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Part I — The Lecture

It was about 50 minutes into another long, boring two-hour lecture by Dr. Foster. The tall, thin, gray-haired biochemistry professor was concluding a chapter on enzymes. The final topic was enzyme inhibition. Sarah, an energetic and outgoing junior, was daydreaming about her upcoming weekend at home for a family reunion. She was not really paying attention, but heard the professor going on and on about alcohol dehydrogenase. At last, Dr. Foster turned to the class and asked, "Any questions?" Sarah, hoping to side-track the professor, enthusiastically waved her hand. As soon as she received a nod from Dr. Foster, she began to recount a story that her grandfather had told her.

"My grandfather said that when he was a teenager, alcohols were used as antifreeze in automobiles. A group of kids was hanging out in a friend's garage. One of them found two bottles of liquid that were marked 'alcohol.' He talked everyone else into trying the alcohol. All of the kids became severely ill, but about half of the teens died from poisoning. Someone later found out that one of the bottles contained methanol and the other a mixture of ethanol and methanol. The kids who lived drank the mixture. Grandpa figured since I was a chemistry major, I'd know why half died and half didn't, but I didn't know. Do you?"

Although Sarah had planned to side-track the professor, her story played nicely into his lesson plan. After all, the incident was related to the current class topic of enzymes and enzyme inhibition. The clever professor began, "Let me remind all of you that the enzyme, alcohol dehydrogenase, catalyzes the first oxidation step in the case of both ethanol and methanol. Methanol is a very common solvent that is quite toxic. I recall an article from a few years ago that described the largest mass methanol poisoning reported to date. It occurred in Nicaragua. Of the approximately 800 poisonings, about 45 patients died and others suffered blindness (SEMP Biot #412, 2006). I seem to recall that poisoned patients received either ethanol or a drug called Fomepizole as an antidote. I think I have some homework that will help you to understand what happened in your grandfather's story."

Questions

- 1. Write the structure of the products for the oxidation of both methanol and ethanol. Name those products. Refer to your textbook and notes as needed.
- 2. Discuss possible hypotheses for why some of the teenagers in the grandfather's story died and the others did not.
- 3. Compare and contrast competitive and noncompetitive inhibition. Show the Michaelis-Menten equation and define all of the variables. Include in your answer the use of Lineweaver-Burk plots in distinguishing between the different types of enzyme inhibition.
- 4. Discuss possible hypotheses for the case that include the role of the enzyme alcohol dehydrogenase. Choose your group's best hypothesis.
- 5. Share your group's hypothesis with the class.
- 6. After the class decides on the best hypothesis, return to your group and devise an experimental procedure to test the hypothesis. Identify environmental factors in the lab that must be held constant. Clearly indicate your experimental control, independent variable and dependent variable.
- 7. Either turn your procedure into the instructor or discuss with the rest of the class.

Part II – An Experiment

Dr. Foster's class carried out an experiment studying a system with the same type of enzyme inhibition as observed in alcohols. They collected the following data.

I	II	III
Methanol (mM)	Rate of Reaction (mMmin-1)	Rate of Reaction in presence of 5.0 μM Ethanol
0.50	23.5	16.67
1.0	32.2	25.25
1.5	36.9	30.49
2.5	41.8	37.04
3.5	44.0	38.91

(Nelson, 2008)

Questions

- 8. Describe the hypothesis that you think Dr. Foster's class is testing.
- 9. Indicate the control, dependent variable, and independent variable used by Dr. Foster's class.
- 10. Compare the type of data that your group suggested collecting with that collected by Dr. Foster's class.
- 11. Using the data above, construct Lineweaver-Burk plots. First, graph the inverse of the reaction velocity (rate of reaction) data in column II versus the inverse of the methanol concentration in column I. Then, on the same graph, plot the inverse of the reaction velocity (rate of reaction) data in column III versus the inverse of the methanol concentration in column I.
- 12. Describe the conclusions that can be supported from the data. What type of inhibition is evident from the plot?
- 13. Suggest ways that the conclusions might explain the case described in the grandfather's story. What would be the substrate and what would be the inhibitor?

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