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Student Document

Context

Currently, a team of researchers at L'Université Laval is working on the development of a vaccine based on a sugar molecule (glucosamine hydrochloride) that could be used to treat certain fungal infections. Indeed, just like viruses or bacteria, some fungi cause serious infections in humans. Currently, only post-infection treatment is available on the market to help infected people treat their symptoms. If successful, the team of Dr. Denis Giguère, an organic chemistry researcher, could be among the first to create a vaccine capable of preventing fungal infections. To learn more about fungal infections and their current treatments, you can watch the following video:

https://www.youtube.com/watch?v=_de4qZpwP8Q



Dr. Denis Giguère is a professor and researcher in the chemistry department at l'Université Laval.

Your Role

If effective, the molecule being developed in Dr. Giguère's lab has the potential to become the basis of a commercial vaccine. Your task is to determine what other components need to be included in this future antifungal vaccine.

A vaccine comprises several components other than the *antigen*, the foreign molecule that triggers a response from the immune system (which may include the production of *antibodies*). You will have to select a *stabilizer* and an *adjuvant* to incorporate into your future vaccine. Both of these additives will need to meet strict criteria to ensure that they are safe for human use.

First, check your prior knowledge of vaccines and how they work by answering the questions on the next page.

Activity 1: Introductory Questions

1- What is a vaccine?

2- How are vaccines administered?

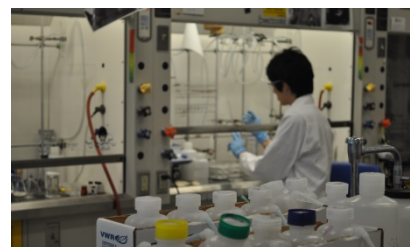
3- Vaccines and pharmaceutical drugs are two methods used to ensure the health of a population. However, their objectives and mechanisms of action differ. Summarize the main differences between pharmaceutical drugs and vaccines by completing the following table.

Characteristics of Drugs and Vaccines

	Médicaments	Vaccins
Main role	Cure or treat an established infection or disease	
Time of administration		Before the infection or disease is contracted
Period of effectiveness	As long as it is administered	
Distribution		Large scale and in specific cases (travellers)

4- In your own words, what do doctors and scientists have to say about the ability of vaccines to control against epidemics and diseases in the general population?

You are now ready to help the team at Laval to complete their antifungal vaccine with a stabilizer and adjuvant!



One of Dr. Giguère's students working on sugar molecules: the basis of the antifungal vaccine.

Activity 2: Choosing a stabilizer for the antifungal vaccine

In order for a vaccine to be widely used, it must be storable for a sufficient period of time. Therefore, a stabilizer is added to all vaccines to extend the shelf life. Stabilizers should not influence the action of the vaccine and therefore, must have the right level of acidity.

Thus, you will have to determine which substance will be the most appropriate stabilizer for your vaccine against fungal infections. You will have two options, and your choice should meet the requirements listed below.

Stabilizer required properties:

- *It must allow the vaccine to be stored for up to one year.*
- *It must react with cobalt dichloride paper.*
- *It must be between 10 and 100 times more alkaline than water.*

In order to make the most informed choice possible, first answer these questions.

1- The stabilizer in a vaccine increases its shelf life. Why do you think this is important? Give at least two reasons.

2- What does a reaction with cobalt dichloride indicate?

3- How is cobalt dichloride paper used to observe this property?

4- What is a synonym for the word “alkaline?” _____

5- What pH range must your stabilizer be within? _____

6- pH indicators are regularly used to measure the acidity or basicity of a substance. However, it is sometimes possible to obtain greater accuracy by mixing indicators. Complete the following table to determine the colors obtained mixtures of indicators.

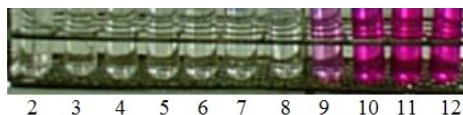
Indicator 1	Indicator 2	Mixture Color
Blue	Transparent	
Blue	Red	
Red		Orange
		Blue-green
		Green

7- Some characteristics of the first stabilizer are given below. After considering the required criteria, would you recommend Abax-3 for use in your vaccine? Why or why not?

