Drug Design Lab

Activity 4.1.5. Engineering an enteric coating

Three class days. Day one is the digestive system and the pH problem a swallowed pill has to solve. Day two you practise coating and testing with the whole class doing the same thing. Day three you design your own experiment, run it, and write a recommendation. Day three is the graded one, and this handout deliberately does not contain its answer.

14, 16 AND 17 DECEMBER | WET LAB | GOGGLES REQUIRED | LAB NOTEBOOK

READ THIS FIRST. WHAT THIS LAB CAN AND CANNOT TELL YOU

- **It is a model of digestion, not digestion.** You are testing coatings in beakers of acidic and basic solution on a bench. A real gut moves, churns, changes pH along its length, and carries enzymes and bile. A coating that behaves well in your beaker has cleared the first and easiest hurdle only.
- **Nothing here tells you whether a drug works.** You are testing delivery, which is the question of whether a pill survives the stomach and opens in the small intestine. Whether the medicine inside it does anything is a completely separate set of studies that take years.
- **Your result is about your coatings, made by your hands, on your day.** Coating thickness, how long the mixture sat before you used it, room temperature, and how evenly you spread it all change the outcome. Two groups can run the same ratio and get different times. That is a real finding about the method, not a mistake to hide.
- **There is no answer key for day three.** No working ratio is printed anywhere in this handout, on the portal, or in the PLTW material you can reach. Finding one is the assignment.

Why a pill has a pH problem

A swallowed pill has to survive one environment and break down in the next one, and the two are only a few centimetres apart.

The gastrointestinal tract is the hollow tube that runs from mouth to anus. Food and anything you swallow with it travels down that tube while accessory organs, the liver and the pancreas chiefly, release secretions into it. Two regions of that tube matter for this lab.

REGION	ROUGHLY WHAT PH	WHAT HAPPENS THERE	WHAT IT MEANS FOR A PILL
Stomach	About 1.5, strongly acidic	Glands release acid and enzymes. Food is churned and partly broken down, then leaves as a thick liquid called chyme.	Very little is absorbed here. A pill that breaks open in the stomach releases its drug where the drug cannot be taken up, and where acid may destroy it.
Small intestine	About 7 to 9, basic	Bile from the liver and enzymes from the pancreas arrive. Bile is basic and raises the pH. Most nutrient absorption happens along this stretch.	This is where you want the pill to open. Absorption happens here, so this is where a released drug can actually reach the bloodstream.

THE PH SCALE, IN ONE PARAGRAPH

pH runs from 0 to 14 and reports how many hydrogen ions are floating free in a solution. More hydrogen ions means more acidic and a lower number. Fewer hydrogen ions than pure water means basic, sometimes called alkaline, and a higher number. Pure water sits at 7. The scale runs backwards from the thing it measures, so a pH of 2 has far more hydrogen ions than a pH of 8, not fewer.

Enteric means relating to the intestines. An enteric coating is a shell put around a tablet so the tablet holds together in stomach acid and then comes apart once it reaches the higher pH of the small intestine. The coating is not the medicine. It is packaging with a timer built into its chemistry.

The two materials you are working with

Polymer

A large molecule built from many repeating subunits linked in a chain. Both of your coating materials are polymers, which is why the mixture behaves like a gel rather than like a solution.

Sodium alginate

Made from seaweed. The chains are strings of linked simple sugars. Mixed with water it turns into a thick, slow-pouring, viscous liquid.

Shellac

A resin secreted by the lac bug of India and Thailand. It is acidic, it is a natural adhesive, and when it dries it hardens into something close to a thin plastic.

Cross-linking

When the two are mixed, links form between chains and the mixture stiffens into a gel. The longer it sits, the more links form, and the harder and more rigid the film becomes. This means the age of your mixture is a variable whether or not you decided to make it one.

THE CONSEQUENCE NOBODY READS UNTIL IT BITES THEM

Because cross-linking keeps going while the mixture sits on the bench, a coating you applied five minutes after mixing is not the same coating you applied twenty five minutes after mixing, even at an identical ratio. If your groups mix once and then coat over a long stretch of the period, mixing time is quietly changing along with the thing you meant to test. Write down the clock time you mix and the clock time you coat. It costs you nothing and it is the first thing to check when two of your own coverslips disagree.

The specification you are designing to

Innovation, Inc. has an allergy pill. The active ingredient reduces the effect of histamines, the chemicals the immune system releases in response to something like pollen or dust. Their chemists already have the active ingredient. What they do not have is a coating.

