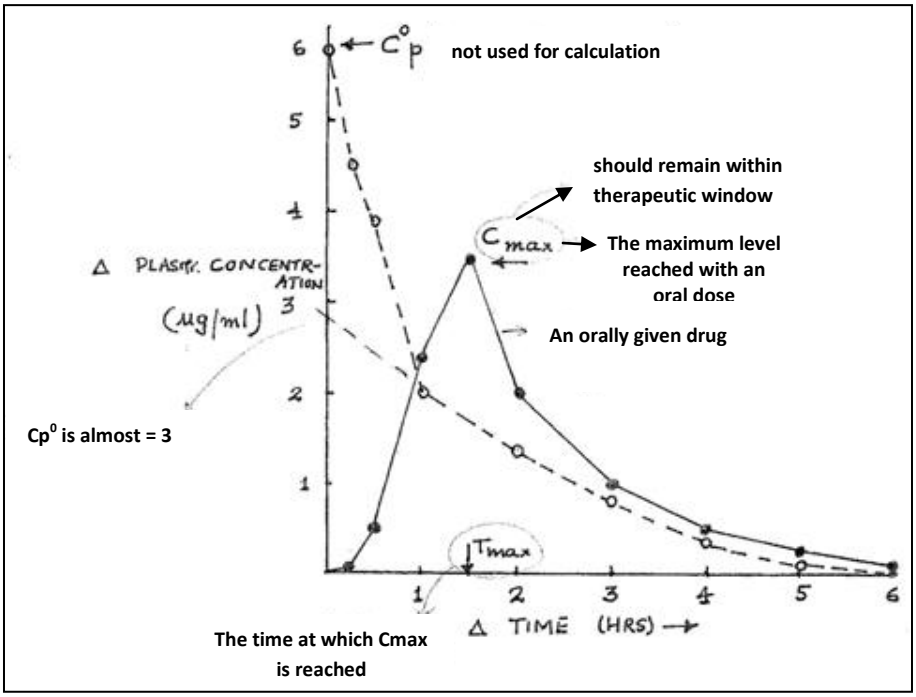
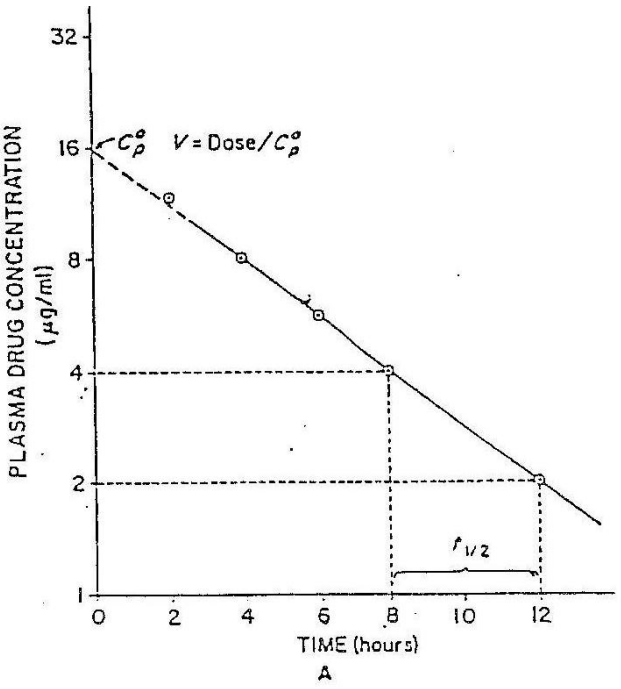
## Unit I – Problem 2 – Pharmacology: Estimation of Pharmacokinetic Parameters of A Drug

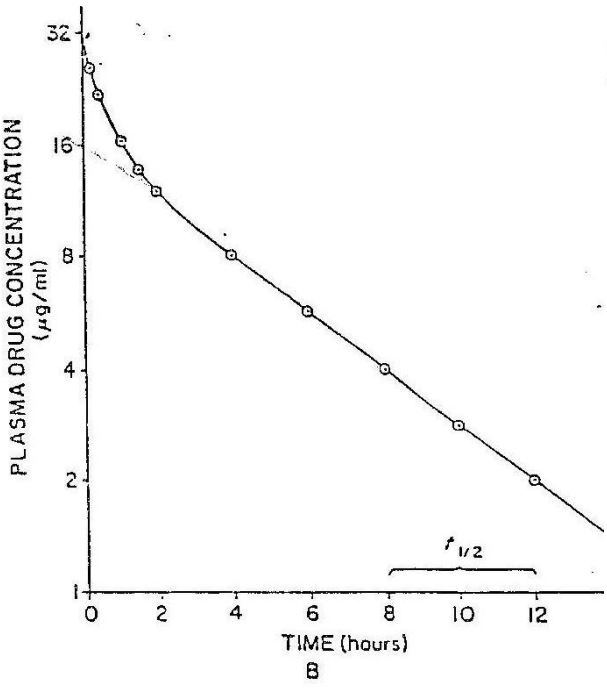
- **Introduction**: it is essential to determine the pharmacokinetic properties of a drug before it is administered to patients. We need to have knowledge about absorption, distribution, biotransformation and excretion of the drug (i.e. pharmacokinetics), so that it can be administered safely to patients. The pharmacokinetics of a drug can be studied in patients, healthy volunteers or animals (rabbits, rats, monkeys… etc).
- **Objective**: to estimate the pharmacokinetic parameters of Paracetamol (Panadol).
- **Parameters measured:**
  - **Plasma Concentration versus Time Curve.**
  - **Maximal (peak) Plasma Concentration ($C_{max}$).**
  - **Time to peak plasma concentration ($T_{max}$).**
  - **Phases of the curve.**
  - **Area under the curve (bioavailability).**
  - **Half-life (t ½).**
  - **Volume of distribution ($V_d$).**

- **Subject**: a 30-year-old male weighing 70 kg.
- **Drug**: Paracetamol 500 mg oral/intravenous.
- **Procedure**: the drug is administered either orally as a tablet or intravenously on different days. Blood samples are collected at 0, 15, 30, 60, 90, 120, 180, 240 and 360 minutes. The plasma levels of the drug at each time are estimated.
- **Results**: the results are presented graphically as plasma concentration versus time curves.




- **Problem solving exercise**: a 70 kg person was administered a drug "X" 650 mg intravenously. A butterfly cannula was fixed and blood samples collected after 30, 60, 90 minutes and subsequently after 2, 4, 6, 8, 10 and 12 hours. The results were plotted on a semi log paper (A & B). Calculate the following pharmacokinetic parameters:
  - **$C_p^0$ (in graph B)** = 16 µg/ml.
  - **Half-life (t ½)** = 4 hours.
  - **Volume of distribution (Vd)** = $\frac{Dose}{Cp^0} = \frac{650{,}000}{16}$ = 40,625 L
  - **After how musch time do you expect approximately 96% of drug to be excreted?**
    - ✓ Steady state = 5 half-lives → 5 x 4 (half-life) = 20 hours.


PLASMA DRUG CONCENTRATION (μg/ml)
32
16
8
4
2
1
$C_p^o$
$V = Dose/C_p^o$
$t_{1/2}$
0
2
4
6
8
10
12
TIME (hours)
A


PLASMA DRUG CONCENTRATION (μg/ml)
32
16
8
4
2
1
$t_{1/2}$
0
2
4
6
8
10
12
TIME (hours)
B