# ORAL Administration
## (One Compartment) Pharmacokinetics
## Method of Residuals

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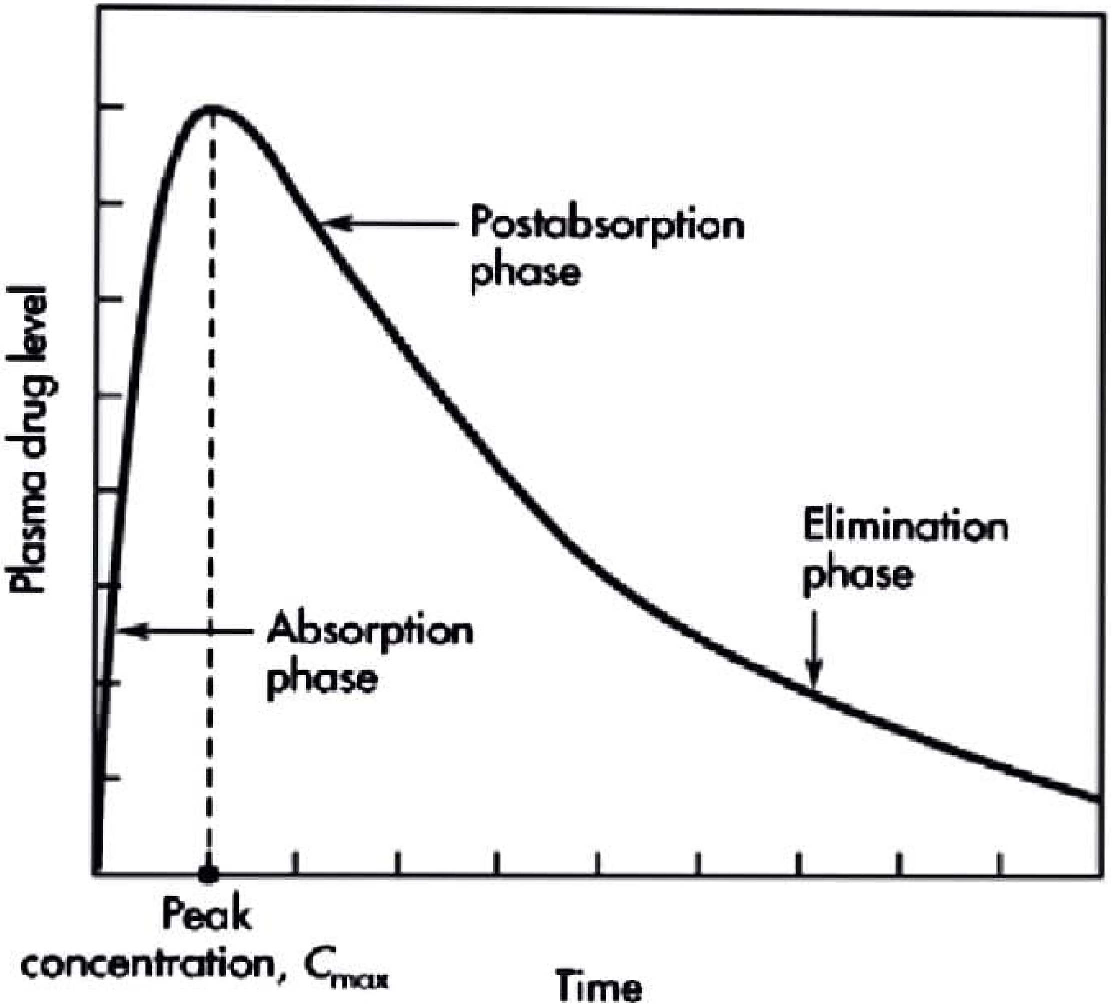
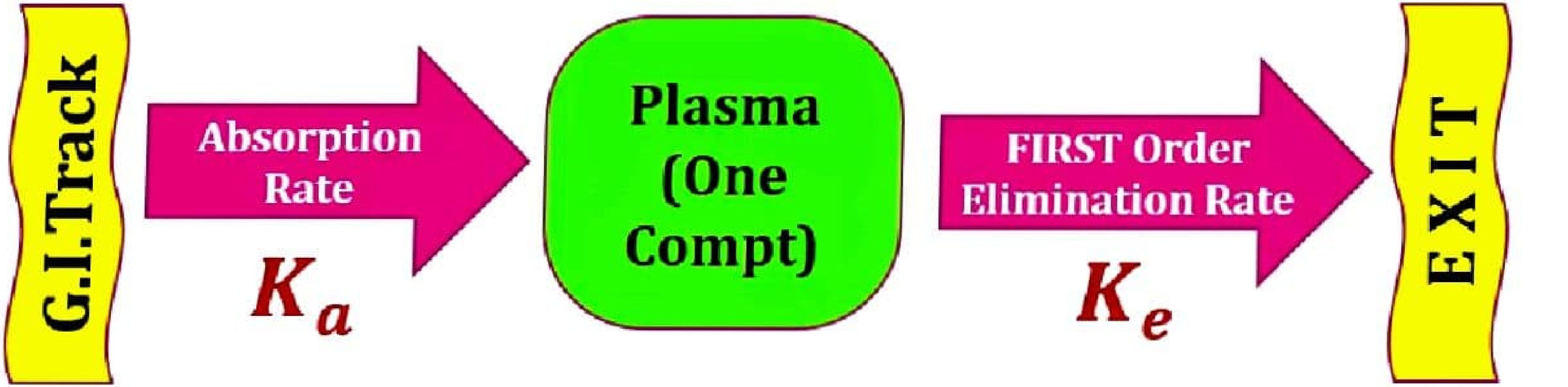
# One Compt ORAL Administration




- **Absorption phase:** absorption rate more than elimination rate
- **Postabsorption phase:** elimination rate more than absorption rate
- **Elimination phase:** no significant absorption occur (only elimination process)

# One Compt ORAL Administration




"Method of Residual" can be used,

Only if "Ka" is FIRST ORDER input Rate

"Wagner Nelson Method" can be used for ZERO Order "Ka" as well as FIRST Order "Ka"

# initial Equation for FIRST Order 'Ka'

Amount of Drug Changed (dX) per unit time change (dt) = Rate Change in Amount in PLASMA

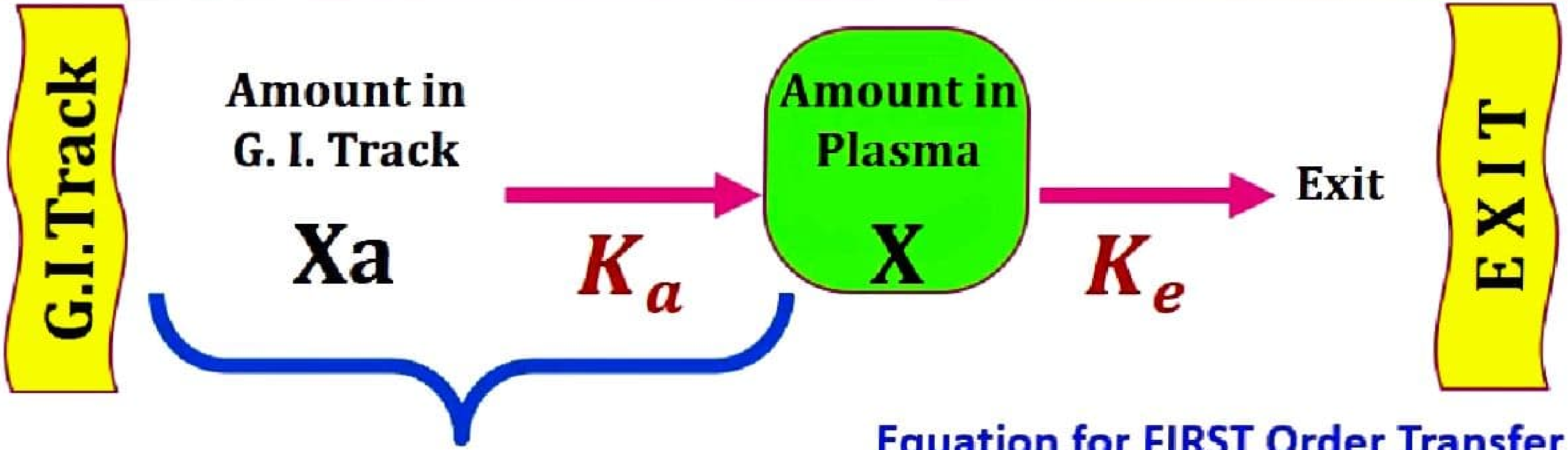
$$\frac{dX}{dt} = \text{Input Rate} - \text{Output Rate}$$

$$\frac{dX}{dt} = k_a X_a - k_e X$$

X = Amount of Drug in Plasma at time 't'

