Degradation of Dissolvable Strips – Instructor's Version
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Date of Experiment:

OBJECTIVES

- Students will learn about mass transfer and degradation rates of drug delivery films
- Students will learn how to properly operate a spectrophotometer
- Students will determine the effect of temperature on this process

INTRODUCTION

In 2000, the pharmaceutical company Pfizer introduced a new over-the-counter product for the treatment of bad breath. This product came in a novel form that was not seen before; a small, orally dissolvable strip. This product revolutionized the industry, generating roughly 250 million dollars in sales. By 2002, many other brands of dissolvable strips were also on the shelves.[1] In 2011, the energy supplement industry also saw the potential profits of sheets. One company, known as Sheets, introduced a caffeine based strip which they claim has zero calories, zero sugar, and has the same caffeine as one cup of coffee, shown in Figure 1. The brand also states that negative side effects, such as a "crash," are not common when taking the product. Although the company has faced controversy, especially with the endorsement of LeBron James, Sheets continues to make energy supplement strips.[2]

Figure 1. The energy strips you will be using in class.

While the use of dissolvable strips is a relatively new delivery method, it has become a popular method of drug delivery. In fact, many other fields of over-the-counter pharmaceutical products have introduced dissolvable strip products. Dissolvable strips that contain medicines for flu and sinus infection symptoms can now be found in most pharmacies.[3]

With dissolvable strips, the delivery vehicle is a thin, flexible sheet of polymer. The active pharmaceutical ingredient (API) is incorporated into this polymer to form the final product. Depending on the nature of the medicine, the API can be incorporated in one

of two ways; either through liquid dissolution or solid suspension in the polymer. The size and thickness of these strips is dependent on the dosage of API that needs to be delivered.[3]

In this experiment, you will investigate the dissolution and degradation rate of a dissolvable strip that contains menthol. You will be using a spectrophotometer to take absorbance readings. These absorbance readings will then be used to find the amount of menthol that was released from the strips. You will also be comparing these rates for two different temperatures; ambient, otherwise known as room (roughly 20°C), and body (37°C).

MATERIALS NEEDED

- 2 Sheets™ brand Mint Boost dissolvable strips
- 2 petri dishes
- 2 timers
- Incubator or oven capable of reaching and maintaining 37°C
- Pair of tweezers
- Deionized water
- 500 µL to 5000 µL pipette
- Spectrophotometer capable of measuring absorbance at 630 nm
- Cuvettes
- Thermometer/thermocouple

INSTRUCTOR'S NOTE

This laboratory requires deionized (DI) water at a temperature of 37 °C (98.6 °F). It may be necessary that you have a batch of DI water kept in an incubator/oven at this temperature overnight or a few hours before the start of experimentation.

In addition, this lab models the release of blue food dye, not caffeine. To model the release of caffeine, an advanced spectrophotometer that can take absorbance readings at 273 nm must be used. While it may be possible to take readings at the 273 nm wavelength, it is encouraged to use the 630 nm for this experiment. A separate time versus absorbance chart is shown in the appendix, along with separate answers based on using this other absorbance.

SAFETY CONDITIONS

Laboratory gloves and eyewear must be worn at all times inside the lab. Be sure to keep water away from the spectrophotometer.

PROCEDURE

1. Start by turning on the spectrophotometer and setting it to take absorbance readings at 630 nm.
2. While the spectrophotometer warms up, place 2.5 mL of deionized water into each of the petri dishes.
3. Place one of the petri dishes into the oven/incubator that is set at 37°C.
4. Allow 20 minutes to pass so that the water may reach 37°C and the spectrophotometer may warm up.
5. After the 20 minutes have passed, fill a cuvette with deionized water and zero the spectrophotometer.
6. Now that the spectrophotometer has been zeroed, use the tweezers to place a strip into one of the petri dishes. Once the strip has been placed in the petri dish, cover and start the timer.

Figures 2 and 3. From left to right, the proper (l) and improper (r) way to take a sample.

