Drug Processing Cheat Sheet

Why is drug delivery important?

_____

_____

Match the pharmacokinetics vocabulary word to its definition.

	Word Bank	
Absorption	Absorption Phase	ADME
Area Under the Curve (AUC)	Bioavailability	Buccal
Clearance	Cmax	Distribution
Duodenal	Duration of Action	Elimination Phase
Excretion	First Pass Metabolism	Intravenous
Lag Time	Liberation	Metabolism
Minimum Toxic Concentration	Oral	Pharmacodynamics
Pharmacokinetics	Pharmacokinetic Models	Sublingual
Subtherapeutic Window	Therapeutic Window	tmax
Toxic Window	Toxicity	Transdermal

_____ What the drug does to the body

_____ What the body does to the drug

_____ Drug release into active form

_____ Uptake of drug

_____ ABCDs of Pharmacokinetics

_____ Transfer of drug in the body

_____ Breakdown of drug into metabolites, resulting in drug deactivation

_____ Removal of drug and metabolites

_____ Depict drug concentration in blood plasma over time

_____ Maximum concentration of drug in the blood

_____ High concentration range where patient may experience toxic effects

_____ Low concentration range where treatment is not effective

_____ Median concentration range where treatment is non-toxic and effective

_____ Length of time that the drug is effective

_____ Time it takes plasma concentration to reach Cmax

_____ Time post-ingestion where drug is taken up into the bloodstream

_____ Time post-ingestion where drug is removed from the bloodstream

_____ Time between drug dosing and increase in plasma concentration

_____ Fraction of drug that is able to yield a therapeutic effect in the body

_____ Used to calculate bioavailability

_____ This type of drug delivery yields a very high bioavailability (100%)

_____ This type of drug delivery yields a very low bioavailability (<1%)

_____ Liver processing that eliminates the majority of orally delivered drug

_____ Damage the drug can cause to the organism

_____ Threshold for drug toxicity

_____ Volume of fluid that is completely freed of drug per unit time

_____ Drug delivery through the skin

_____ Drug delivery through the intestine

_____ Drug delivery through the cheek

_____ Drug delivery under the tongue

Calculating AUC and Assessing Drug Candidates

You are a preclinical researcher at a large pharmaceutical company. You are experimenting with different formulations in order to enhance the delivery of drug molecule Y. High doses of molecule Y are associated with not super fun side effects, so you want to keep the maximum plasma concentration of molecule Y below 1000 $\frac{\mu g}{mL}$. You hypothesize that lipid encapsulation of molecule Y can increase its bioavailability and duration of action while maintaining a drug concentration within the therapeutic window. You test this hypothesis by delivering a single intraduodenal bolus injection of molecule Y into Sprague-Dawley rats and monitoring their plasma concentration of molecule Y over 24 hours. The following formulations were tested:

Active Product Ingredient (API): free molecule Y (no encapsulation)
200 nm Solid Nanoparticle: large droplets of molecule Y in lipid
100 nm Solid Nanoparticle: medium droplets of molecule Y in lipid
10 nm Solid Nanoparticle: small droplets of molecule Y in lipid

The solid Nanoparticles were developed by homogenizing and emulsifying free molecule Y within a lipid carrier and sorting the droplets by size.

The results of this experiment can be found on the Module 9 Data Sheet posted on the Cell Team Website.

Assume that molecule Y has no subtherapeutic threshold unless specified otherwise.

1. The pharmaceutical company hopes to deliver molecule Y orally. Why are you testing its performance through an intraduodenal injection?

2. Calculate the average and standard error plasma concentration of molecule Y for each experimental condition at each time point. Plot average plasma concentration of molecule Y over time for each experimental condition.
    a. What do you notice about the shape of the pharmacokinetic model? Is the absorption phase or elimination phase longer?
    b. You may notice that the error for this dataset is quite large. Why do you think there is such a large difference in plasma concentration of molecule Y between the individual rats?

3. Calculate the average area under the curve (AUC) for each formulation.

    Hint: Dust off your Calculus knowledge and break out Trapezoidal rule

    $$\Delta AUC_{1-2} = \frac{C_1 + C_2}{2} \times (t_2 - t_1)$$

    a. Rank the formulations from highest bioavailability to lowest bioavailability

4. Based on your calculations and plots, which nanoparticle formulation would you recommend for future experimentation?
    a. Why might you hesitate to recommend the API formulation of molecule Y for future studies?
    b. If the subtherapeutic threshold for molecule Y is 500 $\frac{\mu g}{mL}$, would you change your nanoparticle formulation recommendation?

    Note: You don't need to do any calculations to answer this question - just examine the duration of action given this subtherapeutic threshold.