Hydrophilic and Hydrophobic Properties of Dissolvable Thin Films – Instructor's Version
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Date of Experiment:

OBJECTIVES

- Students will learn about the different types of polymers used in oral dissolvable strips
- Students will learn to design an experiment to test for a specific response
- Students will develop a mathematical model to fit experimental data

INTRODUCTION

Thin dissolvable strips often require fast dissolving film that would allow for rapid release of active pharmaceutical ingredients (API). This is accomplished by making a film with hydrophilic polymers that dissolve quickly in water and typically dissolve in a few seconds in the mouth[1]. Certain applications, however, require that the film remains in the mouth for several minutes to provide a slow, controlled release of API. One example of this is using dissolvable strips to treat oral burns. To effectively treat burns in the mouth, it is necessary to have a slow release of topical anesthetic while helping the burned cells inside the mouth regrow. This can be accomplished by blending hydrophilic (water-loving) polymers with hydrophobic (water-avoiding) polymers for use in dissolvable strips. This can slow the release of the API. Using this method, it is possible to have a dissolvable strip that slowly releases the API over 10 minutes[2].

The formulation currently used for this kind of dissolvable strips can be seen below:

Table 1. Patented formulation used for oral thermal burn dissolvable strips[2]

	Materials	**Mass %**
Composition of Solids	Benzocaine	10
(Solids are 15% of the total solution)	Poloxamer 188	20
	HPMC*	55
	Glycerol	15
Composition of solvent	Ethanol	98
	Water	2

*HPMC stands for hyrdoxy-propyl-methylcellulose

INSTRUCTOR'S NOTE

Hydrophobic Polymer

Blue dye or caffeine could be used as a substitute for the Benzocaine as an API. Poloxamer 188 is a hydrophobic block copolymer used to aid in regrowth of damaged cells. Poloxamers have several different trade names such as Pluronic[3], Synperonic[4], which may be used as alternatives if Poloxamer 188 is unavailable.

Apparatus

The stainless steel container will be fabricated beforehand for the students to use. You will have to talk to the mechanical engineering technician to have these made. The steel itself is 304 grade 0.048 inches wide stainless steel with a vinyl coated brush. The stainless steel can be cut out using a water jet with 0.125 inches of tolerance for each the width and length. The sides can be bent up to form the container's shape, and then the corners will be welded together to make the container secure. The edges should be grinded down, so that they will not be sharp.

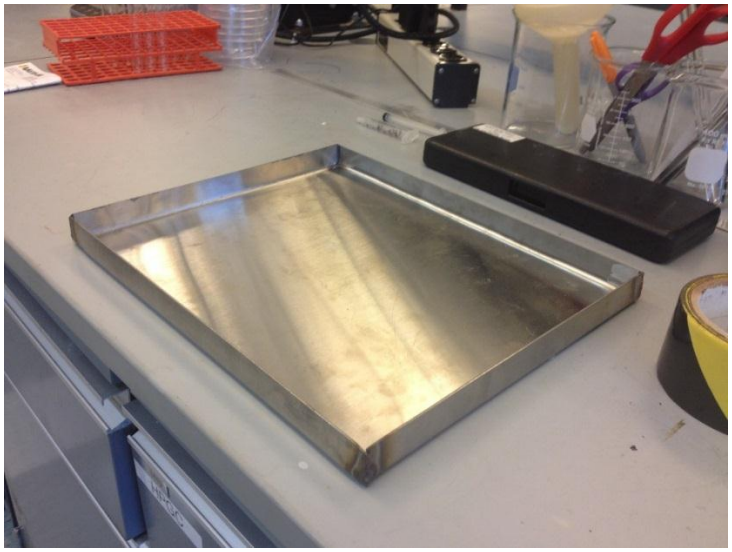


Figure 1. Stainless steel casting tray

MATERIALS NEEDED

- 1000 mL beaker
- Hot plate and mixer
- Magnetic stir bar
- CMC (carboxymethyl cellulose)
- Poloxamer 188
- Sodium lauryl sulfate

- Citric acid (anhydrous)
- Glycerol
- Sucrose
- Peppermint oil
- Dropper
- Deionized water
- 3 mL syringe
- 2 Büchner (vacuum) flasks
- Vegetable oil cooking spray
- Funnel
- Fine mesh screen
- Vacuum tubing
- Vacuum source
- Spatula
- Stainless steel apparatus
- Tubing and stoppers
- Blue food dye (Blue #40)

SAFETY CONDITIONS

Make sure to wear safety glasses, and wear safety gloves when in the lab. Do not consume any materials without your instructor's approval.

