Student Guide

Simulating a Controlled Drug Delivery System

Introduction: Do you use an inhaler to control your asthma? Have you ever taken a cough suppressant to stop your nagging cough? Have you ever used eye drops? Can you think of how all of these "devices" are related? All of these are examples of drug delivery systems; important advances in chemical and biomedical engineering that promote better health through prevention and treatment of diseases and disorders. In developing drug delivery systems, scientists must determine what the body does to the drug and also what the drug does to the body. Significant drug delivery systems including transdermal patches, inhalers, and enteric coating for oral tablets have been in development since the 1970s. But, recent advances in the engineering and design of pharmaceuticals as controlled release and targeted drug delivery systems show promise beyond these conventional systems because they can deliver effective concentrations of a prescribed medication to a specific location at a sustained rate. In this activity, you will learn about alternative drug delivery methods and then prepare a controlled drug delivery system using sodium alginate and glucose to mimic the behavior of a controlled release drug delivery system.

Pre Lab Questions: Scientists are constantly thinking about how to improve experimental designs to overcome challenges and to achieve more profound results. In this investigation you will consider the field of advanced drug delivery as a model for thinking like a scientist. Answer in your lab notebook the following:

- What do you think will happen to the concentration of sugar in your body after you eat a candy bar?
- Does the sugar in your body stay at this concentration? Why?
- Now consider this, if you had a nagging cough, would you prefer that your cough medicine work with several doses or with a single dose and for a longer time? Why?
- Now, consider your answer as you make your own controlled drug delivery system. Would you design a cough drop that behaves in the same way?

Development and distribution funded by the **National Science Foundation**

Materials:

- Laminated Pharma cards
- Prepared alginate-glucose gel in dispenser
- Permanent marker
- Metric ruler
- Small metal strainer
- Plastic spoon
- Disposable pipette
- Glass piece 2.5x35. in.
- 2 plastic cups labeled 1% $CaCl_2$
- 2 plastic cups labeled water
- Stopwatch or similar device
- 1 collection tube with 20mL of water
- Truetrack™ glucose monitor
- 6 Truetrack™ glucose test strips
- Access to Excel application

Procedure:

Day 1: An introduction to drug delivery

1. Your group will be provided with a set of "Pharm Cards". Your teacher will provide you with prompts as you attempt to sort the image cards into categories that you and your partner have agreed upon.
2. Be prepared to discuss the categories that you applied to your selection of cards.
3. You and your classmates will explore advanced drug delivery through the presentation of a PowerPoint slide show. You will discover the design and application of the images on the "Pharm Cards" that you initially sorted.

Day 2: Performing the investigation

1. If you would like to record your experiment using digital photography, feel free to use a digital camera or cellphone. This is optional, but enriches your lab report.

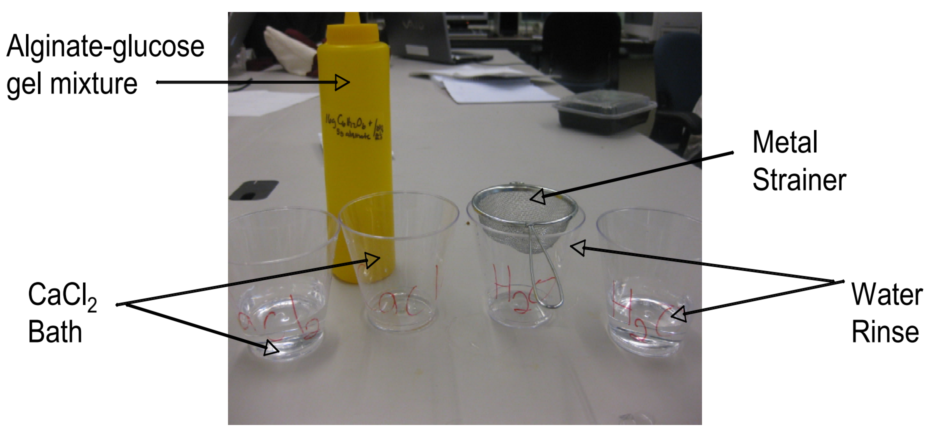


Figure 1. Student Workstation for Microcapsule formation

Development and distribution funded by the **National Science Foundation**

2. Your lab station will be equipped with the materials you will need to carry out this investigation (refer to Figure 1)
3. Label 2 of the plastic cups "$CaCl_2$" and the other 2 "water."
4. Obtain 200mL of 1% $CaCl_2$ solution from the chemical station, and pour it into one of the cups labeled $CaCl_2$.
5. Similarly, obtain 200mL of water from the chemical station, and pour it into one of the plastic cups labeled water.