Xa = Amount of Drug in G.I.T. at time 't'

# Equation for “Xa”




$$X_a = X_{a0} * e^{-k_a t}$$

$$X_a = F\, X_0 * e^{-k_a t}$$

Equation for FIRST Order Transfer

(Similar to that of I.V.Injection)

$X_{a0}$ = Max Amount at time “0”

$X_{a0}$ = Absorbable Dose

F = Fraction of Dose Absorbs (Out of 1)

$X_0$ = Oral Dose

# Final Equation

$$\frac{dX}{dt} = k_a X_a - k_e X$$

$$\frac{dX}{dt} = k_a \left(F\, X_0 * e^{-k_a t}\right) - k_e X$$

***After Integration and Multiple Rearrangements…***

$$X = \frac{k_a F X_0}{(k_a - k_e)}\left(e^{-k_e t} - e^{-k_a t}\right)$$

$$C = \frac{X}{V_d}$$

$$\boxed{C = \frac{k_a F X_0}{V_d\,(k_a - k_e)}\left(e^{-k_e t} - e^{-k_a t}\right)}$$

# Method of Residuals

(Feathering Method)

# Method of Residual

## *Method to Solve any Multi-Exponential Equation...*

$$C = \frac{k_a F X_0}{V_d\,(k_a - k_e)} \left(e^{-k_e t} - e^{-k_a t}\right)$$

**A = All Constants**

$$A = \frac{k_a F X_0}{V_d\,(k_a - k_e)}$$

$$C = \mathrm{A}\left(e^{-k_e t} - e^{-k_a t}\right)$$

$$C_{Actual} = \mathrm{A}\, e^{-k_e t} - A\, e^{-k_a t}$$

***Assumption... Ka >>> Ke***

$$e^{-k_a t} \approx ZERO$$

$$C_{\mathrm{Terminal}} = \mathrm{A}\, e^{-k_e t}$$

# Method of Residual

$$C_{\text{Terminal}} = \mathrm{A}\, e^{-k_e t}$$

$$C_{\text{Back}} = \mathrm{A}\, e^{-k_e t}$$

*Equation of Straight Line*

$$Log\ C_{\text{Back}} = Log\ \mathrm{A} - \frac{K_e}{2.303} t$$

**New Hypothetical Term** $C_{\text{Residual}} = C_{\text{Back}} - C_{\text{Actual}}$

$$C_{Residual} = \mathrm{A}\, e^{-k_e t} - (\mathrm{A}\, e^{-k_e t} - A\, e^{-k_a t})$$

$$C_{Residual} = A\, e^{-k_a t}$$

*Equation of Straight Line*

$$Log\ C_{\text{Residual}} = Log\ \mathrm{A} - \frac{K_a}{2.303} t$$

*Find "Ka" from Slope*

# Absorption Rate Constant “Ka” from SEMI-LOG GRAPH

1

# 'Ka' by SemiLog Graph Paper

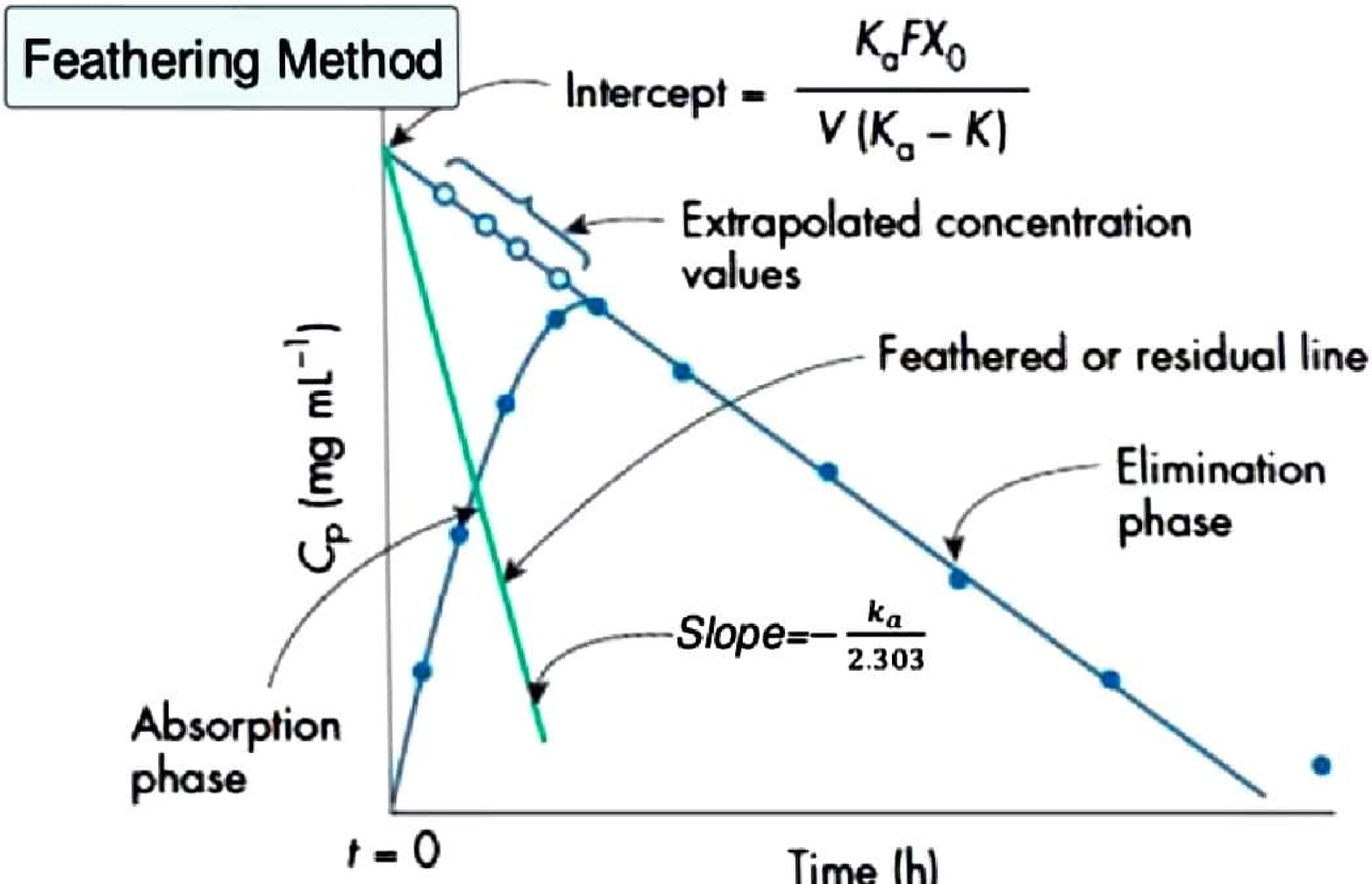
Plot C vs Time on SemiLog Graph Paper, and then Extrapolate Terminal Phase (upto Y-Axis)