PROCEDURE

Each group of students will be assigned the formula to follow in Table 2 below.

Table 2: Recipe for Film Strip Preparation

Species	Mass (g)
CMC	2.4
Poloxamer 188	1.6
Glycerol	2.4
Peppermint oil	0.4
Citric acid	0.8
Sodium lauryl sulfate	0.8
Sucrose	1.2
Water	388
TOTAL	400

1. Weigh out all ingredients for 400 mL solution.
2. Place a beaker with a stir bar in it on a hotplate and set the heat to the lowest setting. Also turn the stir setting to a low setting (around 2).
3. Add water to beaker.
4. Slowly add the polymer mixture in scattering the powder over the surface of the water and wait for it to be absorbed. Once most of the polymer is mixed in, the solution will become very viscous and trap air bubbles.

Once the viscosity increases, you will need to increase the stirring intensity slowly.

5. Once polymer has been fully added, pour in the glycerol from a 3mL syringe. Only approximately 2 mL of glycerol is needed based on the mass from Table 2.
6. Add the rest of the dry ingredients. At this point the solution should be very viscous.
7. Add 3 drops of peppermint oil
8. Add 2 drops of BLUE food dye. The solution should now be a blue color.
9. Transfer the solution into a vacuum flask with a mesh funnel, pouring through the mesh, to catch any large clumps of solidified product and the stir bar. Discard the solidified product.
10. Hook the vacuum flask up to a tube and place a rubber stopper in the top of the flask. Then, connect the tube to the other vacuum flask. Next, place a stopper with an attachment into the top of the other flask and connect this to the vacuum source. See Figure 1 for the appropriate setup. The second beaker will stop any foam from entering the vacuum. We will now make a vacuum filtration system. The purpose of vacuum filtration is to de-aerate the mixture. This minimizes the bubbles in the solution.

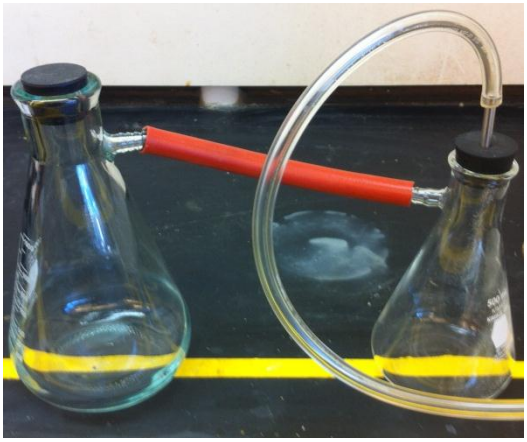


Figure 2: Appropriate Setup for Vacuum Filtration

11. Turn on the vacuum and wait approximately 30 minutes for the gas to leave the solution. The solution should slowly turn clear and may get frothy. The froth will subside.
12. Turn off the vacuum and disconnect the tubing from the vacuum source. Then, remove the beaker with solution from the setup.
13. Pour the contents of the flask into the apparatus
14. Let solution dry for several days until a dry film forms.

DEGREDATION PROCEDURE

The following procedure is a modification from the Degradation Lab

1. Cut out strips about 1 in. x 1 in. from the sheet of dried film.
2. Turn on the spectrophotometer and set it to take absorbance readings at 630 nm.
3. Place 25 mL of deionized water into a petri dish.
4. Fill a cuvette with deionized water and zero the spectrophotometer.
5. Using tweezers, place the strip into the petri dish and start the timer.
6. After five minutes, take a sample of the water into a cuvette. Make sure the sample does not contain any large portions of the dissolvable strip.
7. Take an absorbance reading and return the sample to the petri dish.
8. 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.

RESULTS

Record the time when a sample was taken and the corresponding absorbance.

QUESTIONS

1. Make a plot of absorbance vs time. Below is data for a batch containing only CMC. Plot should include both the mixed polymer batch and the CMC only batch.

