الكلية	الصيدلة
القسم	الصيدلانيات
المادة باللغة الانجليزية	Practical Biopharmaceutics
المادة باللغة العربية	عملي صيدلة حياتية
المرحلة الدراسية	الرابعة
اسم التدريسي	م.م. علي فخري جميل
عنوان المحاضرة باللغة الانجليزية	Introduction to Biopharmaceutics
عنوان المحاضرة باللغة العربية	مقدمة الى الصيدلة الحياتية
رقم المحاضرة	1
المصادر والمراجع	Laboratory Manual of Biopharmaceutics and Pharmacokinetics, S. B. Bhise, R. J. Dias, S. C. Dhawale, K. K. Mali
	Applied Biopharmaceutics and Pharmacokinetics

محتوى المحاضرة

Biopharmaceutics explain the effect and relationship of physical/chemical properties of the drug, dosage form in which the drug is given, and route of administration on the rate and extent of systemic drug absorption, then distribution in vivo to the site of action, metabolism and excretion.
i.e. "Pharmacokinetics"

Biopharmaceutics provides the scientific basis for drug product design and drug product development. Each step in the manufacturing process of a finished dosage form may potentially affect the release of the drug from the drug product and the availability of the drug at the site of action.

Biopharmaceutic considerations in drug product design:

Therapeutic objective: acute relief or chronic use, local or systemic .

Drug: physico-chemical properties.

Route of administration: oral, topical, parenteral.

Drug dosage and dosage regimen: small or large dose, frequency of administration, patient compliance.

Type of drug product: orally disintegrating tablet, extended-release tablet, injection.

Excipients: may affect drug product performance.

Method of manufacture: weighing accuracy, mixing uniformity, sterility, releasing tests.

Biopharmaceutics and mathematics:

Biopharmaceutics based on predicting values of drug release, bioavailability, elimination, … etc. by using mathematical laws, relationships, and plotting graphs.

One of the most important considerations in this relation is the "units" that must be established properly.

The most common units in biopharmaceutics are listed in the following table:

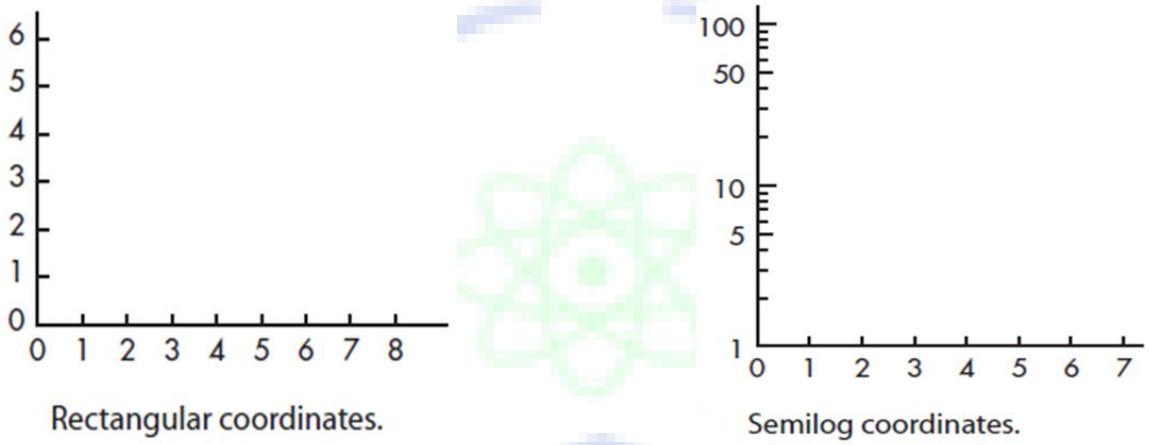
Parameter	Symbol	Unit	Example
Rate	$\frac{dD}{dt}$	$\frac{\text{Mass}}{\text{Time}}$	mg/h
	$\frac{dC}{dt}$	$\frac{\text{Concentration}}{\text{Time}}$	ug/mL/h
Zero-order rate constant	K_0	$\frac{\text{Concentration}}{\text{Time}}$	μg/mL/h
		$\frac{\text{Mass}}{\text{Time}}$	mg/h
First-order rate constant	k	$\frac{1}{\text{Time}}$	1/h or h^{-1}
Drug dose	D_0	Mass	mg
Concentration	C	$\frac{\text{Mass}}{\text{Volume}}$	μg/mL
Plasma drug concentration	Cp	$\frac{\text{Drug}}{\text{Volume}}$	μg/mL
Volume	V	Volume	mL or L
Area under the curve	AUC	Constration × time	μg·h/mL
Fraction of drug absorbed	F	No units	0 to 1
Clearance	Cl	$\frac{\text{Volume}}{\text{Time}}$	mL/h
Half-life	$t_{1/2}$	Time	H

Terms to be remembered in our course:

Calibration curve

Area under the curve "AUC"

Semi-log graph paper



Calibration curve:

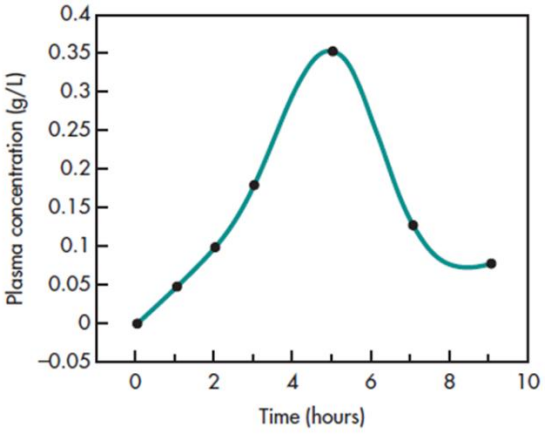
It is a plot that shows the relation between two variables, i.e. the changes that take place in the value of one variable depending on increasing or decreasing in the value of the second one.