Note-down Value of $C_{Back}$ for initial Time Points from GRAPH

Calculate $C_{Residual} = C_{back} - C_{Actual}$

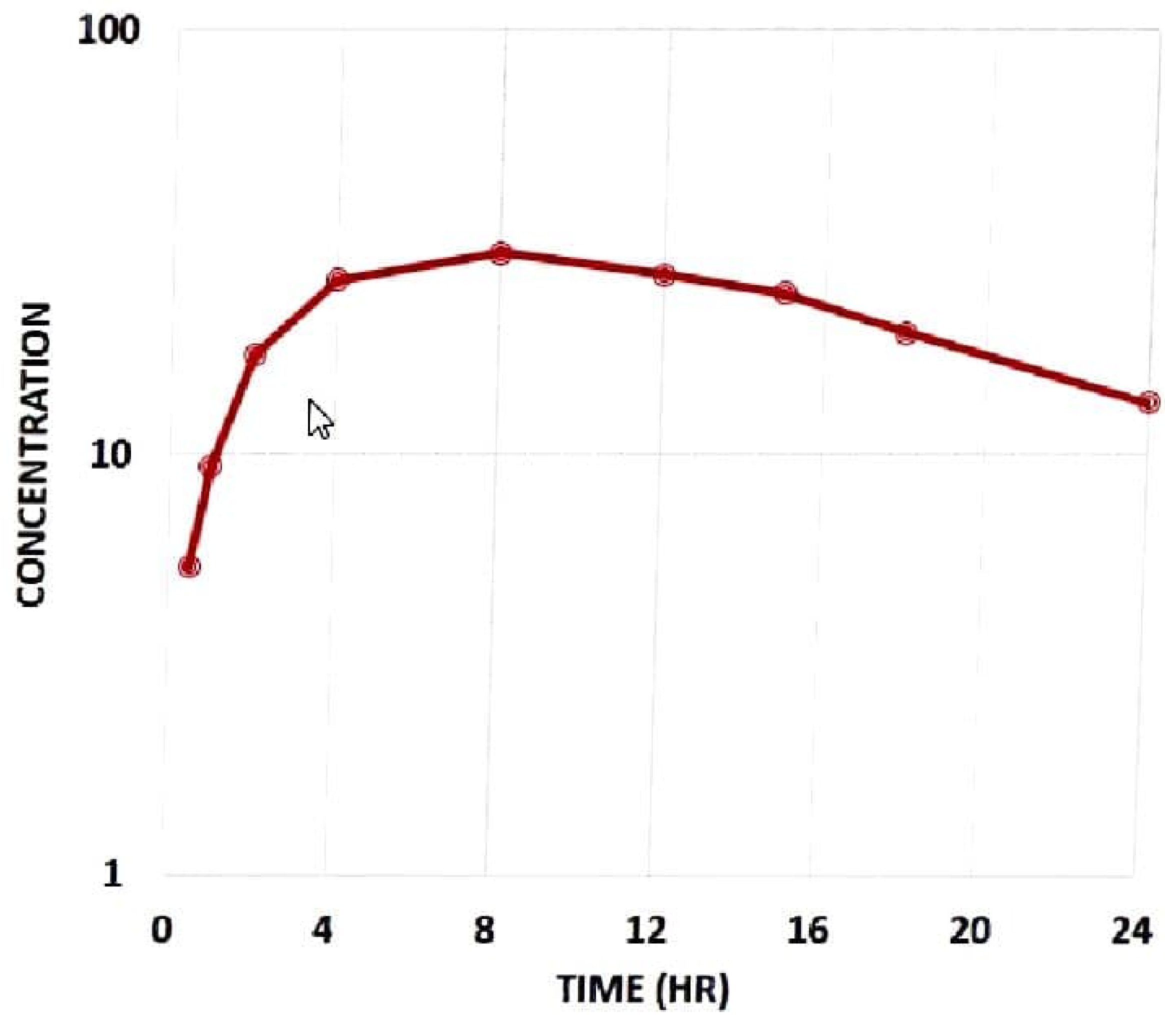
Plot Graph of $C_{Residual}$ Vs Time, Calculate "Ka" from Slope

# Method of Residual



# Start with Data – SemiLog Graph

| Time (Hr) | Plasma Conc (mcg/ml) |
|---|---|
| 0 | 0 |
| 0.5 | 5.4 |
| 1 | 9.4 |
| 2 | 17.2 |
| 4 | 25.8 |
| 8 | 29.8 |
| 12 | 26.6 |
| 15 | 24.1 |
| 18 | 19.4 |
| 24 | 13.3 |



