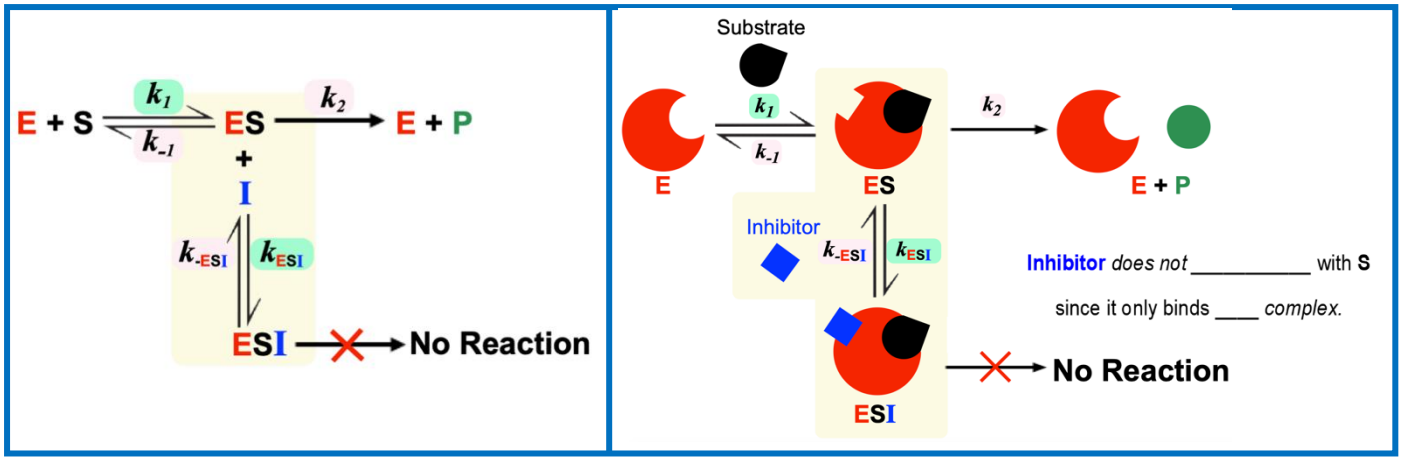
CONCEPT: UNCOMPETITIVE INHIBITION

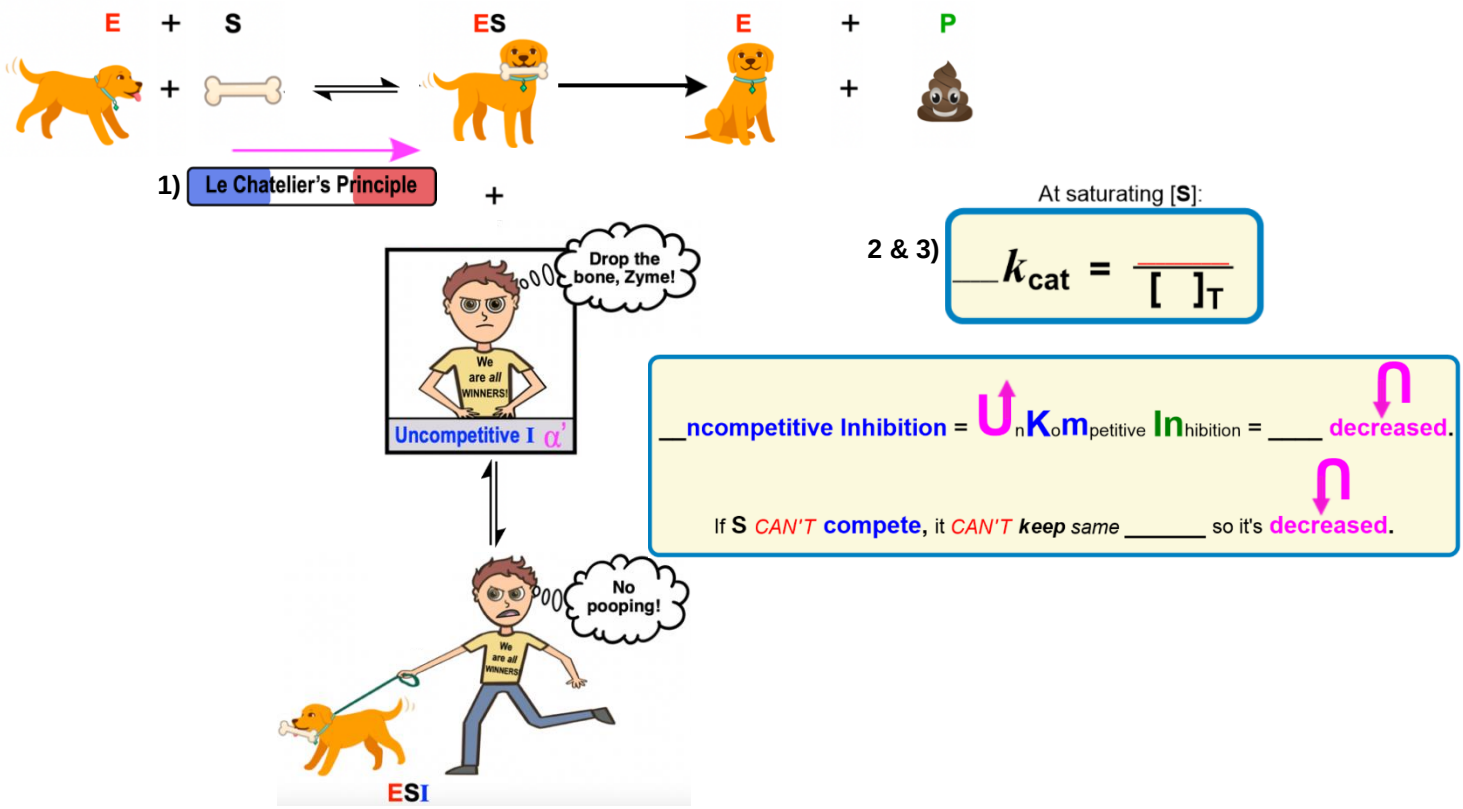
- _____ *inhibitors*: *only* bind _____-complex (***NOT*** free enzyme) to form an ESI-complex & *decrease* V_0.
  - □ _____ competition: Uncompetitive inhibitor's binding-site *only* created when **S** binds **E** to form the ES-complex.
  - □ Binding of an *uncompetitive inhibitor* to ES-complex _____ conversion of **S** → **P**.

EXAMPLE: Uncompetitive inhibition.



Uncompetitive Inhibitor Effects

- Recall: No competition between **S** & *uncompetitive* inhibitors & they *proportionally* _____ both K_m^{app} & V_{max}^{app}.