Characteristics of Stabilizer Abax-3	
Color in presence of phenol red	Yellow
Color in presence of methyl orange	Yellow
Color in presence of phenolphthalein	Transparent
Storage life	9 000 hours
Solvent	Water

Indicator Color Ranges (for reference)

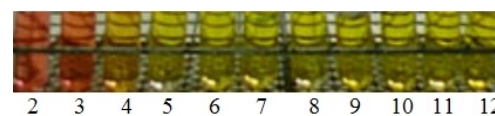
Phenolphthalein



Phenol Red



Methyl Orange



a- Based on the color of **phenolphthalein** in Abax-3 solution, what pH might this stabilizer possess? _____

b- Based on the color of **phenol red** in Abax-3 solution, what pH might this stabilizer possess? _____

c- Based on the color of **methyl orange** in Abax-3 solution, what pH might this stabilizer possess? _____

d- Therefore, what is the pH of the Abax-3 stabilizer? _____

e- Could this stabilizer be used in your vaccine? Why or why not? _____

8- Some notes about stabilizer **Baxat-4_(aq)** gathered by your team of researchers are presented below.

Indicators	Color
Bromothymol blue + methyl orange	Green
Bromocresol purple + thymol blue	Green
Storage life	9600 hours

Indicator Color Ranges (for reference)

Bromocresol purple



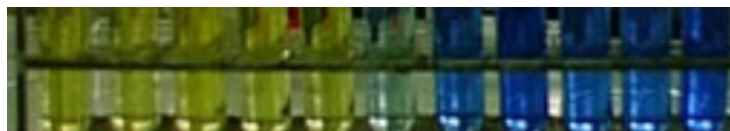
Thymol blue



Methyl orange



Bromothymol blue



a- According to the result of the **bromothymol blue + methyl orange test**, what pH range must Baxat-4 be within? _____

b- According to the result of the **bromocresol purple + thymol blue test**, what pH range must Baxat-4 be within? _____

c- Therefore, what is the pH of the Baxat-4 stabilizer? _____

d- Could this stabilizer be used in your vaccine? Why or why not?

Activity 3: Choosing an adjuvant for the antifungal vaccine

In most vaccines, an adjuvant is added in order to improve the immune response and increase the number of antibodies. As a result, a vaccinated person will be able to fight off an infection more easily.

Like the stabilizer, the adjuvant must not interfere in the vaccine's mechanism of action, and it must also be present in a sufficient concentration. In this activity, you will compare two adjuvants used in the biopharmaceutical industry and then use a set of criteria to choose the best one for your antifungal vaccine.

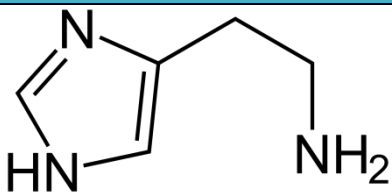
Adjuvant required properties:

- It must have a maximum concentration of 0.005 mol/L.
- It must have a minimum concentration of 0.0002 mol/L.

Did you know?
 Aluminum salts are the most commonly used adjuvants in the pharmaceutical industry

In order to make the most informed choice possible, first answer these questions.

1- Two potential adjuvants are presented in the following table. Fill in the missing information.

Adjuvant Name	Molecular Formula	Molecule Structure
Histamine		

Aluminum potassium sulfate	$KAl(SO_4)_2$	
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2- Determine the molar mass of these two adjuvants. Show your calculations in the space below.

Adjuvant	Molar mass
Histamine	
Aluminum potassium sulfate	

3- Based on the masses given, calculate the concentration of each adjuvant in 0.05 mL of vaccine solution. Show your work.

Adjuvant	Mass (mg)	Adjuvant concentration (mol/L)
Histamine	0.017 mg	

Aluminum potassium sulfate	0.08 mg	
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4- Which of these two adjuvants is available in the proper concentration for your antifungal vaccine?

5- Although these two adjuvants have proved their worth in the past, current studies are trying to develop other molecules that may be even more effective and less costly to produce. Although the World Health Organization has recently demonstrated that aluminum salts do not pose any serious health risks, some people are still afraid to use them.

In 2015, the Giguère group attempted to develop a type of adjuvant based upon sugar molecules, which would be very compatible with the human immune system. Moreover, this type of adjuvant would be very stable in the human body, which possesses a great tolerance to these types of molecules since they are already found in a number of tissues.

Using the Internet, determine what motivates researchers to find alternatives to aluminum-based adjuvants. You may want to start with this [article](#) from the U.S. FDA or this [article](#) from vaccines.gov.
