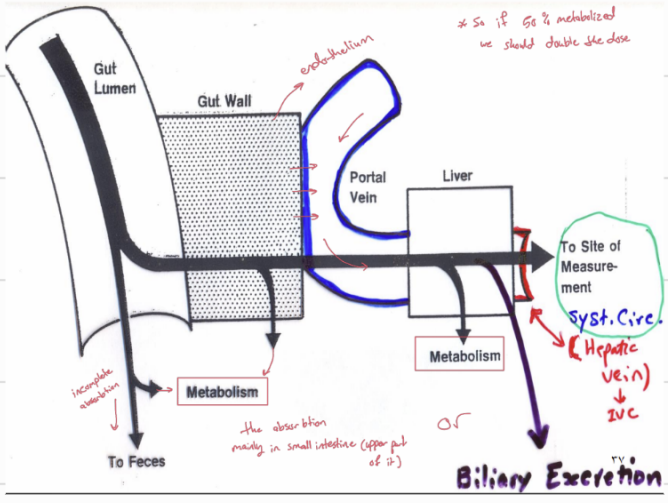
plecental barrier : semipermeable membrane made up of plecental tissues where are maternal and fetal circulation remains completely separated Because of precese of tight junction that Allow slow possage of ions and slow molecules only and restricted to larger one.

* first pass - effect or first pass effect : incomplete delivery of dose to systemic circulation or pre systemic elimination

* Drug pathway when it is givin orally

gut lumen → gut wall → portal vain → liver → systemic circulation By IVC (from hepatic vain)



* method of elimination

- metabolism in
  - Gut wall
  - Gut lumen
  - liver
  - All organs metabolise drug but with different percents
  - * if the patient has liver cirrhosis it will not metabolise the drug → we should reduce the dose
- incomplete absorbition → The main site of absorbtion is first part of small intistine
- Biliary execretion

* So due to these eliminations we should give the drug with higher dose orally than intravenous.

* Bio availability : is percentage of UNchanced active Drug that reach the systemic Circulation following Drug adminstration irrespective to the route if Drug is givin IV ⟹ Bio availibility = 100 %

Bio Availability factors

- Faulty manufacturing of dosage form
- incomplete Absorbtion
- incomplete Disintegration and dissolution
- Enterhepatic cycling
- ① first pass effect
- Destruction By gastric acid in the Gut as penicillin