  - **1)** By Le Chatelier's Principle, lower [ES] causes k_1 reaction to shift _____, strengthening ES affinity & ___ K_m^{app}.
  - **2)** Since **S** *can't* outcompete uncompetitive inhibitors, effects are *NOT reversed* by ____ [**S**], so V_{max}^{app} is *decreased*.
  - **3)** Since uncompetitive inhibitors *decrease* V_{max}^{app}, k_{cat} is also _____.



CONCEPT: UNCOMPETITIVE INHIBITION

Uncompetitive Inhibition & Michaelis-Menten-Plots

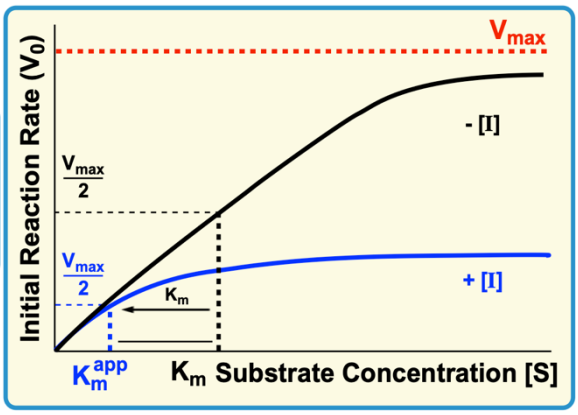
●Recall: All inhibitors, including uncompetitive inhibitors, _____ V_0 of an enzyme-catalyzed-reaction.