7. Place the other strip in the other petri dish using the tweezers. Once placed, close the petri dish and start a secondary timer. NOTE: It is a good idea to stagger the starting times so that you do not find yourself rushing to take two measurements. It may also be a good idea if you are working in teams to split the team so that one section of the group is in charge of one specific temperature study.
8. After five minutes have elapsed, take a sample of your water into a cuvette. Make sure that this sample is relatively far from the dissolvable strip so that you do not accidentally pick up any large portions of the dissolvable strip, as in Figures 2 and 3.
9. Take an absorbance reading then return the sample to the corresponding petri dish.
10. Take absorbance readings every five minutes for the first thirty minutes. After that, take absorbance readings every ten minutes until you have reached 90 minutes. You may use Table 1, but you should also record your results in your laboratory notebook.

Table 1. Empty data table to record absorbance at 630 nm data for the dissolvable strips laboratory.

Time (min)	Absorbance readings at 630 nm	
	Room Temperature (20°C)	Body Temperature (37°C)
0	0	0
5		
10		
15		
20		
25		
30		
40		
50		
60		
70		
80		
90		

11. Once you have taken all the necessary measurements, make sure to turn off the spectrophotometer and the incubator/oven.
12. Dispose of all equipment used in this lab, and make sure that any water spills were cleaned up before exiting the laboratory.

RESULTS

Be sure to record all the data you collected in this experiment into your laboratory notebook. If you split into two groups to complete this experiment, be sure that you share the data sets.

DATA ANALYSIS

To analyze the data, the best method is to create a graph of the time versus absorbance reading. In this case, the x-axis will be the time axis and the y-axis will be the absorbance axis. Create one of these graphs using Excel or another program and turn it in along with the rest of your laboratory report.

QUESTIONS

1. Now, you will take your absorbance readings and figure out the concentration of menthol in your solutions. You will do this using the following graph, which correlates absorbance at 630 nm to concentration in mg/mL. Once you have the concentrations, create another graph of concentration versus time for both temperature sets. In addition, fill in Table 2. Make a copy of this table and turn in along with the rest of the deliverables for this experiment.

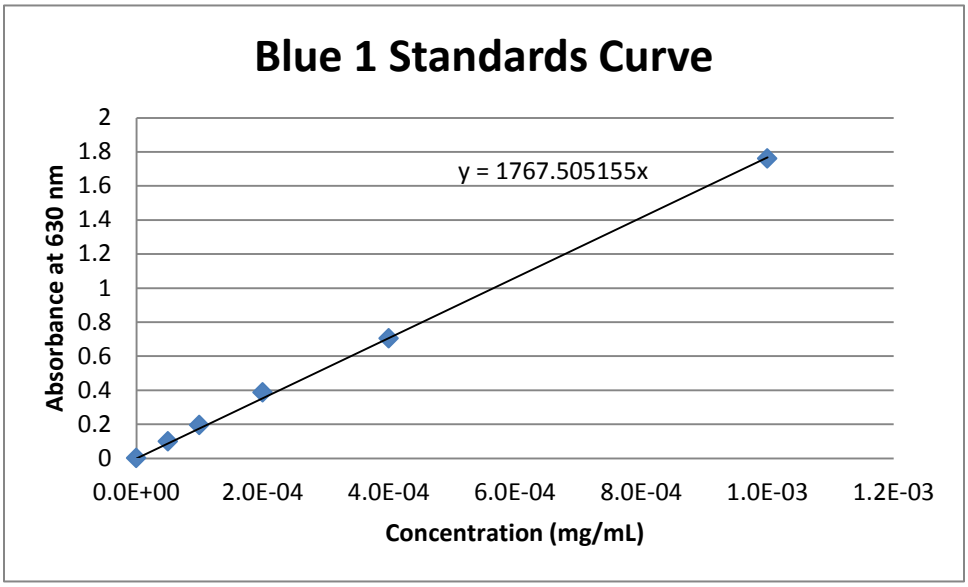


Table 2. Empty data table for recording concentrations in the dissolvable strips laboratory.

