija	D (mg)	τ	k_a (h^{-1})	V_D (L)	k_{el} (h^{-1})	$t_{1/2}$ (h)
3 x dnevno	3 x 50	8 h	0.72	100	0.17	4
2 x dnevno	2 x 75	12 h	0.72	100	0.17	4



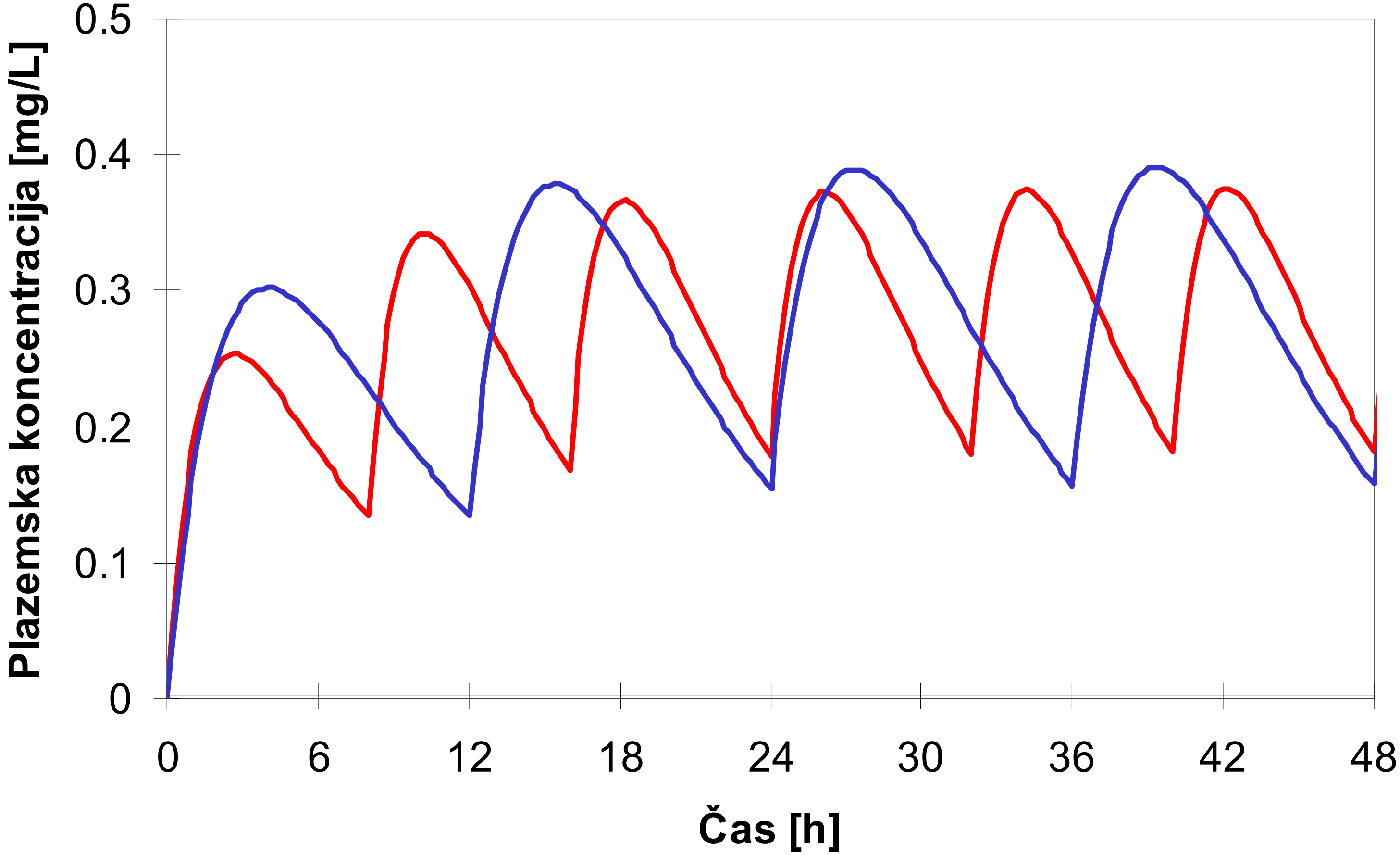
C_{SS}^{max} = 0.475 mg/L

C_{SS}^{max} = 0.375 mg/L

C_{SS}^{min} = 0.181 mg/L

C_{SS}^{min} = 0.119mg/L

Aplikacija	D (mg)	τ	k_a (h^{-1})	V_D (L)	k_{el} (h^{-1})	$t_{1/2}$ (h)
3 x dnevno	3 x 50	8 h	0.72	100	0.17	4
2 x dnevno	2 x 75	12 h	0.36	100	0.17	4