# Find "Ke" from Terminal Phase

*'Ke' is NOT Required to find 'Ka'*

**But, it can be Obtained from Terminal Phase (Whereby Only Elimination & NO Absorption)**

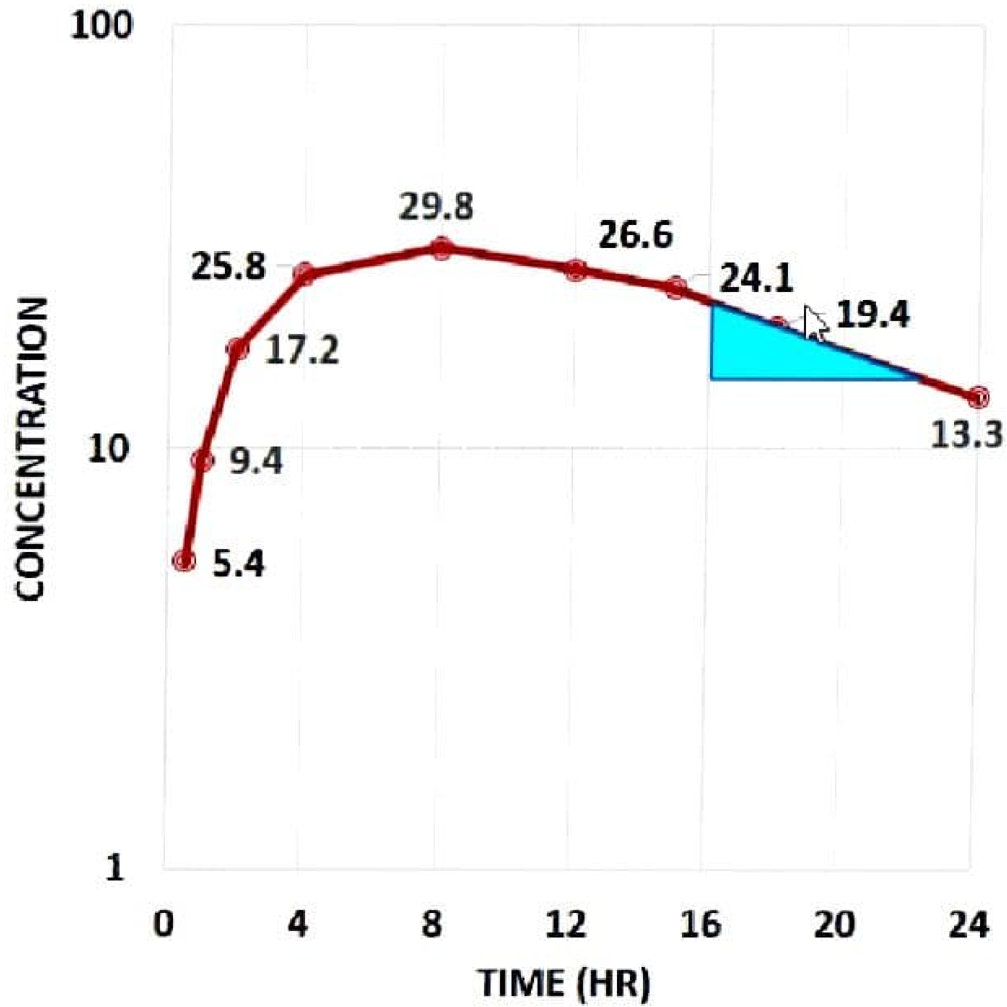
*Method is SAME as I.V.Injection*

$$Slope = m = \frac{Log\ y_2 - Log\ y_1}{x_2 - x_1}$$

**Ke = - Slope * 2.303**

**Ke = -(-0.0285) * 2.303**

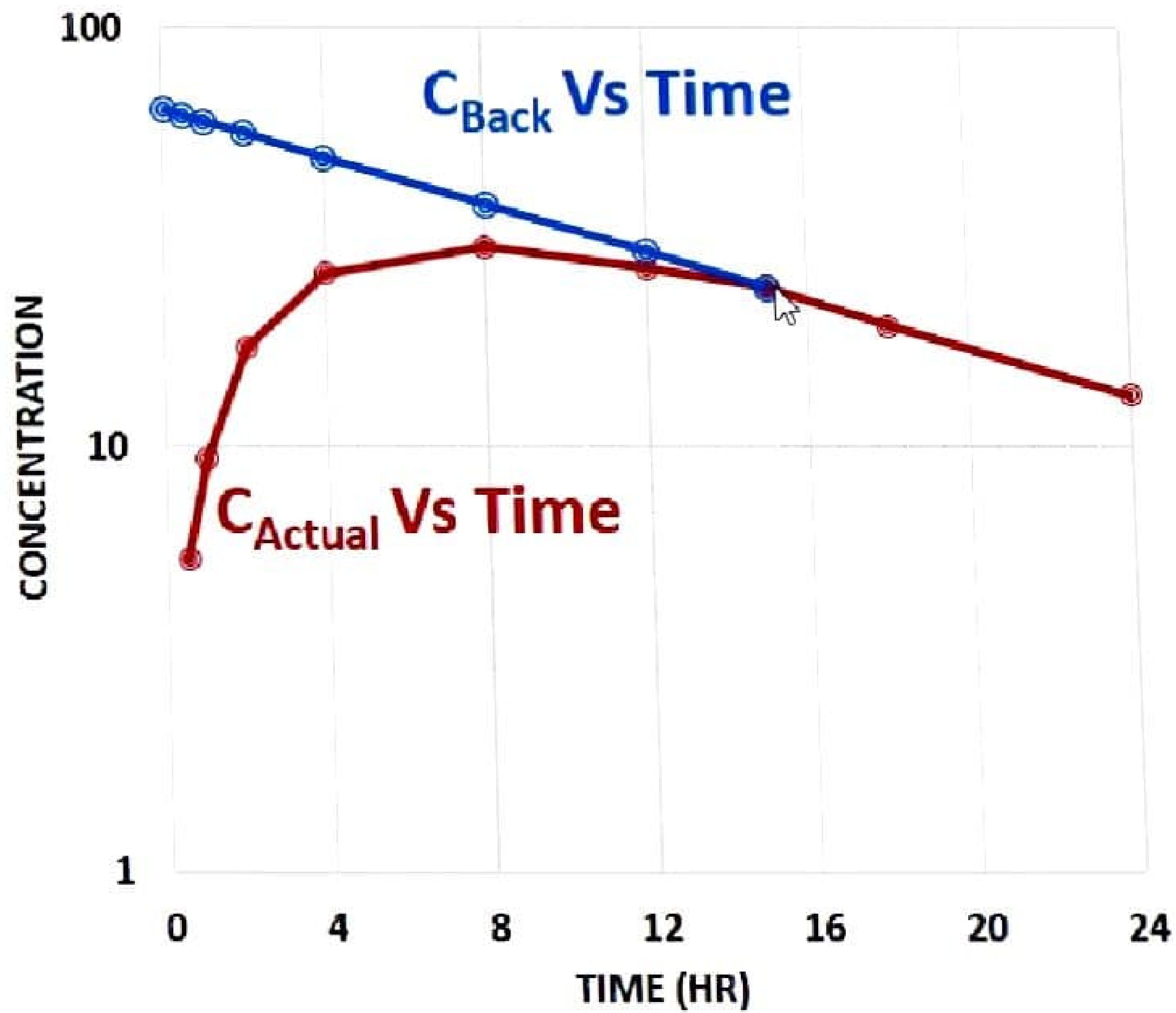
**Ke = 0.0656 hr$^{-1}$**



# Extrapolate Terminal Phase

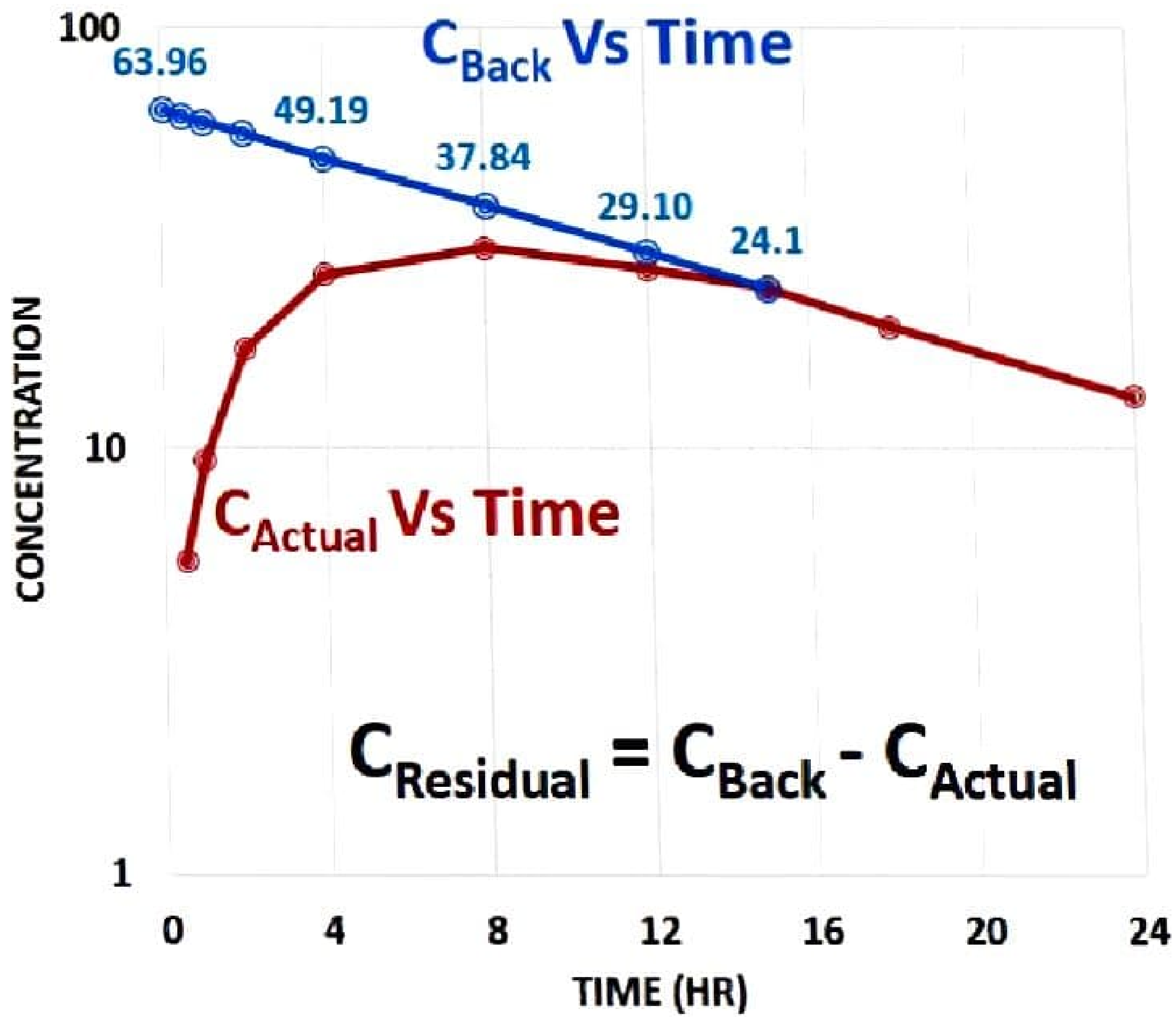
Extrapolate Terminal Phase upto Y-Axis.

Note Down Value of $C_{Back}$ for Initial Time Points from GRAPH



# Find $C_{Back}$ from Graph & Calculate $C_{Residual}$

| Time (Hr) | $C_{Actual}$ | $C_{Back}$ | $C_{Residual}$ |
|---|---|---|---|
| 0 | 0 | 63.96 | 63.96 |
| 0.5 | 5.4 | 61.89 | 56.49 |
| 1 | 9.4 | 59.90 | 50.50 |
| 2 | 17.2 | 56.09 | 38.89 |
| 4 | 25.8 | 49.19 | 23.39 |
| 8 | 29.8 | 37.84 | 8.04 |
| 12 | 26.6 | 29.10 | 2.50 |
| 15 | 24.1 | | |
| 18 | 19.4 | | |
| 24 | 13.3 | | |