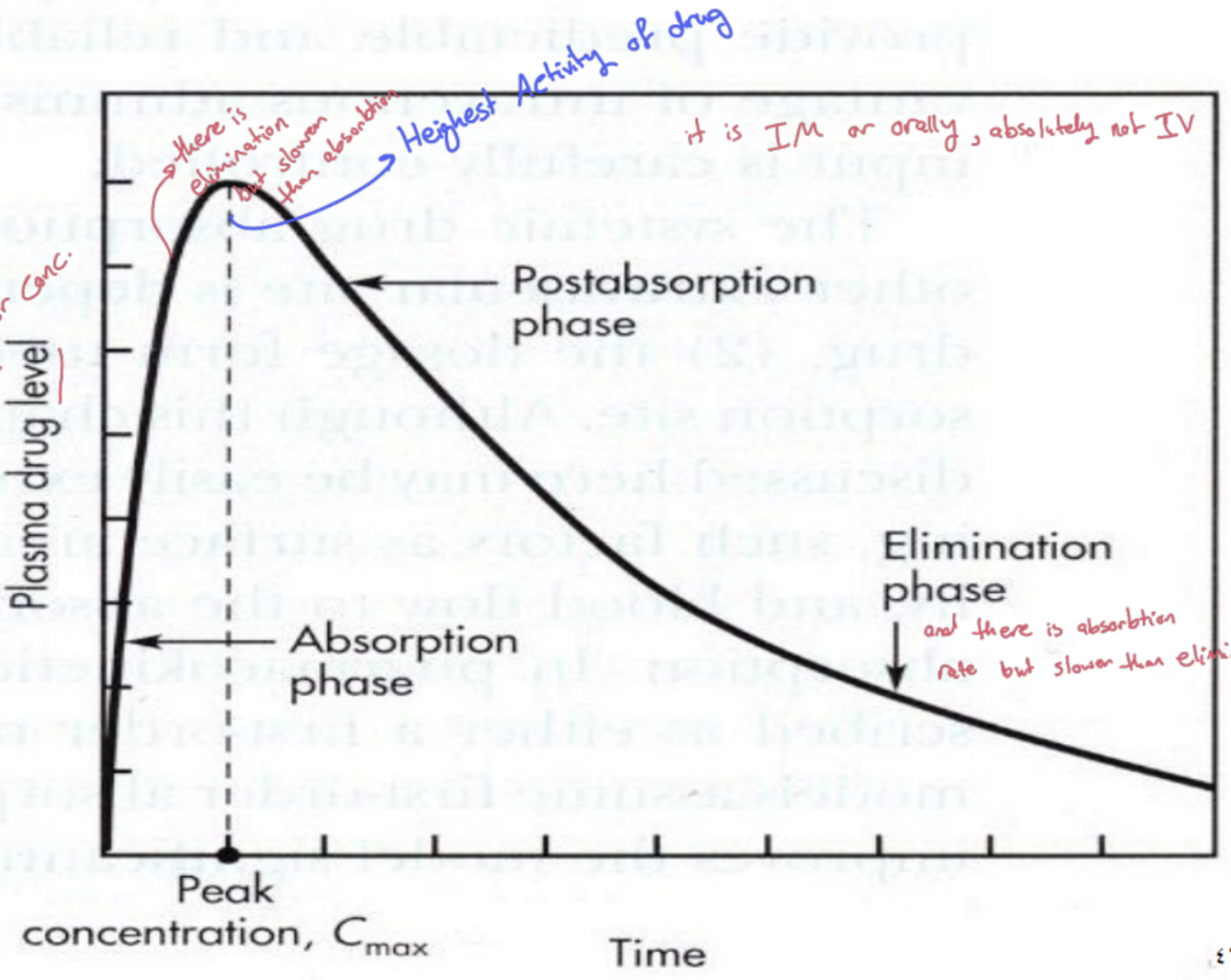
* We can Calculate the Bio availability By Calculating Area Under the Curve (AUC) in Concentration versus Time. and it represent the extent of Bio availability and it is reduced by