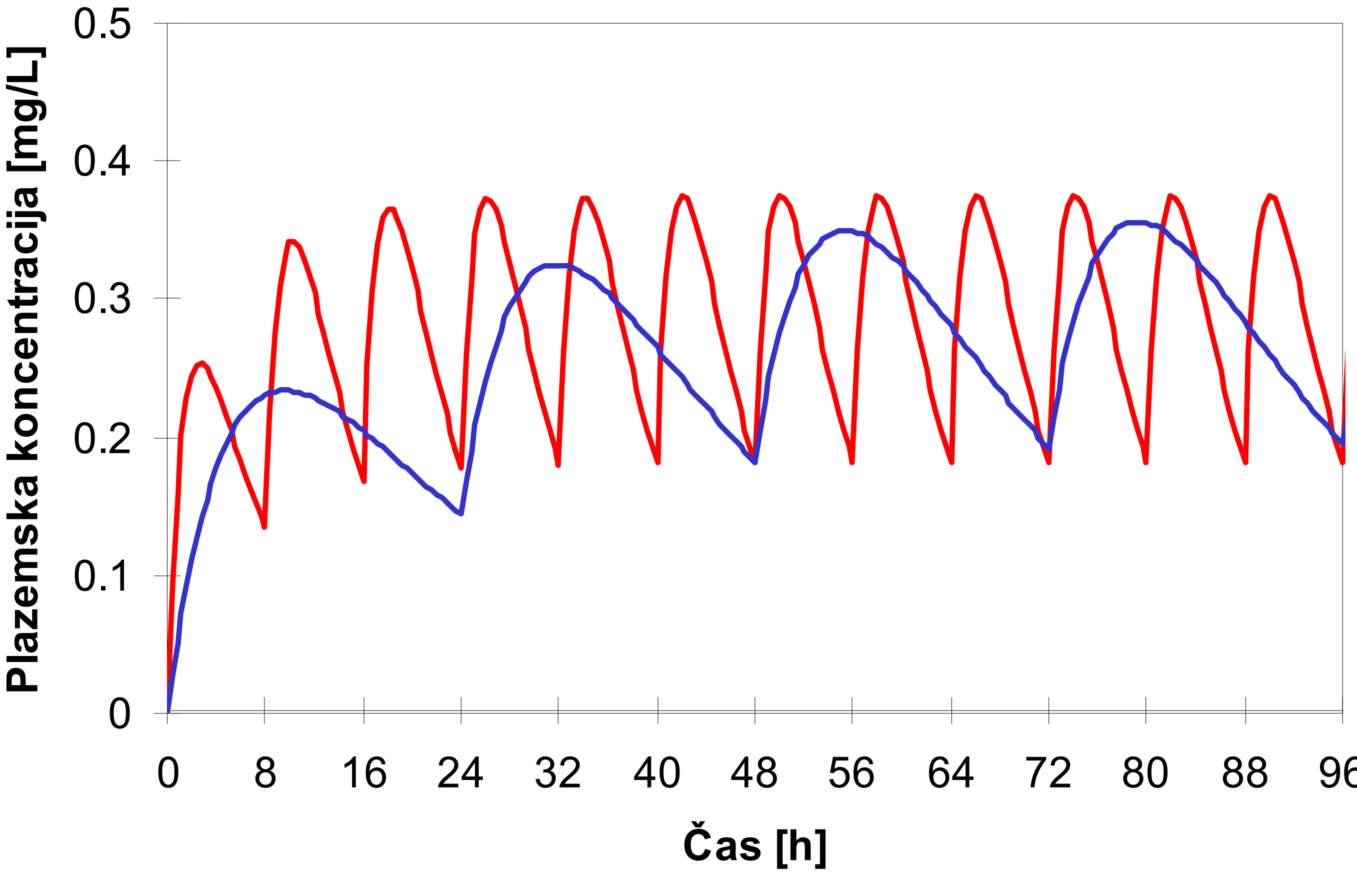
C_{SS}^{max} = 0.391 mg/L

C_{SS}^{max} = 0.375 mg/L

C_{SS}^{min} = 0.181 mg/L

C_{SS}^{min} = 0.157mg/L

Aplikacija	D (mg)	τ	k_a (h^{-1})	V_D (L)	k_{el} (h^{-1})	$t_{1/2}$ (h)
3 x dnevno	3 x 50	8 h	0.70	100	0.17	4 (el.)
1 x dnevno	1 x 150	24 h	0.06	100	0.17	12 (abs.)