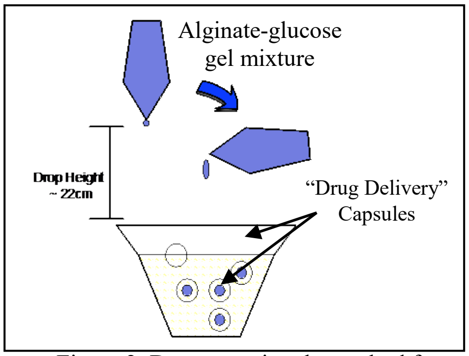


Figure 2. Demonstrating the method for drop formation in $CaCl_2$

6. Hold the container labeled "alginate-glucose" in a vertical position and from a height of approximately 22cm over the cup labeled "$CaCl_2$" and gently squeeze the container until you observe the formation of a drop from the tip of the container. Then, rotate your container 90 degrees so that it is parallel with the cup containing $CaCl_2$. Allow the drop that was forming to fall into the $CaCl_2$ solution (refer to Figure 2).
7. Immediately start your stopwatch. Gently stir the drop in the $CaCl_2$ for 30 seconds.
8. When 30 seconds up, place the small metal strainer on top of the second empty cup labeled "$CaCl_2$." Pour the contents of the first $CaCl_2$ solution with the recently formed capsule into the second cup.
9. Place the strainer containing the capsule on top of the empty cup labeled "water."
10. Rinse the capsule by pouring the water from the full cup of water into this apparatus.
11. Use the plastic spoon to collect the capsule and place into a collection tube (Note: **Do Not** add water to the collection tube until all capsules have been formed).
12. Repeat this procedure 7 more times for a total of 8 capsules.
13. You will be sharing your glucose monitor with another lab group. Make sure that the glucose test strips are used properly and ONLY with the glucose monitor at your station. Your group will be provided with 5 test strips to collect your data. If you obtain and "Error" reading, please notify your teacher so you can use the teacher designated backup monitor.
14. When all the capsules have been formed and placed into the collection tube, add 20mL of water to the collection tube and IMMEDIATELY start your stopwatch. Continue to gently agitate the contents of the collection tube for 5 minutes.
15. After 5 minutes has elapsed, withdraw a sample of the liquid from your collection tube. Place a drop of the sample onto the glass grid labeled "1".
16. Insert an unused test strip into the glucose monitor. Wait for the blood drop icon to flash. When you see this, the machine is ready to test.
17. Hold the glucose monitor in a vertical position, and place the tip of the test strip directly into the liquid sample. Wait for the monitor to determine the glucose concentration in your sample drop.
18. Record this numerical value in the data table provided.

Development and distribution funded by the **National Science Foundation**

19. Continue to agitate the contents of the collection tube while waiting for the next 5-minute interval to elapse. Repeat steps 16-18 until 20 minutes has passed. This will ensure that you and your partner will have recorded a minimum of 4 data points. If time is not a constraint, continue recording measurements until you reach "HI" as a data point. Record this as >600mg/dL in your data table.

Cleanup:

1. Alginate-glucose capsules and leftover mixtures should be strained and further disposed of into a compost or common waste receptacle.
2. Do not pour the $CaCl_2$ solution down the sink. Return the USED $CaCl_2$ to the stock container labeled "USED $CaCl_2$" to avoid cross-contaminating the unused batch. $CaCl_2$ can be saved and reused.
3. Rinse all cups, pipets, and collection tubes with water and let dry.
4. Dispose of glucose test strips in a common waste receptacle.
5. Return glucose monitor and test strip vial to its carrying case.
6. Wipe down your station.
7. If you were borrowing a digital camera, download your photos, delete them from the camera, and store the camera properly.

Day 3: Using Excel®

Now that you have collected some data, you will be compiling it into a form that is more easily interpreted.

1. Open a new spreadsheet from the Excel program on your computer.
2. Type the title of your investigation in the spreadsheet for reference.
3. Insert the Time (minutes) and record the time intervals vertically by starting with "0".
4. Repeat this in the adjacent column for Glucose (mg/dL) and record the glucose values you measured.
5. Highlight the content of both columns and then click on the "chart" icon in the Excel® toolbar. This will open another window. Select the scatter plot graph option and click XY (scatter) chart type and the scatter plot graph with just data points as your chart sub-type. Click "Next".
6. The screen will display a graph of your data points. Click "Next".
7. The screen that appears should display chart options for title, x-axis, and y-axis. Fill in these labels as appropriate, including units.
8. Click on the toolbar option entitled "legend" and click off the "show legend" mode.
9. Click "next" and the "Finish" to complete your graph.
10. Your graph should appear on the spreadsheet with your data. Feel free to move the graph over if it is obscuring your data table.
11. Use the Excel toolbar to select "Chart" and then "Add Trendline" in the drop down menu.
12. Once in this dialogue box, click on the "Linear trend/regression" line. Then, select "Options" from the menu bar in this window. Once there, click on the "Display equation on chart" and "Display R-squared value in chart". This will display the slope of your best fit line as well as how well this equation describes the data (R^2).