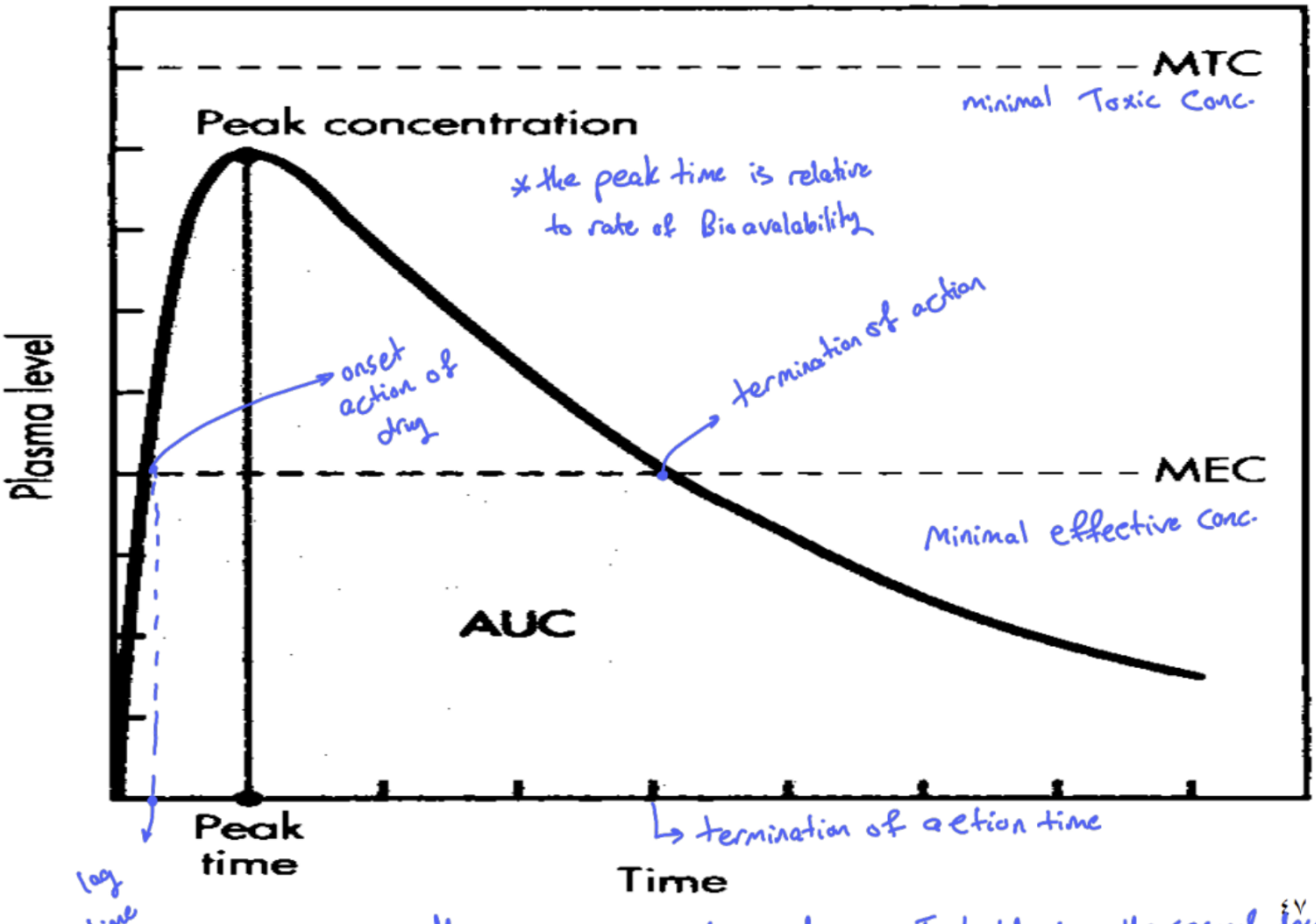
① Drug may too hydrophilic (atenolo) to be absorbed

② or it is too lipophilic (acyclovir) to reach the cell

③ presence of reverse transporters (P-Glycoprotein) That pump the drug out Back to the Gut

* Some Drug (as Grapefruit) may inhibit these transporter so the Bio availability will increase and we should reduce the dose





This curve represent one dose, so I should give the second dose before elimination time

* Bioequivalence: term used to compare the rate and extent of absorbtion of Different formulations of the same active drug

* The Bioequivalence Drug must have same extent and Rate of Bioavalibility

* the extent availability measured By the AUC

* the Rate of availability assessed By Cmax and Tmax
  - Cmax → peak concentration
  - Tmax → time for peak conc.