This plotting can be used to determine other variables, by using area under the curve for example.

Or to predict the value of one variable by extrapolation of the straight line.

The general format for a linear relationship is often expressed as:
$y=mx+b$

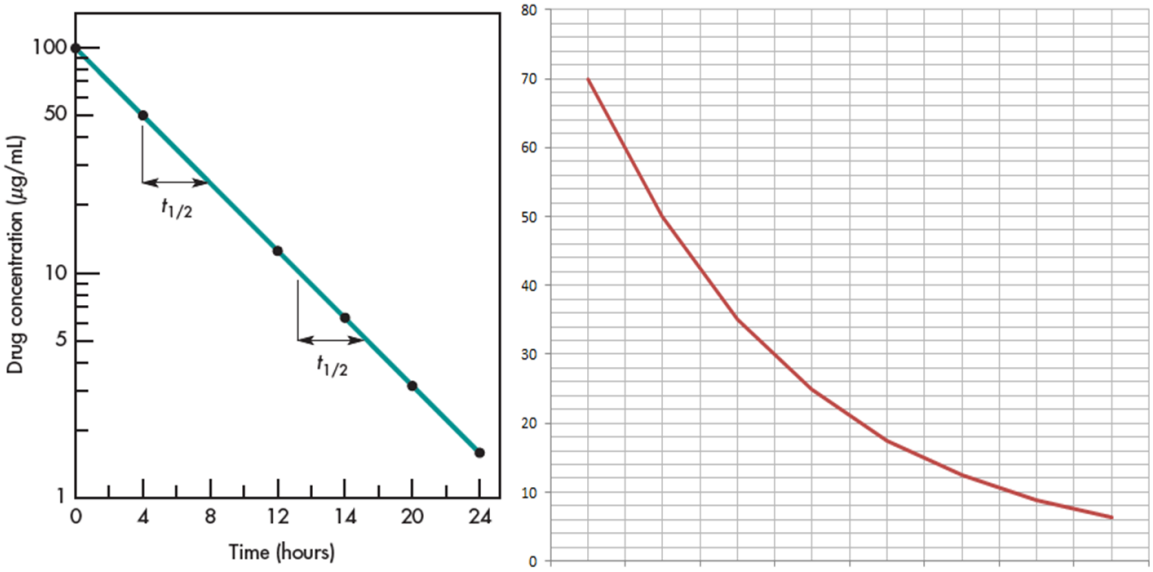
Plasma Concentration (ng/L)	Time (hours)	AUC (ng·h/L)
0	0	0
0.05	1	0.025
0.10	2	0.075
0.18	3	0.140
0.36	5	0.540
0.13	7	0.490
0.08	9	0.210



Semi-log graph:

Semi-logarithmic allows placement of the data at logarithmic intervals so that the numbers need not be converted to their corresponding log values prior to plotting on the graph .

Some of nonlinear curves in rectangular graph is converted to linear in semi-log graph. (1st order kinetics)



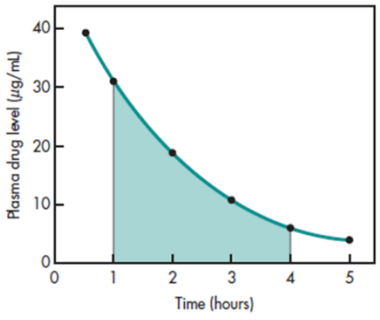
Calculation of AUC "Trapezoidal rule":

Considering the plot below, AUC from time 1h to 4h is the area that indicated by blue color.

The area is divided to smaller areas(from 1-2h, 2-3h...) and calculated individually by using:

$$[\mathrm{AUC}]_{t_{n-1}}^{t_n} = \frac{C_{n-1} + C_n}{2}(t_n - t_{n-1})$$

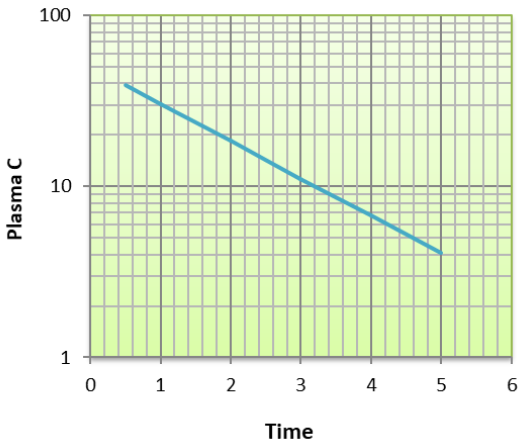
AUC can reflect the extent of drug absorption.



To calculate the total AUC from zero time to infinity, the concentration at zero time is estimated by back extrapolation of data points using a log linear plot (or semi-log plot).
The last plasma level–time curve is extrapolated to t = ∞.

$$[\mathrm{AUC}]_{t_n}^{t_\infty} = \frac{C_{pn}}{k}$$

Time (hours)	Plasma Drug Level (μg/mL)
0.5	38.9
1.0	30.3
2.0	18.4
3.0	11.1
4.0	6.77
5.0	4.10



The trapezoidal rule written in its full form to calculate the AUC from t = 0 to t = ∞ is as follows:

$$[\mathrm{AUC}]_0^\infty = \Sigma[\mathrm{AUC}]_{t_{n-1}}^{t_n} + \frac{C_{pn}}{k}$$