THE SPEC, EXACTLY AS THE LAB WROTE IT

- The coating must **not** break down in stomach acid.
- Once the pill enters the small intestine, the coating must dissolve **between five and six minutes**. Not sooner. Not later.
- Prior research found that this window gives the fastest and strongest response. That window is a given. You are not being asked to justify it.

Note the shape of that specification. It is two sided. A coating that never dissolves passes the first requirement and fails the whole job. Most groups who fail this lab fail it by optimising only one side.

Safety

BEFORE ANYTHING COMES OUT OF THE KIT

- **Splash goggles on before the first container is opened, and they stay on until every container is closed and the bench is wiped.** Not on your forehead. Over your eyes.
- Long hair tied back. Sleeves pushed up. Bags and coats off the floor near the bench and out of the walkway.
- Nothing goes near your mouth. Shellac and sodium alginate are food-adjacent materials and that is exactly why people get casual with them. This is a laboratory, not a kitchen. No tasting, no smelling by waving it under your nose, no eating or drinking at the bench.
- The simulated stomach solution is acidic. Treat it as an irritant. If any of it reaches skin, rinse with running water for a full minute and tell Mr. Mendoza. If any of it reaches an eye, go straight to the eyewash, hold your eyelid open, rinse for fifteen minutes, and someone else tells Mr. Mendoza while you rinse.
- Glass: beakers, stirring rods and coverslips. **Coverslips are thin glass and they break into pieces you cannot see.** Handle them with forceps. Never push down on one with a finger. Broken glass goes in the sharps container, never in the regular bin and never in the sink.
- Report every spill, every crack, and every splash, including the small ones. A reported small problem is a two minute problem.

CLEANUP AND DISPOSAL

- Liquid waste goes where Mr. Mendoza directs it. Ask before you pour anything down a drain. Neutralising an acid before disposal is a real step, not a formality.
- Coated coverslips and used gel go in the solid waste container Mr. Mendoza sets out, not in the sink, where the gel sets and blocks it.
- Rinse beakers and stirring rods before the gel hardens. Dried cross-linked shellac is genuinely difficult to remove and the next class inherits it.
- Wipe the bench. Then wash your hands with soap and water, whether or not you wore gloves.

Day two. Part I, the practice run

Everybody does the same thing on day two. This is not the graded experiment. The point is to find out what these materials feel like and how the test behaves before your own design depends on it. Read all the way through the procedure before you touch anything.

1. Collect your Laboratory Procedure sheet and your Data Analysis sheet. Read the Part I procedure end to end. Do not start at step one and read as you go.

   Done when: you can say out loud what the last step is before you have done the first.

2. Write in your notebook, in one sentence, what Part I is for. Not what you will do. What it is for.

   Done when: one sentence exists and it names a purpose, not an action.

3. Set up your bench: goggles on, materials laid out, a timer you can see, and your data sheet open with a pen already on it.

   Done when: you are not going to be hunting for a pen while a timer runs.

4. Follow the Part I procedure to coat your practice pills and set up the simulated digestive system.

5. Run the test. **Record an observation every 30 seconds** on the Data Analysis sheet. Every thirty seconds, including the ones where nothing appears to be happening.

   Done when: the 30 second column has no gaps in it.

6. Attach the Part I data table into your notebook and write a conclusion. What did this investigation teach you about how the coating behaves?

   Done when: the data table is in your notebook and a written conclusion sits under it.

THE ROWS WHERE NOTHING HAPPENS ARE THE USEFUL ROWS

An observation of no visible change is data. It is how you find the point where the change starts. A sheet with gaps in it cannot tell you when anything began, which is the only quantity this whole lab is about. Write *no visible change* and move on.

Day three. Part II, the part that is graded

Your goal: design a shellac-based coating that survives the acid stage and then dissolves between five and six minutes after it enters the simulated small intestine. You will test your coatings on coverslips rather than on whole pills.

Here is the honest description of what is being graded. It is not the ratio you land on. Groups who land on a good ratio by luck and cannot say how they got there score badly, and groups who miss the window but can show exactly what they varied, what they measured, and what they would change score well. **The experiment is the deliverable.**

FIVE DECISIONS THIS HANDOUT WILL NOT MAKE FOR YOU

Every one of these is part of the graded design. If you find yourself waiting for a number to appear, it is not going to. Write your own and defend it.