Time (min)	Absorbance (nm)
5	0.13
10	0.16
15	0.13
20	0.16
25	0.16
30	0.17
40	0.165
50	0.16
60	0.18
70	0.17
80	0.17
90	0.17

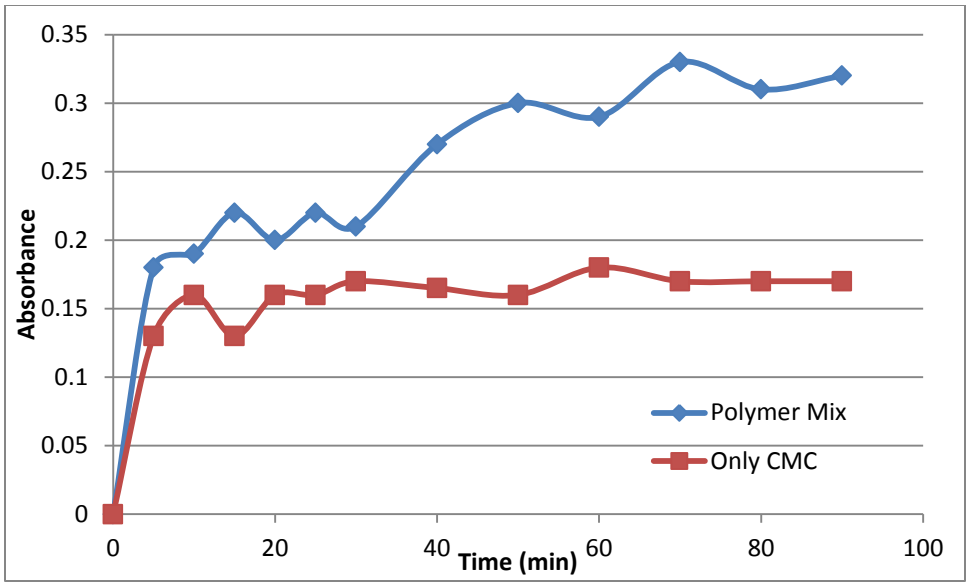


Figure 3: Example Plot of Absorbance vs. Time for both Trials

2. Are the two sets of data similar? What differences, if any, are there in the data? If there are differences, what caused them?
   Ans: Based on the slopes the two sets of data are not similar. The polymer mix had an unsteady absorbance rate while the batch with only CMC had an almost constant absorbance rate. The differences come from the type of polymer used.

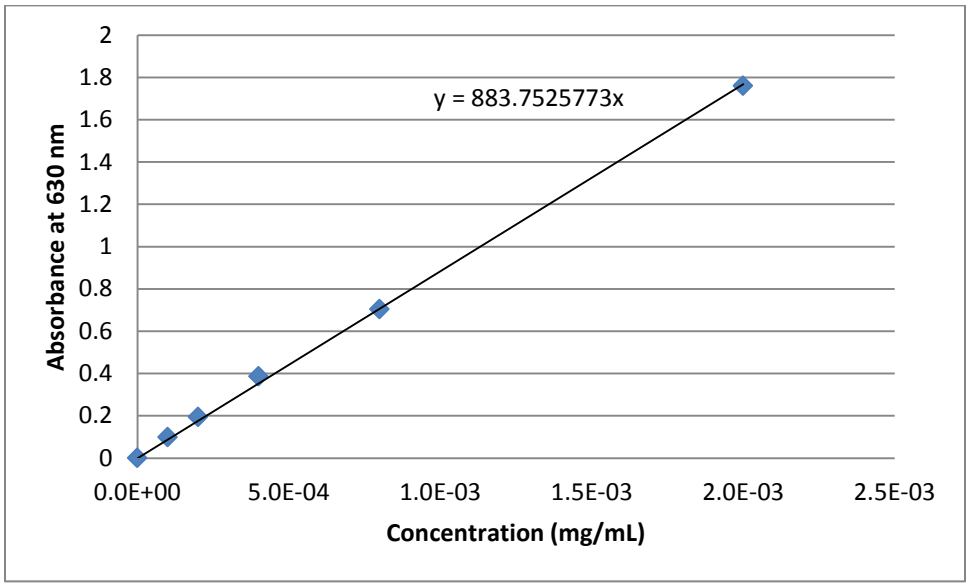
3. What are the differences between hydrophobic and hydrophilic polymers? Explain using your data.
   Ans: Hydrophobic is repelling water or water fearing. Hydrophilic is readily absorbed or dissolved in water, water loving. Hydrophobic polymers are polymers with long hydrocarbon chains that repel water. Hydrophilic polymers are polymers with groups that readily interact with water. Based on the data, hydrophobic polymers take longer to release the blue food dye while hydrophilic polymers release the blue food dye quickly.