Development and distribution funded by the **National Science Foundation**

13. Click “OK” and the dialogue box will disappear and the final graph will appear on your spreadsheet.
14. Save your spreadsheet to a thumb drive, email it to yourself, or print it to a local printer so that you can include it in your lab report.

Record Your Observations:

Monitoring Glucose Concentration

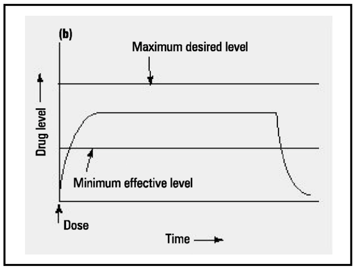
Time (minutes)	Glucose Concentration (mg/dL)
0	
5	
10	
15	
20	
25	
30	
35	
40	

Draw Conclusions:

1. What part of this experiment did you purposely change or manipulate?
2. What variable changed as a result of the variable in #1? How much did that responding variable change?
3. Does this investigation have a control? If yes, identify it.
4. What did you keep the same during this experiment? In other words, what were the constants in your experiment?
5. What is the slope of your line? Compare the slope of your line with that of 3 other groups. Provide a reason for any apparent differences.
6. What is the relationship between the slope of your line and the rate of glucose release?
7. If we continued recording measurements, what do you predict would happen to your slope? Explain.
8. Predict what would happen to the slope of the line if you increased the concentration of glucose in the alginate capsule? Decreased the concentration of glucose in the alginate capsule?

Development and distribution funded by the **National Science Foundation**

9. Compare the graph of your data with the conventional and controlled release drug delivery profiles below. Identify which graph your data most closely represents and why.



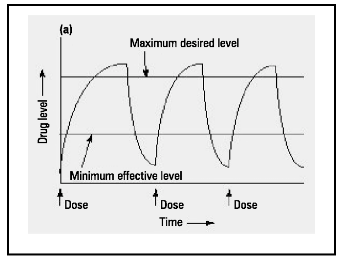


Image Source: http://www.emeraldinsight.com/fig/1560070504001.png

10. Is this simulation an accurate representation of how a controlled release drug delivery system behaves? Why or why not?
11. Identify at least 3 sources of error in this investigation, and explain how this error could affect your results.

Enhancing understanding:

1. What diffused in this investigation? How do you know?
2. Was your answer to #1 the only material that diffused in this investigation? Explain.
3. What other variables could you test in this experimental design?
4. Create your own experiment using this system and a variable you identified in the previous question. Provide a possible question, and then design a potential experiment that could be designed to test your idea.

Review the findings as a class discussion.

Going Further:

1. In order to design a new drug delivery system, what questions might a bioengineer consider before initiating its development?
2. Assume that the glucose represents a new prescription medication. Construct a print advertisement that accurately represents your results.
3. What are the benefits of controlled release drug delivery over conventional forms?

Engineering Design Extension: Your teacher may extend this investigation to students as an engineering design challenge. You will consider the following:

1. How does altering the time in the $CaCl_2$ bath change the rate of glucose release;
2. How can this system be designed to achieve a zero order release;
3. Can this system be redesigned to release glucose at a lower rate based on the health of an individual (i.e., diabetic vs. non-diabetic);
4. Can other materials be encapsulated in this manner and then tested using an alternative to the glucose monitor and test strips?

Development and distribution funded by the **National Science Foundation**

Assessment: You will be evaluated on your lab technique and your written formal lab report for this investigation. The rubric for both criteria are listed below:

Rubric for Lab Technique	
Category	**Points**
Participation in lab	20 points
Accuracy of data	10 points
Adherence to safety rules	10 points
Cleaning of equipment and lab station	10 points

Rubric for Evaluating Lab Reports	
Component	**Points**
1. Attribution	2
2.Title	3
3. Introduction	5
4. Purpose	2
5. Materials	3
6. Safety	5
7. Procedure	10
8. Results	10
9. Calculations (when applicable)	10
10. Graphs	10-20
11. Discussion	20
12. Conclusion	5
13. Works Cited	5

Development and distribution funded by the **National Science Foundation**