$$C_{Residual} = C_{Back} - C_{Actual}$$

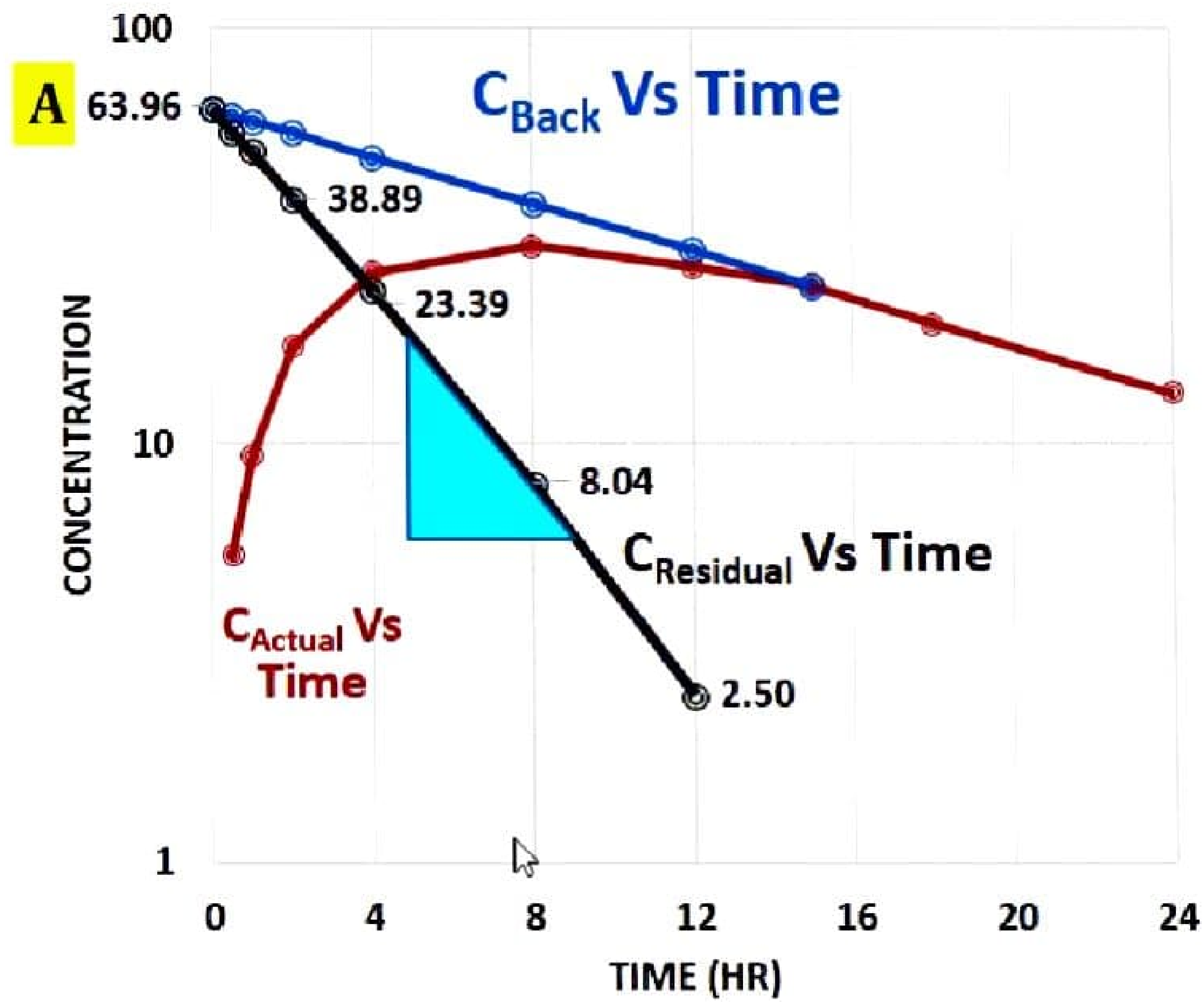
# Find "Ka" from Slope of $C_R$ vs t

$$Slope = \frac{Log\, y_2 - Log\, y_1}{x_2 - x_1}$$

Ka = - Slope * 2.303

Ka = -(-0.1168) * 2.303

Ka = 0.269 $hr^{-1}$




$$A = \frac{k_a F X_0}{V_d\,(k_a - k_e)}$$

# Absorption Rate Constant “Ka” from SIMPLE GRAPH PAPER

2

# 'Ka' by Simple Graph Paper

Plot Log C vs Time, and then Extrapolate Terminal Phase (upto Y-Axis)

Note-down Value of Log ($C_{Back}$) for initial Time Points from GRAPH

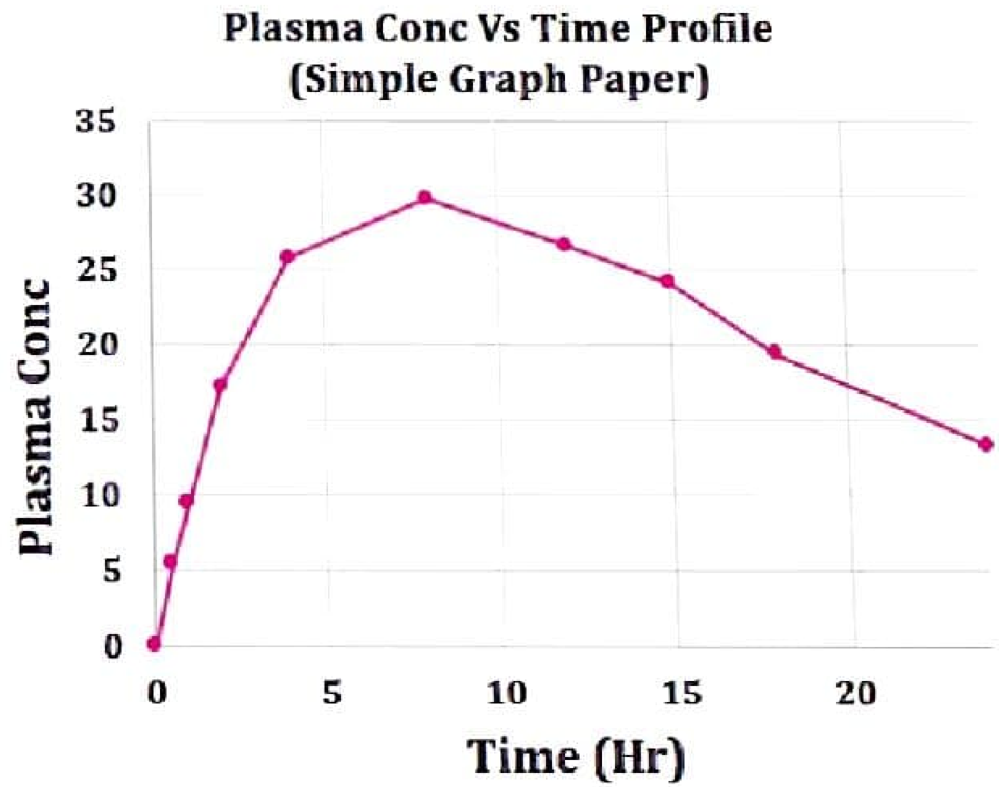
Calculate $C_{back}$ i.e. Anti-log of Log $C_{back}$

Calculate $C_{Residual} = C_{back} - C_{Actual}$

Plot Graph of Log $C_{Residual}$ Vs Time, Calculate "Ka" from Slope

# Start with Data

| Time (Hr) | Plasma Conc (mcg/ml) |
|---|---|
| 0 | 0 |
| 0.5 | 5.4 |
| 1 | 9.4 |
| 2 | 17.2 |
| 4 | 25.8 |
| 8 | 29.8 |
| 12 | 26.6 |
| 15 | 24.1 |
| 18 | 19.4 |
| 24 | 13.3 |

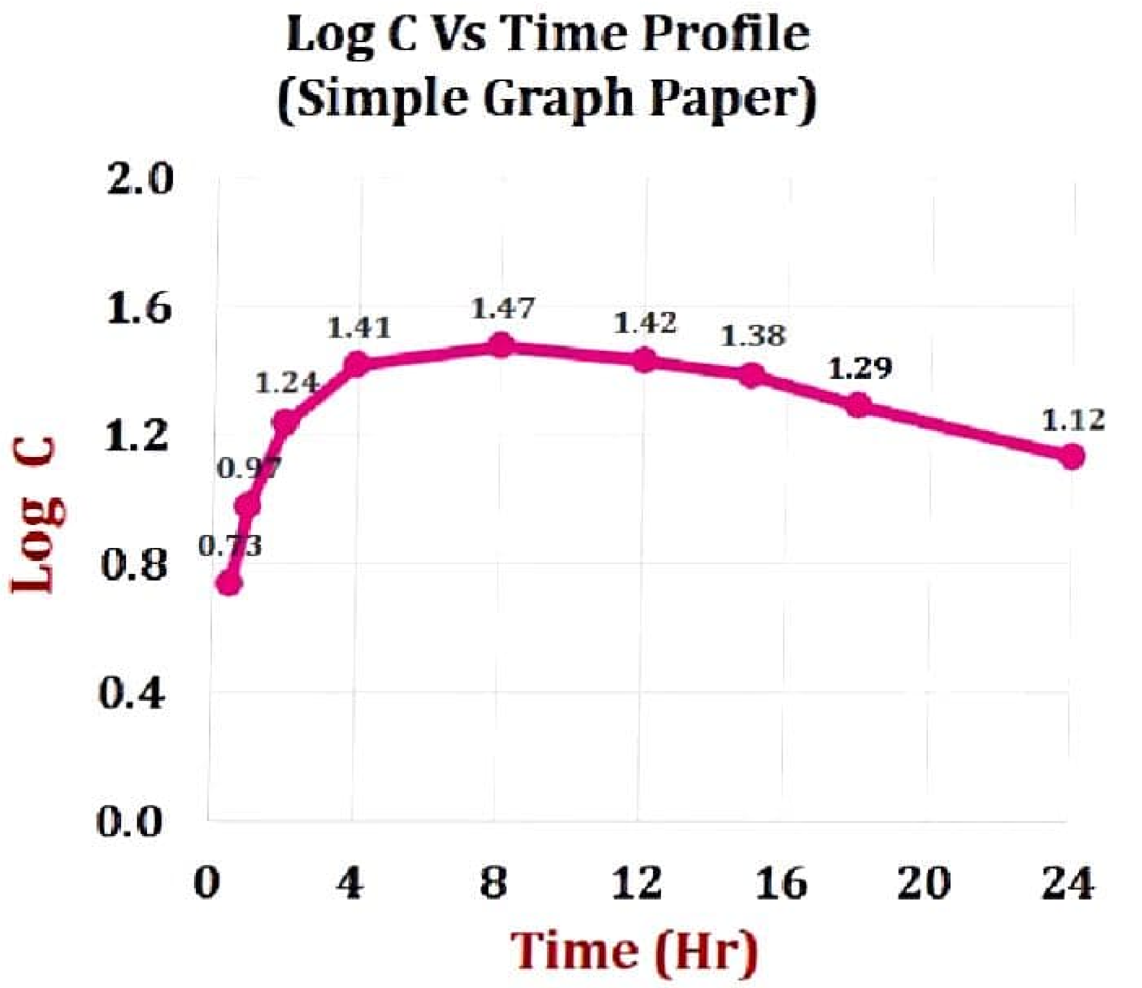



## No Need to Plot

"C vs t" on Simple Graph

# Plot Log C vs Time on Simple Graph

| Time (Hr) | Plasma Conc (mcg/ml) | Log C |
|---|---|---|
| 0 | 0 | |
| 0.5 | 5.4 | 0.73 |
| 1 | 9.4 | 0.97 |
| 2 | 17.2 | 1.24 |
| 4 | 25.8 | 1.41 |
| 8 | 29.8 | 1.47 |
| 12 | 26.6 | 1.42 |
| 15 | 24.1 | 1.38 |
| 18 | 19.4 | 1.29 |
| 24 | 13.3 | 1.12 |