1. **Which ratios to test, and how many.** You need a range wide enough that the coatings actually behave differently, and spaced closely enough that you can tell which direction to move. Two ratios that both fail tell you almost nothing.
2. **How many times to run each ratio.** One run of a ratio gives you a number with no idea how much it wobbles. Decide what you need in order to believe your own result, and write down the reason.
3. **What counts as dissolved.** This is the one that decides your whole dataset. Dissolving is not an instant. It is a process with a beginning, a middle and an end, and different people watching the same coverslip will call it at different moments unless the group agrees on a rule first. Write your rule in your notebook *before* you run anything, and hold every coverslip to the same rule.
4. **What you hold constant.** List the things that could change the result and are not the ratio. Coating thickness. Mixing time before coating. Solution temperature. How long the coating dried. How you agitate. Then decide which ones you will actually control and how.
5. **Who does what, and who calls the time.** If two different people time two different coverslips, you have added a variable you did not intend. Assign the timer to one person.

1 Review the Part II procedure. Note that coatings go on coverslips.

> **Done when:** you know how the coverslips get coated and how they get into the test solutions.

2 **Design your experiment and write it down before you touch a material.** Use the design record on the next page. Fill in every box including your definition of dissolved. Refer to the Experimental Design resource if you want a checklist for what a complete design contains.

> **Done when:** every box in the design record is filled in, and none of them say *as directed*.

3 Show your written design to Mr. Mendoza. This is not an approval gate. It is a two minute read so that a design fault does not cost you the whole period.

> **Done when:** someone other than your group has read your design.

4 Run your experiment. Record on the Data Analysis sheet as you go, not from memory afterwards.

> **Done when:** every run you performed has a row, including the ones that went wrong.

5 Use the Scientific Numeracy resource if you need to review significant figures, units, or how to report an average and a spread honestly.

6 Write your recommendation to Innovation, Inc. Which ratio, and why. See the write-up section for what a complete recommendation contains.

> **Done when:** your recommendation names a ratio, cites your own data, and states at least one thing you are not sure about.

7 Clean up as directed. Wash your hands.

Your design record

Fill this in before you run anything. Copy it into your notebook if you would rather write there.

DECISION	WHAT WE DECIDED	WHY
Question we are answering		
Ratios we will test		
Runs per ratio		
Our rule for *dissolved*		
Held constant, and how		
Who times, who records		
What would make us wrong		

DATA TABLE

RUN	RATIO TESTED	MIXED AT (TIME)	COATED AT (TIME)	SURVIVED ACID STAGE?	TIME TO DISSOLVED (MIN:SEC)	IN THE 5 TO 6 WINDOW?	NOTES

RUN	RATIO TESTED	MIXED AT (TIME)	COATED AT (TIME)	SURVIVED ACID STAGE?	TIME TO DISSOLVED (MIN:SEC)	IN THE 5 TO 6 WINDOW?	NOTES

What a finished write-up looks like

Below is a worked example of the **format**. The scenario is invented and it is not this lab: different materials, a different target window, and numbers made up for practice. Copy the shape of it. Nothing in it transfers to the coating you are testing.

PRACTICE EXAMPLE PRACTICE-COAT-1. INVENTED MATERIALS, INVENTED TARGET, INVENTED DATA

> **Claim.** We recommend a 5 to 1 ratio of Material X to Material Y for the target window of 9 to 10 minutes.
>
> **Evidence.** We tested four ratios, four coverslips each, sixteen runs total. All sixteen survived the acid stage with no visible change at four minutes. We defined dissolved as the first moment at which the film no longer held together as one piece when the beaker was swirled once. Mean times to dissolved were: 3 to 1, 6 min 10 sec (range 5:40 to 6:35); 4 to 1, 7 min 50 sec (range 7:20 to 8:15); 5 to 1, 9 min 25 sec (range 8:55 to 9:50); 6 to 1, 12 min 05 sec (range 11:10 to 13:00). Only 5 to 1 put every one of its four runs inside the 9 to 10 minute window.
>
> **Reasoning.** More Material X means a thicker cross-linked film, and a thicker film takes longer to come apart, which is why time rises steadily as the ratio rises. The 4 to 1 mean of 7:50 is outside the window even though its slowest run at 8:15 is closer to it than the fastest 5 to 1 run, so picking on best single runs rather than on whole sets would have chosen wrongly. We also note the spread widens as the ratio rises, from 55 seconds at 3 to 1 to 110 seconds at 6 to 1, which means the thicker films are less repeatable and 5 to 1 is near the edge of where we can control the result.
>
> **What we are not sure about.** We mixed once at 9:05 and coated over the following eighteen minutes, so our later coverslips sat in a more cross-linked mixture than our earlier ones. We did not measure coating thickness at all, so some of the spread we blamed on ratio may be thickness. If we ran this again we would mix a fresh batch for each ratio and weigh each coverslip before and after coating.

