

Dr. Casey
Exam 2
Fall 2004
CHEM 480/580

Name: _____

Signature: _____

Honor Statement: By signing this exam, you indicate that you have neither given nor received aid from any unauthorized source.

Each question (each number) is worth 20 points. Answer 10 of the questions. If you answer more than 10, I will grade only the first 10. Answer each question in the space provided. If you need more space, use the back of the sheet. Answer thoroughly!

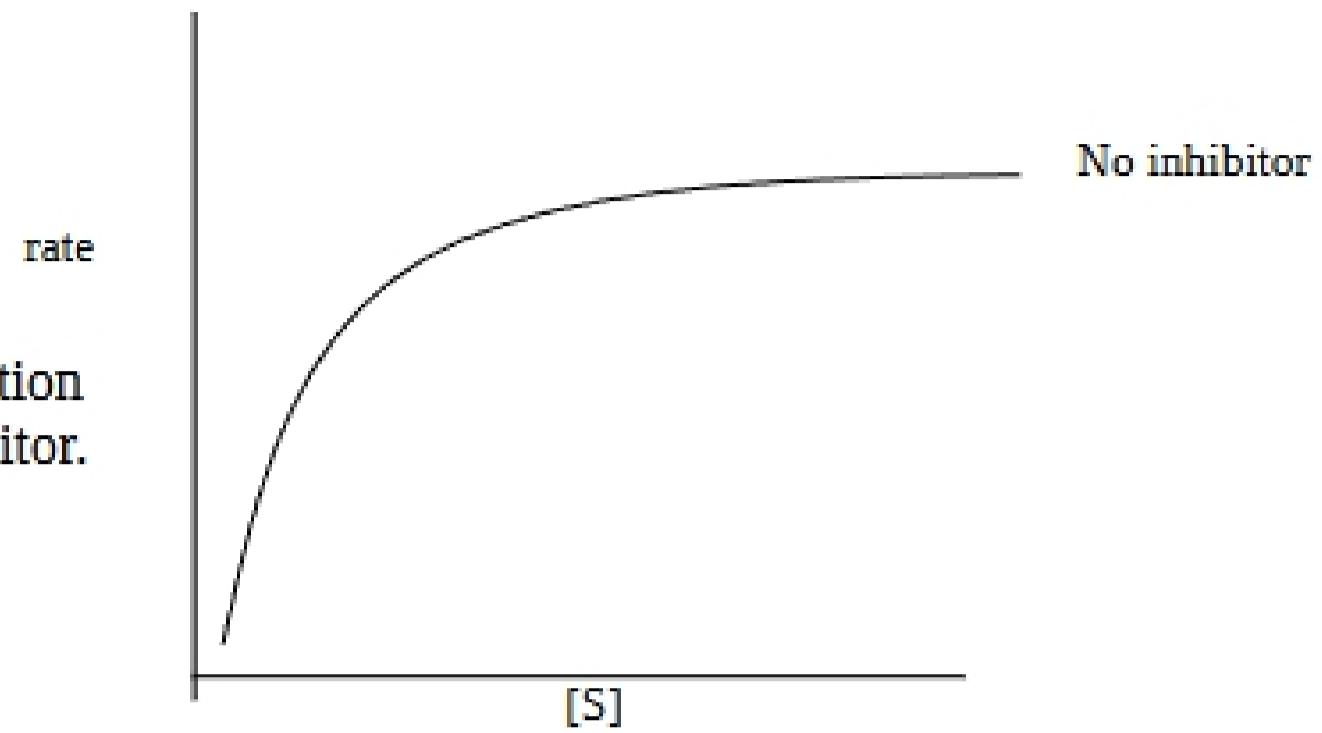
1. Rodenticides are often more toxic to humans than fungicides. Explain how this could be true in terms of both receptor sites for toxicity and differences in metabolic enzymes.

2. Hexobarbital is a sedative and is metabolized by P450 enzymes. Metyrapone is an inhibitor of P450 enzymes. 2,3,7,8-TCDD is a planar nonpolar organochlorine that binds well with the Ah receptor. An experiment is conducted in which mice are dosed in the following scheme (X indicates that the chemical was included in the dose). Explain how the administered substances cause the observed sleep times (time until the mouse awakens from the sedative effects of hexobarbital).

	<u>Hexobarbital</u>	<u>Metyrapone</u>	<u>TCDD</u>	<u>Sleep Time (h)</u>
Group 1	X			2.1
Group 2	X	X		5.3
Group 3	X		X	1.4
Group 4	X	X	X	2.8

3. In competitive inhibition, K_m increases and V_{max} stays constant (in comparison with the case of no inhibitor) in the Michaelis-Menton equation of enzyme kinetics.

$$\text{Rate} = \frac{V_{max} [S]}{K_m + [S]}$$



a. Draw the curve for the rate of reaction in the presence of a competitive inhibitor.

b. Explain the interactions that are occurring between the enzyme, substrate and inhibitor and how those interactions explain the line that you drew on the graph above.

4. Benzo[a]pyrene induces the production of new P450 enzymes. Explain how this occurs. Also explain whether this effect is beneficial, detrimental or both to the organism.

5. Explain the role of the protein metallothionein (MT) in metal toxicity. Where is MT produced? How does it interact with metals? What can go wrong with MT as a means for removing metals from an organism?

6. a. Amphotericin is an antifungal drug which can bind to cholesterol and create an aqueous pore in a cell membrane. Explain why this makes the kidney particularly susceptible to malfunction due to amphotericin. Be specific.

b. Pb^{2+} ions are taken up by proximal tubule cells in the kidney and interfere with energy generation by mitochondria. How will this impact the function of the kidney? How could a urine test reveal that this sort of damage had occurred?