4. Given the two scenarios below; determine what type of drug release agent (hydrophobic versus hydrophilic polymers) would be the best. Explain your choice and why it is the best option.

   a. A person is suffering a heart attack.
   Ans: Hydrophilic polymers are useful in quickly releasing the API into the body. Therefore, someone having a heart attack would need a hydrophilic release agent. This is because the drug needs to start working quickly in order to alleviate symptoms before they become fatal.

b. A person taking an anti-nausea medication during chemotherapy.
Ans: Hydrophobic polymers slowly release the drug into the body. This helps to prolong the release of the drug, which allows the medication to last longer. This would be helpful during chemotherapy, as it is a lengthy process. Hydrophobic polymers would therefore allow the anti-nausea medication to be released throughout the therapy, keeping the patient comfortable.

5. You are working for Pastemaker Inc., a pharmaceutical company that has developed a new drug. While this new drug is helpful in treating symptoms of multiple sclerosis (MS), it can be fatal in large doses. If the mass of the medicine delivered increases by 1.0 mg over a period of 10 minutes, then the patient will go into shock and possibly die. Previous researchers have developed a figure that relates the absorbance readings of a solution at 630nm to the concentration of the drug in the solution. You are tasked with determining if the CMC or CMC/Poloxamer blend of thin films that the company makes would be appropriate for delivering this medication. Using the absorbance data you collected in this lab, determine if either of these thin films is a viable film for drug delivery. Assume that there is 5L of blood in the body.



Ans:

$C = \frac{m}{V}$ $C = \frac{1.0\ mg}{5L} \times \frac{1L}{1000mL} \times \frac{1}{10\ min}$ $C = 2 \times 10^{-5}\ \frac{mg}{mL}$

Using the trendline from the figure above, you can calculate the concentration of your sample at the various absorbencies measured in the lab.

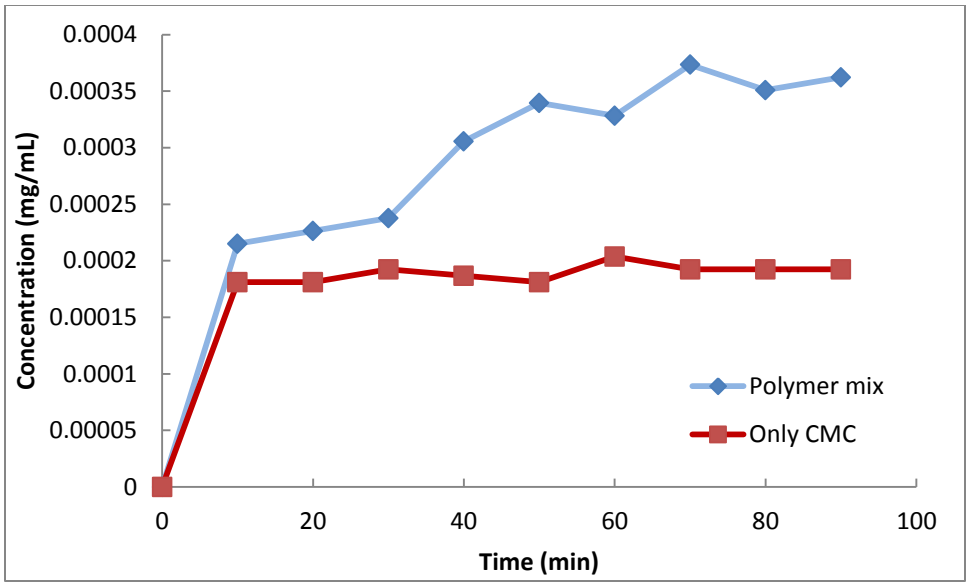


Figure 4: Concentration vs Time Plot used in solving this problem.

Table: Used in solving problem

T (min)	Slope	
	Mix	CMC
0-10	2.15E-05	1.81E-05
10-20	1.13E-06	0
20-30	1.13E-06	1.13E-06
30-40	6.79E-06	-5.7E-07
40-50	3.39E-06	-5.7E-07
50-60	-1.1E-06	2.26E-06
60-70	4.53E-06	-1.1E-06
70-80	-2.3E-06	0
80-90	1.13E-06	0

Compare the slopes at each point and see which value is over the toxic amount. In this case the polymer mix is over the toxic amount, so the hydrophilic drug release method, CMC only, would be the best suited for this drug.

REFERENCES

1. Patil, S. L., “Fast Dissolving Oral Films: An Innovative Drug Delivery System.” *International Journal of Research and Reviews in Pharmacy and Applied Science*, 2(3), 482-496.
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