C_{SS}^{max} = 0.375 mg/L

C_{SS}^{max} = 0.327 mg/L

C_{SS}^{min} = 0.195 mg/L

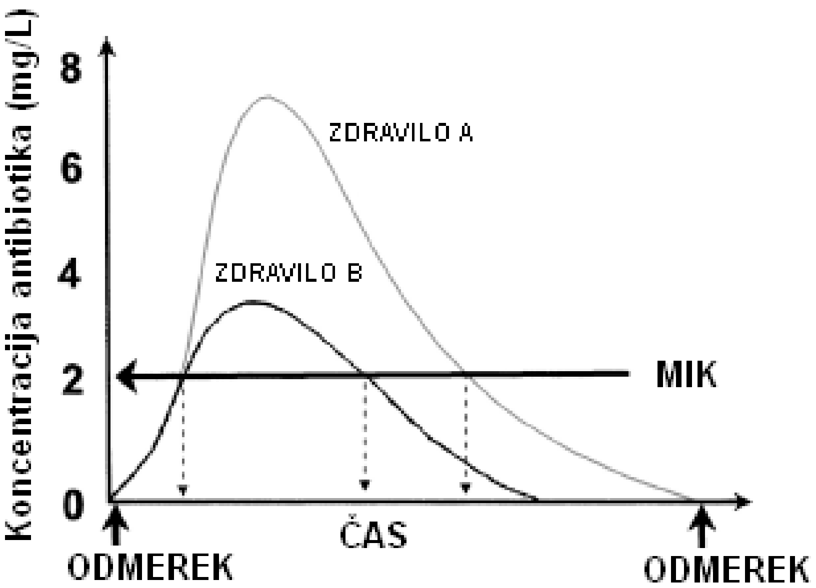
C_{SS}^{min} = 0.181mg/L

VZORCI PROTIMIKROBNEGA DELOVANJA

- Časovno odvisno delovanje
  - C(antib) > MIK: z ↑c(antib) se hitrost uničevanja mikroorganizmov NE povečuje
  - ↓ PAU
- Koncentracijsko odvisno delovanje
  - Baktericidnost = f (c(antib))
  - ↑ PAU

INDEKSI UČINKOVITOSTI

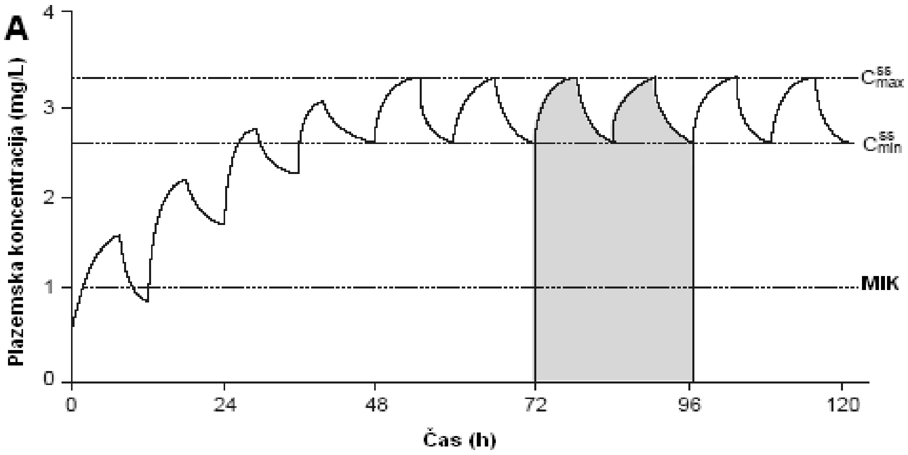
- **Čas, ko koncentracija protimikrobne učinkovine preseže MIK** (t>MIK) – izražen kot % dozirnega intervala



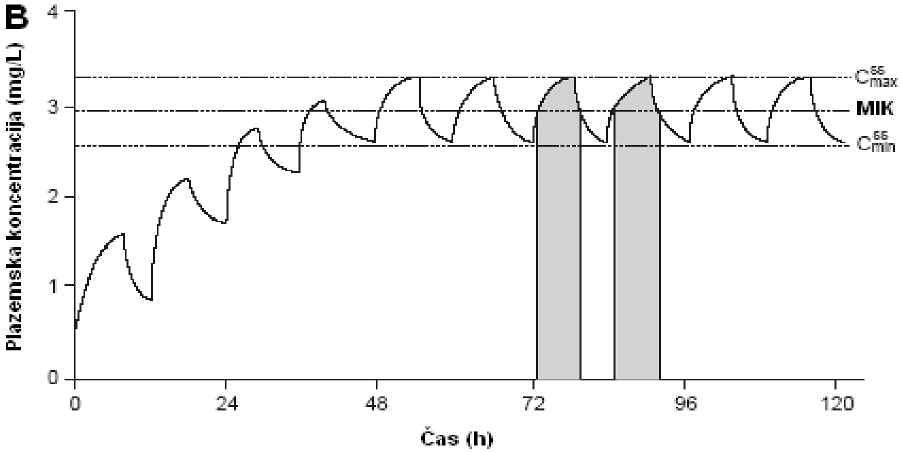
- **Razmerje med C_{max}^{ss} in MIK** (C_{max}^{ss}/MIK)

Razmerje med površino pod krivuljo in MIK (PPK^{ss}/MIK)

Površina pod krivuljo (PPK^{ss})



$Cmin^{SS}$ > MIK



$Cmin^{SS}$ < MIK