# Find “Ke” from Terminal Phase

***‘Ke’ is NOT Required to find ‘Ka’***

**But, it can be Obtained from Terminal Phase (Whereby Only Elimination & NO Absorption)**

***Method is SAME as I.V.Injection***

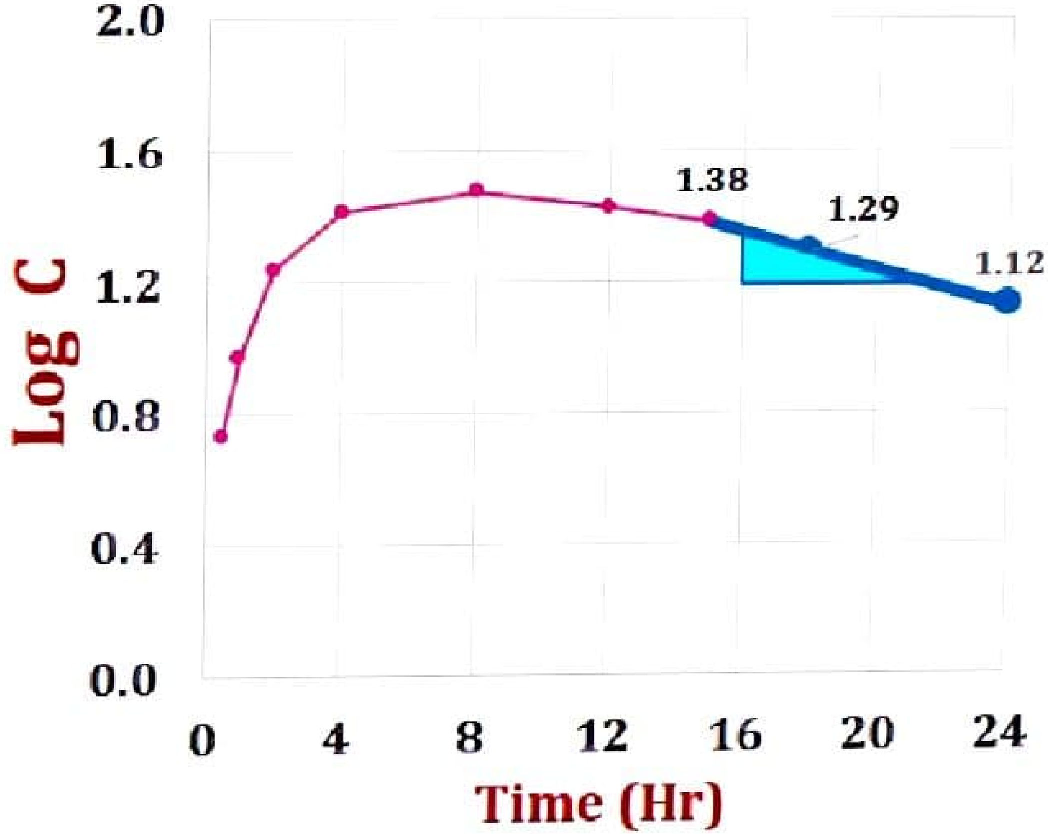
$$Slope = m = \frac{dy}{dx} = \frac{y_2 - y_1}{x_2 - x_1}$$