Time (min)	Concentration (mg/mL)	
	Room Temperature (20°C)	Body Temperature (37°C)
0	0	0
5		
10		
15		
20		
25		
30		
40		
50		
60		
70		
80		
90		

2. Now that you have found the concentration of the solution over time, you will need to use concentration and absorbance readings to determine the molar absorptivity of the blue food dye. The molar absorptivity, or the molar absorption coefficient, is defined as how strongly a substance absorbs light at a particular wavelength[4]. This coefficient is seen in the Beer-Lambert Law, an important law that governs the absorbance of light. This law is shown below:

$$A = \varepsilon \ell c \quad (1)$$

With:

$$A = absorbance\ (dimensionless)$$
$$\varepsilon = molar\ absorption\ coefficient$$
$$\ell = length\ the\ light\ has\ to\ travel\ through\ the\ solution\ (cm)$$
$$c = concentration\ of\ solution\ in\ moles\ per\ liter\ (M)$$

   a) Use one of the higher time points (70 to 90 minutes) of both the room temperature and body temperature experimental runs to determine the molar absorption coefficients of both runs. Use the following constants to help you in this calculation.

$$\ell = 1\ cm$$
$$molar\ mass\ of\ Blue\ 1 = 793\ \frac{g}{mol}$$

   b) Based on the values, do you think that the temperature affects the molar absorption coefficient?

3. Determine how well the molar absorption coefficients can determine the concentration of the solution based on absorbance readings. Use the molar coefficients you previously found and determine the concentration that the solution should be at based on the Beer-Lambert Law. Use a time point between 30 and 50 minutes in both cases. Determine how different these two numbers are by using percent difference. The equation for percent difference is shown below. In this case, the "E" terms are the molar concentrations. It should be noted that percent difference is a dimensionless number. Make sure you do all the necessary unit conversions before calculating the percent difference.

$$Percent\ Difference = \frac{|E_1 - E_2|}{\left(\frac{E_1 + E_2}{2}\right)} * 100\% \quad (2)$$

4. It is known that the molar absorptivity coefficient of the blue food dye used in these sheets is 1.3×10^6 $M^{-1}cm^{-1}$.[5]

    a) How different is the molar absorptivity coefficient that you found using your experimental data from this known value? Use experimental error to determine this difference. The equation for percent error is shown below.

$$Percent\ Error = \frac{|E - A|}{A} * 100\% \quad (3)$$

    Here, the "E" term is the molar absorptivity coefficient obtained through the experimental data, while the "A" term is the molar absorptivity coefficient given to you above. It should be noted that when using this equation, the two terms need to be in the same units. It should be noted that percent error is also a dimensionless number.

    b) Now, use the same time point that you used in Question 6 and determine the concentration based on the given molar absorptivity coefficient. Again, compare using percent error. Do this for both experimental runs. Here, the "E" term will be the concentration that you obtained during experimentation, while the "A" term will be the concentration that you obtained using the given molar absorptivity coefficient.

5. The Beer-Lambert Law is one of the most important laws used in spectroscopy (the interactions between light and matter). How could you use this law in an engineering aspect?

6. Now, we will discuss a rate law. A rate law, or rate equation, is an equation that governs the rate of a process as a function of a variable, such as time. These laws are used by engineers to determine the design of a chemical process. Rate laws applied to this experiment relate absorbance with time. For example, an important variable of a rate law, the rate coefficient/constant (k), can be determined using absorbance data. This can be done using the following equation:

$$\ln \frac{(A - A_\infty)}{(A_0 - A_\infty)} = -k * t \quad (4)$$

Where:

t	Time
A	Absorbance at time t
A_0	Absorbance at t=0
A_∞	Absorbance at t=∞
k	Rate coefficient