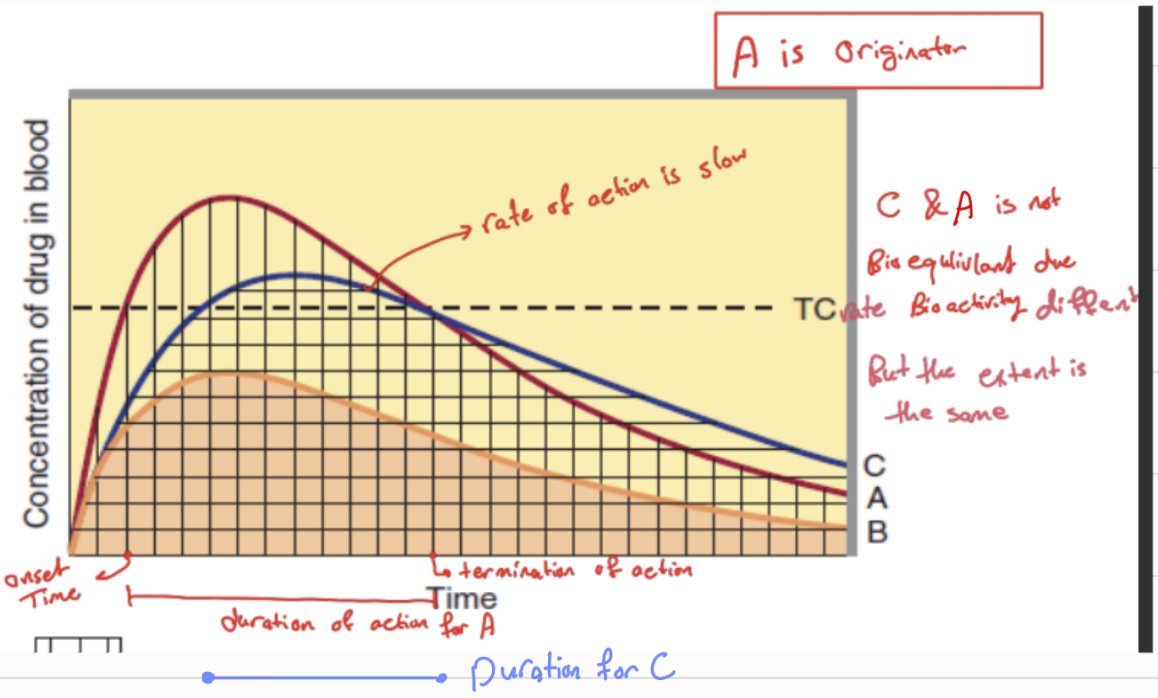
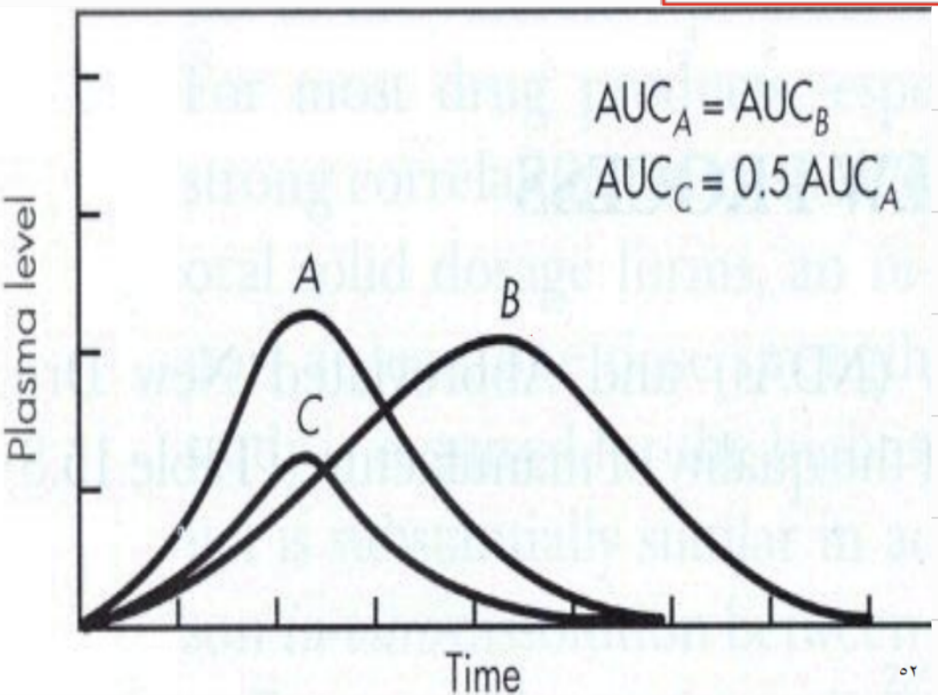


FIGURE 3-4 Blood concentration-time curves, illustrating how changes in the rate of absorption and extent of bioavailability can influence both the duration of action and the effectiveness of the same total dose of a drug administered in three different formulations. The dashed line indicates the target concentration (TC) of the drug in the blood.

therapeutic conc. (target conc.)



extent of A & B is the same

extent of C < extent A

rate A = rate C, rate A > rate B

No one is Bioequivalence to another

* rate is related to time took to reach peak