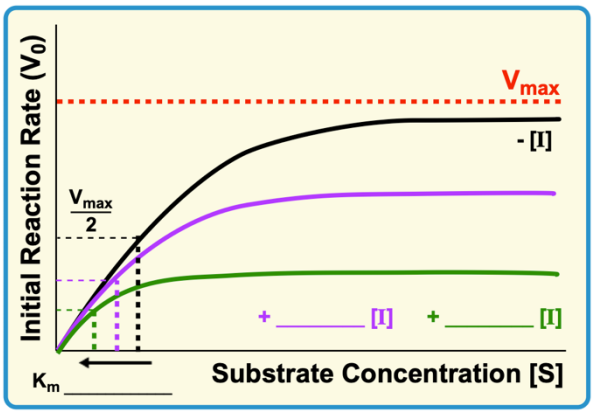
●Recall: uncompetitive inhibitors *only* bind to ES-complexes, so ____ measures its *degree of inhibition* on the ES-complex.

□ α' of an uncompetitive inhibitor _____ both the K_m^{app} & V_{max}^{app} of an enzyme (K_m/α' and V_{max}/α').

Uncompetitive Inhibitor Michaelis-Menten Equation:

$$V_0 = \frac{\left(\frac{V_{max}}{\alpha'}\right)[S]}{\left(\frac{K_m}{\alpha'}\right) + [S]}$$





Uncompetitive Inhibition & Lineweaver-Burk-Plots

●Recall: Uncompetitive inhibitors *proportionally* _____ both the K_m^{app} & the V_{max}^{app} of an enzyme.

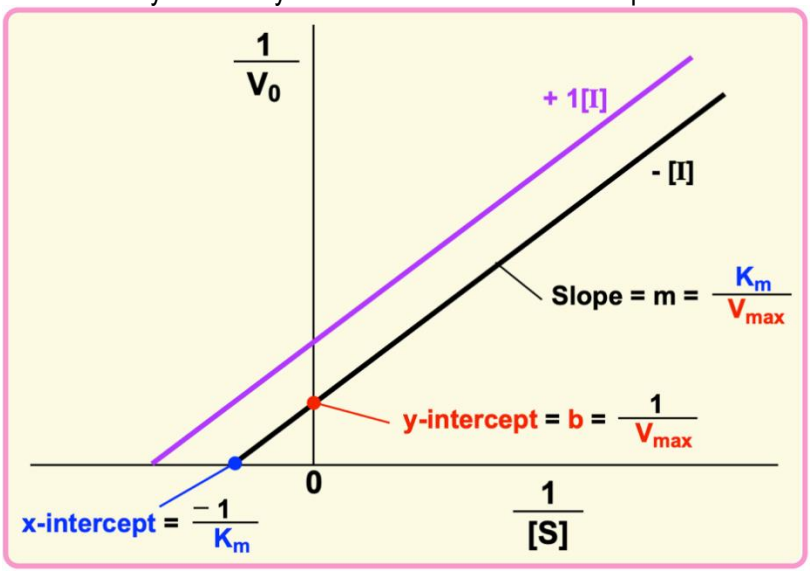
●Though K_m^{app} & V_{max}^{app} are *decreased*, uncompetitive inhibitors do *not* change the line's _____ (slope = K_m/V_{max}).

●Both the ____-intercept ($1/V_{max}$) & the absolute value of the ____-intercept ($-1/K_m$) are *proportionally* _____.

EXAMPLE: Draw the representative line for the enzyme activity if the concentration of uncompetitive inhibitor was doubled.

Uncompetitive Inhibitor Lineweaver-Burk Equation:

$$\frac{1}{V_0} = \frac{K_m}{V_{max}}\left(\frac{1}{[S]}\right) + \frac{\alpha'}{V_{max}}$$



*Parallel Lines

PRACTICE: True or false: Increasing [S] in the presence of an uncompetitive inhibitor will lower the inhibition constant (K_I).

a) True. b) False.

CONCEPT: UNCOMPETITIVE INHIBITION

PRACTICE: In the presence of an uncompetitive inhibitor that binds _____ the substrate, the apparent V_{max} _____ and the apparent K_m _____ with respect to the V_{max} and K_m of the uninhibited enzyme.

a) Before, Decreases, Increases.
b) After, Decreases, Decreases.
c) After, Increases, Increases.
d) Before, Stays the same, Decreases.
e) After, Decreases, Stays the same.

PRACTICE: What is the effect of an uncompetitive inhibitor on the equilibrium between free enzyme & the ES-complex?

a) A shift to the right due to decreased [ES].
b) A shift to the left due to decreased [ES].
c) A shift to the right due to increased [ES].
d) A shift to the left due to increased [ES].