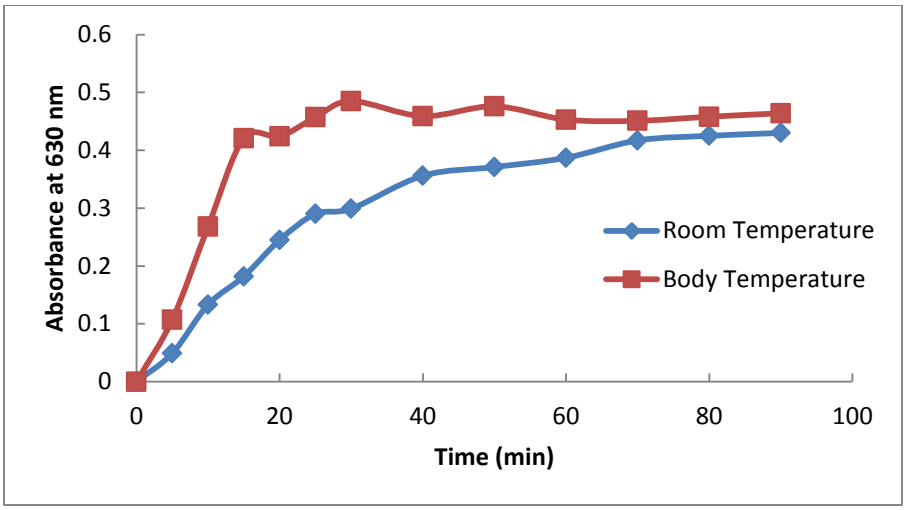
a) Determine the rate coefficient from your absorbance data. To do this, you will need to determine A_∞ based on your data. Use a point earlier in your experiment, and determine a rate coefficient for both sets of data.
b) Based on these results, does temperature affect the dissolution rate? Use the rate constant values you obtained to verify your answer.

ANSWER KEY

The following data shown in Table 3 will be used when answering the questions section of this report:

Table 3. Sample absorbance readings at 630 nm for the dissolvable strips laboratory

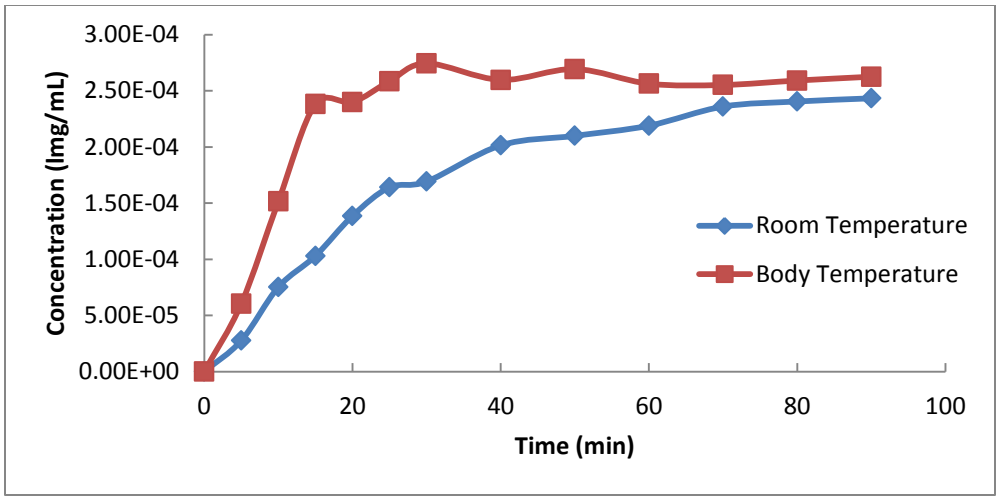
Time (min)	Absorbance readings at 630 nm	
	Room Temperature (20°C)	Body Temperature (37°C)
0	0	0
5	0.049	0.107
10	0.133	0.268
15	0.182	0.421
20	0.245	0.424
25	0.29	0.457
30	0.299	0.485
40	0.356	0.459
50	0.371	0.476
60	0.387	0.453
70	0.417	0.451
80	0.425	0.458
90	0.43	0.464



1. Once you have the concentrations, create another graph of concentration versus time for both temperature sets. Fill in the table and turn in along with the graphs generated and the rest of the report.
   Ans: The unit conversions were made and the table was filled in with the following data points, yielding the graph shown below.