WHAT THAT EXAMPLE DOES THAT YOU SHOULD COPY

- The claim is one sentence and it answers the question that was asked.
- The evidence is *their own numbers*, with the spread reported and not just the average. Reporting only an average hides whether the result is repeatable.
- The definition of dissolved is stated, so a reader knows what was being timed.
- The reasoning connects the chemistry to the pattern in the numbers, and it names a rival reading of the data and says why it was rejected.
- The last paragraph gives away a weakness in their own work. That paragraph gains marks. It does not lose them.

Where people get stuck

Waiting for the ratio to be given to them.

It is not in this handout, it is not on the portal, and it is not in the PLTW student material. Roughly half of every class loses twenty minutes of a fifty minute period looking for it. Start testing.

Never defining dissolved, then arguing about the data afterwards.

Two people watch the same coverslip and call it thirty seconds apart, and now the group cannot tell whether ratios differ or observers do. Agree the rule in writing before the first timer starts.

Testing ratios that are all nearly the same.

If every coating behaves the same, you have learned nothing and you have no direction to move in. Spread your first ratios wide, see which direction time moves, then close in.

Running each ratio once.

One run gives you a number and no idea whether the same coating would do it again. If a single run lands inside the window you cannot tell luck from design, which is exactly what the recommendation is supposed to distinguish.

Forgetting the acid stage.

A coating that dissolves at 5 min 30 sec in the intestinal solution is worthless if it already came apart in the stomach solution. Both halves of the spec are the spec. Record the acid result for every run.

Mixing one batch and using it all period.

Cross-linking continues while it sits. Your last coverslip was coated with a different material from your first. Note your times or mix fresh.

Treating a failed run as something to hide.

A run that failed and that you can explain is stronger evidence than a run that worked and that you cannot. Put every run in the table, including the spilled one, and label it.

Writing the conclusion from memory after cleanup.

Details you were certain you would remember are gone within ten minutes. Write while the timer is still on the bench.

Words this activity uses

Active ingredient

The chemical in a medicine that actually causes a change in the body.

Inactive ingredient

Everything else in the tablet. It may hold the pill together, mask a bitter taste, or extend shelf life. Inactive does not mean pointless.

Formulation

The particular mixture of chemicals used to get a drug into the body and to the place it is needed. Two pills with the same active ingredient and different formulations behave differently.

Enteric

Relating to the intestines.

Enteric coating

A shell around a tablet designed to hold in stomach acid and come apart at the higher pH of the small intestine.

Gastrointestinal tract

The hollow tube food and waste travel through, mouth to anus. Sometimes shortened to GI tract.

Accessory organ

A digestive organ that is not part of the tube itself but releases something into it. The liver and the pancreas are the two that matter here.

Chyme

The thick liquid that food has become by the time it leaves the stomach.

Bile

A basic fluid made by the liver and released into the small intestine. It helps raise the pH there.

Enzyme

A protein that speeds up a chemical reaction.

pH

A 0 to 14 scale reporting how many hydrogen ions are free in a solution. Lower is more acidic, higher is more basic, 7 is neutral.

Histamine

A chemical the immune system releases in response to an allergen such as pollen or dust. It causes much of what an allergic reaction feels like.

Operational definition

A rule that says exactly how you will decide whether something counts, stated before you measure. Your rule for *dissolved* is an operational definition.

Independent variable

The thing you deliberately change. Here, the ratio.

Dependent variable

The thing you measure. Here, the time to dissolved.

Controlled variable

Something you deliberately hold the same across every run so it cannot explain your result.

> CAREERS THIS LAB TOUCHES
>
> **Pharmaceutical scientist.** Works on getting new and better medications to market. Days are spent in a laboratory investigating how compounds interact with cells. The field splits roughly into three stages: **discovery**, finding compounds that could treat a disease or injury; **development**, testing to establish that a candidate is safe and effective; and **manufacturing**, producing it at scale for patients. Activity 4.1.5 also asks you to read two candidate resumes and cover letters for an open position in this lab and to say which one you would interview and why. A resume is a brief summary of who someone is and what they have done. A cover letter is where they argue why they fit this particular job.