**Ke = - Slope * 2.303**

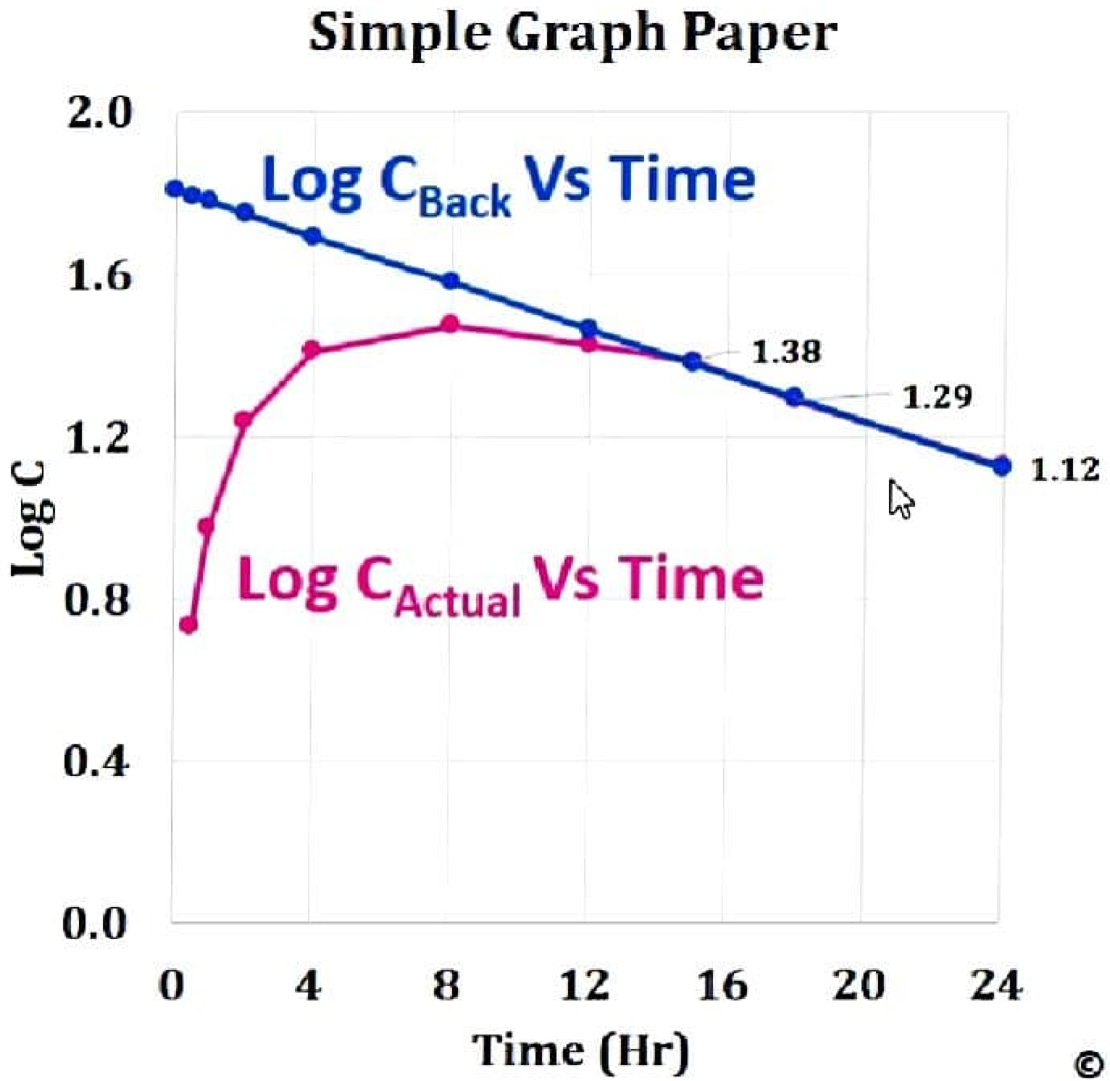
**Ke = -(-0.0285) * 2.303**

**Ke = 0.0656 $hr^{-1}$**

**Log C Vs Time Profile (Simple Graph Paper)**



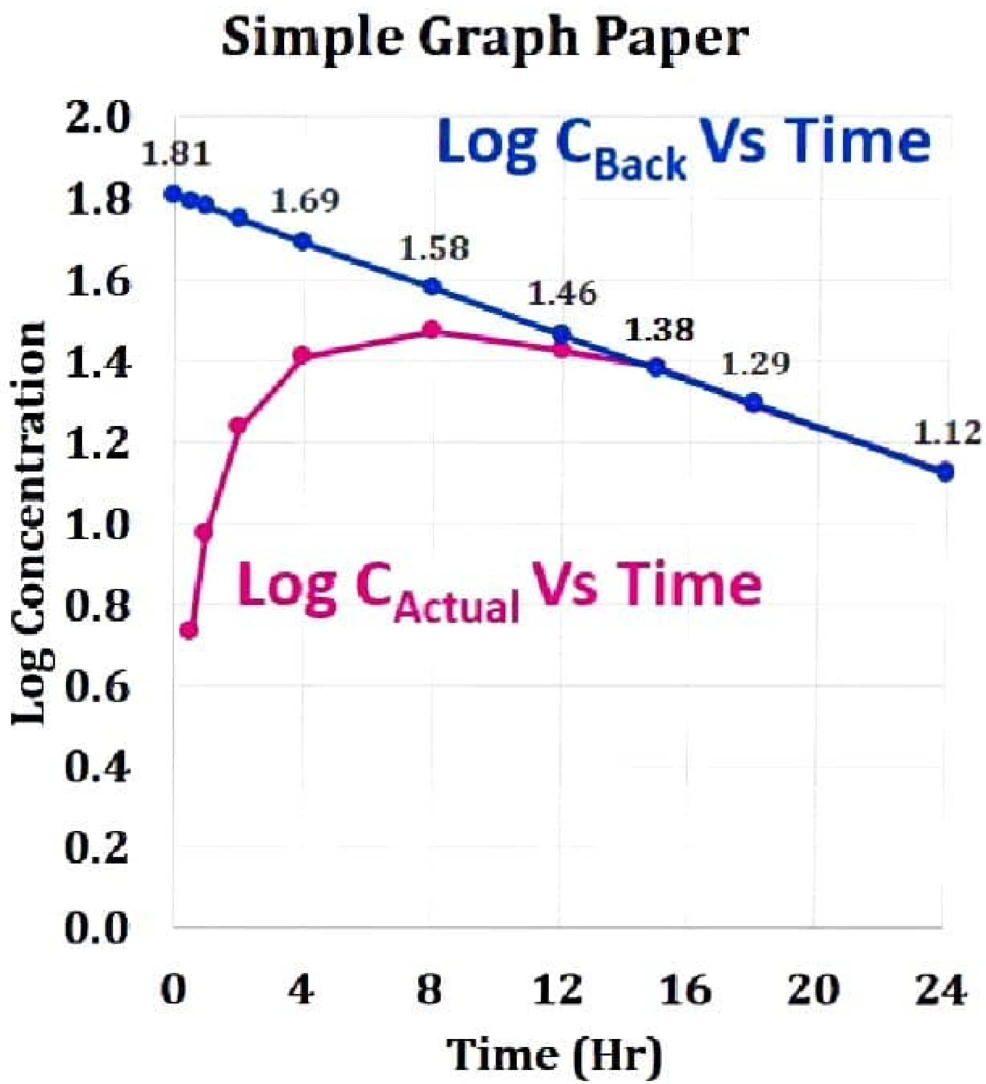
# Extrapolate Terminal Phase




Extrapolate Terminal Phase upto Y-Axis.

Note Down Value of Log $C_{Back}$ for Initial Time Points from GRAPH

# Log $C_{Back}$ from Graph

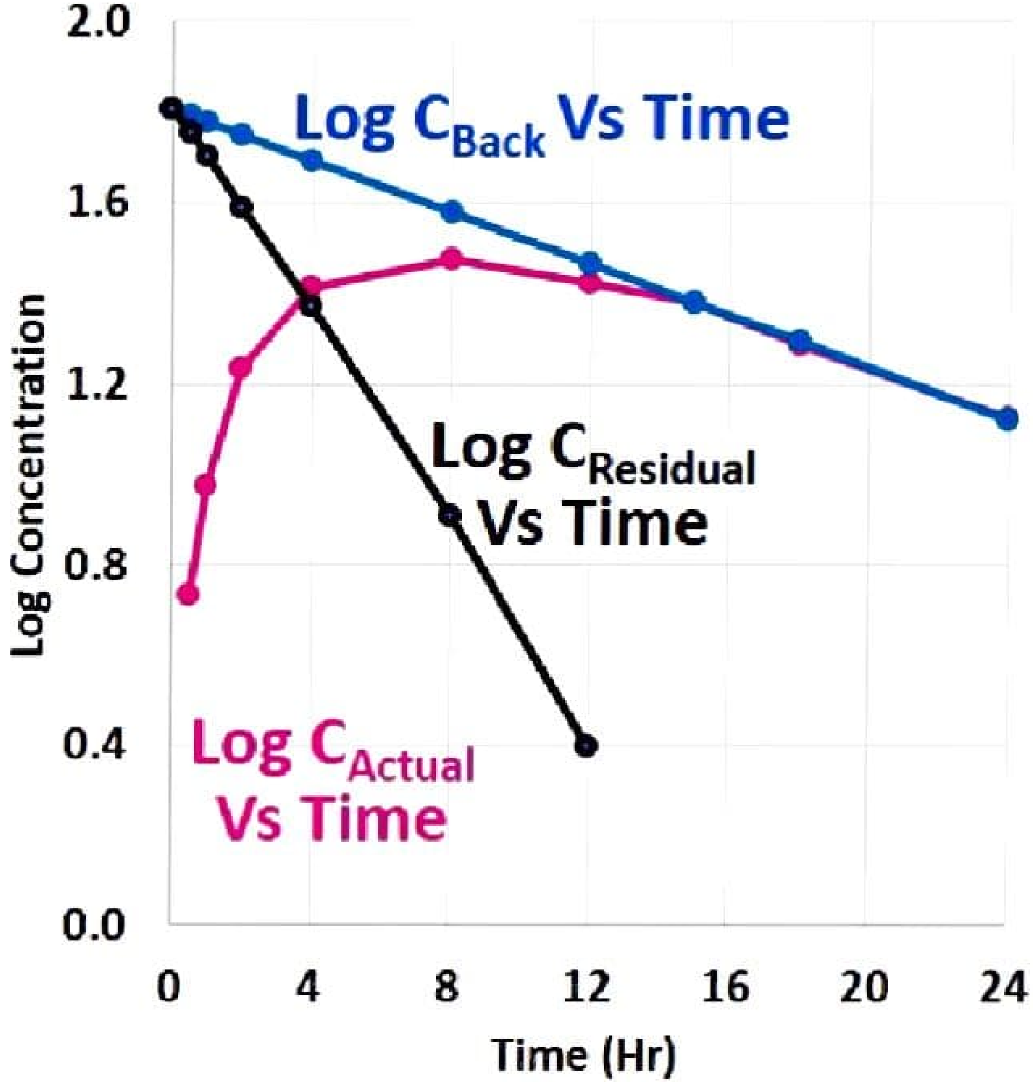



| Time (Hr) | $C_{Actual}$ | Log $C_{Actual}$ | Log $C_{Back}$ |
|---|---|---|---|
| 0 | 0 | - - - | 1.81 |
| 0.5 | 5.4 | 0.73 | 1.79 |
| 1 | 9.4 | 0.97 | 1.78 |
| 2 | 17.2 | 1.24 | 1.75 |
| 4 | 25.8 | 1.41 | 1.69 |
| 8 | 29.8 | 1.47 | 1.58 |
| 12 | 26.6 | 1.42 | 1.46 |
| 15 | 24.1 | 1.38 | 1.38 |
| 18 | 19.4 | 1.29 | 1.29 |
| 24 | 13.3 | 1.12 | 1.12 |

# Calculate $C_{Back}$ and $C_{Residual}$

| Time (Hr) | $C_{Actual}$ | Log $C_{Actual}$ | Log $C_{Back}$ | $C_{Back}$ | $C_{Residual}$ | Log $C_{residual}$ |
|---|---|---|---|---|---|---|
| 0 | 0 | --- | 1.81 | 63.96 | 63.96 | 1.81 |
| 0.5 | 5.4 | 0.73 | 1.79 | 61.89 | 56.49 | 1.75 |
| 1 | 9.4 | 0.97 | 1.78 | 59.90 | 50.50 | 1.70 |
| 2 | 17.2 | 1.24 | 1.75 | 56.09 | 38.89 | 1.59 |
| 4 | 25.8 | 1.41 | 1.69 | 49.19 | 23.39 | 1.37 |
| 8 | 29.8 | 1.47 | 1.58 | 37.84 | 8.04 | 0.91 |
| 12 | 26.6 | 1.42 | 1.46 | 29.10 | 2.50 | 0.40 |
| 15 | 24.1 | 1.38 | 1.38 | $C_{residual} = C_{back} - C_{Actual}$ | | |
| 18 | 19.4 | 1.29 | 1.29 | | | |
| 24 | 13.3 | 1.12 | 1.12 | | | |