Table 4. Sample data for the concentrations in the dissolvable strips laboratory

	Concentration (mg/mL)	
Time	Room Temp (20°C)	Body Temp (37 °C)
0	0.00E+00	0.00E+00
5	2.77E-05	6.05E-05
10	7.52E-05	1.52E-04
15	1.03E-04	2.38E-04
20	1.39E-04	2.40E-04
25	1.64E-04	2.59E-04
30	1.69E-04	2.74E-04
40	2.01E-04	2.60E-04
50	2.10E-04	2.69E-04
60	2.19E-04	2.56E-04
70	2.36E-04	2.55E-04
80	2.40E-04	2.59E-04
90	2.43E-04	2.63E-04



2. a) Use one of the higher time points (70 to 90 minutes) of both the room temperature and body temperature experimental runs to determine the molar absorption coefficients of both runs. **Ans.** For this answer, the time point of 80 minutes was used. The molar absorption constants were found to be:

ε at room temperature = $1.401 * 10^{6}\ M^{-1}\ cm^{-1}$
ε at body temperature = $1.401 * 10^{6}\ M^{-1}\ cm^{-1}$

This was found by first calculating the molar concentration:

$$Concentration\ at\ 80\,min = 2.40 * 10^{-4}\ \frac{mg}{mL} = 2.4 * 10^{-4}\frac{g}{L}$$

$$Molar\ Concentration\ at\ 80\,min = c = \frac{2.4 * 10^{-4}\ \frac{g}{L}}{793\ \frac{g}{mol}} = 3.03 * 10^{-7}\ \frac{mol}{L} = 3.03 * 10^{-7} M$$

Now, using the Beer-Lambert Law:

$$\varepsilon = \frac{A}{\ell\, c}$$

$$\varepsilon = \frac{0.425}{1\ cm * 3.03 * 10^{-7} M} = 1.40 * 10^{-6}\ M^{-1} cm^{-1}$$

b) Based on the values, do you think that the temperature affects the molar absorption coefficient? **Ans.** Since the molar absorptivity coefficient is identical between the two sets of data, the temperature of the system does not affect the molar absorption coefficient. This is interesting, considering that it is mentioned in several articles that the molar absorptivity coefficient does depend on the temperature of the system.[6,7] Then again, it might be different since we are

working in the visible spectrum range, and not the ultra violet region or the infrared region. It should also be noted that we are only working in a temperature range of 17 °C. This might not be enough of a difference to thoroughly conclude that temperature has no effect on the molar absorption coefficient.

3. Determine how well the molar absorption coefficients can determine the concentration of the solution based on absorbance readings. Use the molar coefficients you found previously and determine the concentration that the solution should be at based on the Beer-Lambert Law. Use a time point between 30 and 50 minutes in both cases. Determine how different these two numbers are by using percent difference. **Ans.** Using the time of 40 min, the Beer-Lambert Law was completed:

$$A = \varepsilon lc = 1.40 * 10^{-6} M^{-1} cm^{-1} * 1 cm * \frac{2.01 * 10^{-4} \, {}^{g}/_{L}}{793 \, {}^{g}/_{mol}} = 0.355$$

Then, find the percent difference:

$$Percent\ Difference = \frac{|0.355 - 0.356|}{\left(\frac{0.355 + 0.356}{2}\right)} * 100\% = 0.28\%$$

The percent difference should be very small, as the molar absorption coefficient was found using these readings.