# "Log $C_{Residual}$ vs t" on Simple Graph

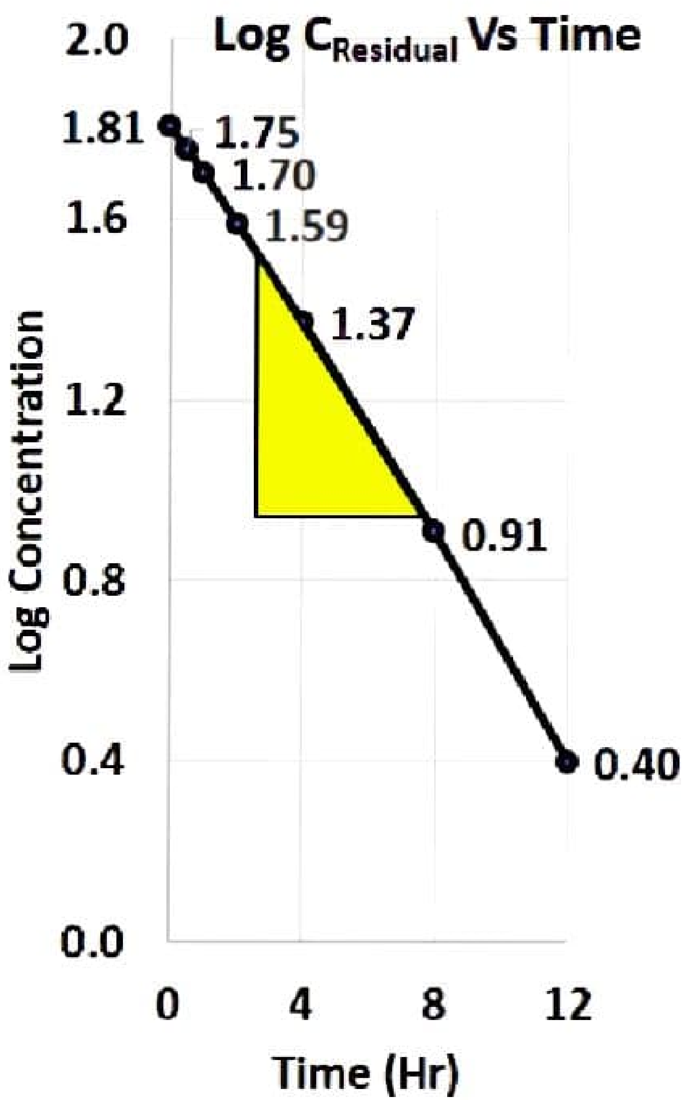



Plot on SAME Graph Paper or Another Graph Paper.

Plotting on Another Graph Paper is Better, as X-Axis Scale Unit Can be increase for Better Plotting of Data

**Calculate Slope of Log $C_{Residual}$ Vs Time and Multiply with 2.303 is the Value "Ka"**

# Calculate "Ka" from Slope




$$Slope = m = \frac{dy}{dx} = \frac{y_2 - y_1}{x_2 - x_1}$$

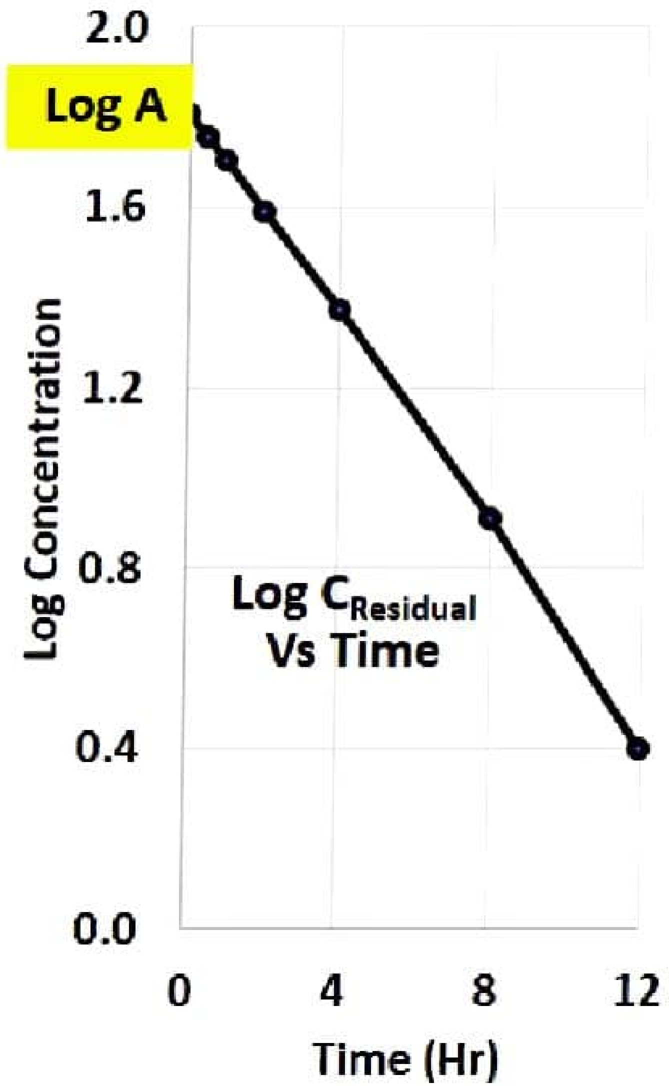
Ka = - Slope * 2.303

Ka = -(-0.1168) * 2.303

Ka = 0.269 $hr^{-1}$

| Ka | >> | Ke |
|---|---|---|
| 0.269 | >> | 0.0656 |

# Intercept Value




A = Antilog of intercept

$$A = \frac{k_a F X_0}{V_d \, (k_a - k_e)}$$

By Keeping the Value of known Parameters, the Unknown Parameters may be Calculated from it

# Practice Numerical – 1

| Time (Hr) | $C_{Actual}$ | Log $C_{Actual}$ | Log $C_{Back}$ | $C_{Back}$ | $C_{Residual}$ | Log $C_{residual}$ |
|---|---|---|---|---|---|---|
| 0 | 0 | --- | | | | |
| 0.25 | 2.85 | | | | | |
| 0.5 | 5.43 | | | | | |
| 0.75 | 7.75 | | | | | |
| 1 | 9.84 | | | | | |
| 2 | 16.2 | | | | | |
| 4 | 22.15 | | | | | |
| 6 | 23.01 | | | | | |
| 10 | 19.09 | | | | | |
| 14 | 13.9 | | | | | |
| 16 | 11.3 | | | | | |
| 20 | 7.97 | | | | | |

Dose = 10 mg , Fraction Absorb = 0.8

# Practice Numerical – 2

| Time (Hr) | $C_{Actual}$ | Log $C_{Actual}$ | Log $C_{Back}$ | $C_{Back}$ | $C_{Residual}$ | Log $C_{residual}$ |
|---|---|---|---|---|---|---|
| 0 | 0 | --- | | | | |
| 0.5 | 5.36 | | | | | |
| 1 | 9.35 | | | | | |
| 2 | 17.18 | | | | | |
| 4 | 25.78 | | | | | |
| 8 | 29.78 | | | | | |
| 12 | 26.63 | | | | | |
| 18 | 19.4 | | | | | |
| 24 | 13.26 | | | | | |
| 36 | 5.88 | | | | | |
| 48 | 2.56 | | | | | |
| 72 | 0.49 | | | | | |

Dose = 500 mg , Fraction Absorb = 1

# Practice Numerical – 3

| Time (Hr) | $C_{Actual}$ | Log $C_{Actual}$ | Log $C_{Back}$ | $C_{Back}$ | $C_{Residual}$ | Log $C_{residual}$ |
|---|---|---|---|---|---|---|
| 0 | 0 | --- | | | | |
| 1 | 0.38 | | | | | |
| 2 | 0.73 | | | | | |
| 3 | 0.91 | | | | | |
| 4 | 0.97 | | | | | |
| 5 | 0.97 | | | | | |
| 6 | 0.92 | | | | | |
| 8 | 0.71 | | | | | |
| 10 | 0.53 | | | | | |
| 12 | 0.4 | | | | | |
| 14 | 0.3 | | | | | |

Dose = 100 mg , Fraction Absorb = 1

# Practice Numerical – 4

| Time (Hr) | $C_{Actual}$ | Log $C_{Actual}$ | Log $C_{Back}$ | $C_{Back}$ | $C_{Residual}$ | Log $C_{residual}$ |
|---|---|---|---|---|---|---|
| 0 | 0 | --- | | | | |
| 0.25 | 2.2 | | | | | |
| 0.5 | 3.8 | | | | | |
| 0.75 | 5 | | | | | |
| 1 | 5.8 | | | | | |
| 1.5 | 6.8 | | | | | |
| 2 | 7.1 | | | | | |
| 2.5 | 7.1 | | | | | |
| 3 | 6.9 | | | | | |
| 4 | 6.2 | | | | | |
| 6 | 4.8 | | | | | |
| 8 | 3.5 | | | | | |
| 12 | 1.9 | | | | | |
| 18 | 0.8 | | | | | |
| 24 | 0.3 | | | | | |