4. a) How different is the molar absorptivity coefficient that you found using your experimental data from this known value? Use experimental error to determine this difference. **Ans.** Using the percent error equation, the percent error was found to be:

$$Percent\ Error = \frac{|1.4 * 10^{6}\ M^{-1} cm^{-1} - 1.3 * 10^{6} M^{-1} cm^{-1}|}{1.3 * 10^{6} M^{-1} cm^{-1}} * 100\% = 7.69\%$$

b) Now, use the same time point that you used in Question 6 and determine the concentration based on the given molar absorptivity coefficient. Again, compare using percent error. Do this for both experimental runs. **Ans.** The sample calculations were done with the room temperature experimental run. Using the Beer-Lambert Equation:

$$A = 1.3 * 10^{6} M^{-1} cm^{-1} * 1\ cm * c$$

$$c = 2.74 * 10^{-7} M * 793\ \frac{g}{mol} = 2.17 * 10^{-4}\ \frac{g}{L} = 2.17 * 10^{-4}\ \frac{mg}{mL}$$

Now, find the percent difference:

$$Percent\ difference = \frac{\left|2.01 * 10^{-4}\ {}^{mg}/_{mL} - 2.17 * 10^{-4}\ {}^{mg}/_{mL}\right|}{2.17 * 10^{-4}\ {}^{mg}/_{mL}} * 100\% = 7.25\%$$

The same was done for the body temperature experimental run. The concentration was found to be 2.27 *10^{-4} and a percent error of 14.5%.

5. How could you use this law in an engineering aspect? **Ans.** This law is one of the governing laws of spectrophotometry. This is used in several areas for determining concentrations based on absorbance data. Some of these areas are analytical chemistry, algal studies, and organic chemistry. In the case of engineering aspects, this can be useful to chemical and civil/environmental engineers. For example, civil/environmental engineers would use this to determine the growth of algae or the concentration of a contaminant in water. Chemical engineers can use this to determine contaminants in a system, determine the dissolution rate of a drug, and determine the concentration of product in a chemical reaction.

6. a) Determine the rate coefficient from your absorbance data. To do this, you will need to determine A_∞ based on your data. Use a point earlier in your experiment, and determine a rate coefficient for both sets of data. **Ans.** Using the time of 15 minutes, the calculations were followed, and k was determined for both of the data sets. These values are shown below:

k @ room temperature	0.0374 min^{-1}
k @ body temperature	0.1683 min^{-1}

This is obtained through the following calculation:

$$\ln\frac{(A - A_\infty)}{(A_0 - A_\infty)} = -k * t$$

$$\ln\frac{(0.182 - 0.424)}{(0 - 0.424)} = -k * (15\ min)$$

$$k = 0.0374\ min^{-1}$$

A_∞ was determined taking the average of the last three points of the absorbance data.

b) Based on these results, does temperature affect the dissolution rate? Use the rate constant values you obtained to back up your answer. **Ans.** Based on the rate constants, the temperature of the system does affect the dissolution rate.

From the values obtained, we can see that the rate constant increases as the temperature increases. This means that the dissolution rate also increases with temperature. This makes sense, especially when you look at the graph made of the absorbance data.

REFERENCES

1. InnovateUs, Inc. “What are Breath Strips?” http://www.innovateus.net/health/what-are-breath-strips.
2. Donaldson James, Susan. “Sheets Give Caffeine Jolt, Potential for Abuse.” ABC News. 10 June, 2011. http://abcnews.go.com/Health/lebron-james-shills-sheets-caffeine-strips-bad-idea/story?id=13805037#.UeWj2m1nA6e.
3. Particle Sciences Drug Development Services. “Dissolving Films.” 2010. Volume 3.
4. Biology Online. Molar Extinction Coefficient. Biology Online.org. 22 June 2008. Accessed 11 September 2013. http://www.biology-online.org/dictionary/Molar_extinction_coefficient.
5. Reeves, J. Beer’s Law. Laboratory for science majors at The University of North Carolina Wilmington. Accessed 12 September 2013. http://uncw.edu/chem/Courses/Reeves/OnLineLabs/scienceMajors/BeersLaw_PH.pdf.
6. Seton Hall University. UV Absorbance. HPLC Book for the Chemistry Department. http://hplc.chem.shu.edu/NEW/HPLC_Book/Detectors/det_uvab.html.
7. McComb, R.B., Bond, L.W., Burnett, R.W., Keech, R.C., Bowers, G.N. Jr. Determination of the Molar Absorptivity of NADH. Clinical Chemistry. Vol. 2. pp. 141-150. 1976.