Teacher's Preparatory Guide

THE BLOOD GLUCOSE MONITOR

Overview

Diabetes mellitus is a metabolic disorder that is characterized by the lack of insulin production, which results in elevated blood glucose. Insulin is a protein that allows cells to take up glucose from the blood for metabolism into energy (ATP) for bodily functions. To manage diabetes, patients require multiple insulin injections daily and rely on glucose monitors to measure their blood glucose for accurate insulin dosage [1].

Blood glucose monitors are sensors that use chemistry and electricity to measure the concentration of glucose in the blood. These fall under the growing number of devices called "lab-on-a chip." Many people are familiar with home pregnancy tests and instant strep tests. The use of nanotechnology has allowed monitors to become smaller, more sensitive, and measure smaller volumes of blood or other fluids. Blood glucose monitors operate using basic chemistry concepts. Blood is placed on the testing strip and the glucose in the sample reacts with glucose oxidase, an enzyme, to produce gluconic acid. The gluconic acid reacts with ferricyanide, a chemical on the testing strip, to produce ferrocyanide. The ferrocyanide reacts with the electricity generated by the meter to produce a reading of the blood glucose concentration of the patient [2].

Nanotechnology researchers have also been able to develop a detector that allows diabetics to monitor glucose levels in their blood using single-walled carbon nanotubes. The carbon nanotubes are formed from millions of carbon atoms and fluoresce (glow) at particular wavelengths in the electromagnetic spectrum in the presence of blood glucose. Scientist have inserted the detectors into human tissue samples and illuminated it with an infrared laser, which has allowed them to relate the glucose concentration to the strength of the fluorescence. Transducers were used to convert the florescence into an electrical signal that can be displayed on a digital screen as the glucose concentration. Lab

You may want to explore the *Nanooze* issue on nanomedicine which has an article on nano tattoos and blood glucose. (http://www.nanooze.org/english/pdfs/nanoozeissue_08.pdf) This lesson connects with Big Ideas: forces and interactions and structure of matter.

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Purpose: The purpose of the lab is to measure the glucose concentration of several synthetic blood and urine samples to determine which patients have diabetes. Students will also build models based on the conservation of mass to further their understanding of the role of insulin on the concentration of glucose in the blood.

Time Required: 90 Minute Class Period

Level: High School Chemistry and Biology

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

NNIN Document: NNIN-1243
Rev: 03/2012

Safety Information

The blood glucose monitor comes with a lancet, which is used to prick the skin for blood. Remove it from the kit prior to beginning the lab. The monitor comes with test strips, but the students may not insert the strips into the monitors properly, which could damage the device. Thus, instructions need to be given several times to the students on the operation of the monitors. Gloves may be needed; some students may be sensitive to the synthetic blood samples. Also, discourage students from ingesting the solutions and from taking measurements of their own blood, due to the risk of blood-borne diseases (HIV, etc).

Advance Preparation

The following items are needed for this activity: blood glucose meter, batteries for meter, control blood samples, blood glucose testing strips, urine glucose testing strips, and simulated "blood" and "urine" samples. Commercially available glucose monitoring kits typically contain a monitor, a few strips, and a control blood sample. In addition, the teacher should check to make sure the monitors work by testing them the day before the activity. Change the batteries in the meter if necessary. Make sure the blood and urine testing strips are not expired. Also, if you are using technology to present your lectures, make sure that your equipment operates correctly by testing it at least 15 minutes before the start of class. If you do not have a computer projector in your classroom, check one out of the media center the day before.

Materials per class (20 students)

- Blood Glucose Monitor kits (5, recommend NovaMax meter)
- Blood glucose standard (5, included with monitor kit)
- 2 mL of simulated blood samples (3 samples/group, See protocol below)
- 2 mL simulated urine samples (3 samples/group, See protocol below)
- Microscope Slides
- Blood glucose test Strips
- Urine glucose test strips
- Gloves
- Paper Towels
- Glucose tablets or glucose powder
- Yellow food coloring
- Red food coloring
- Disposable transfer pipets
- Beakers
- Graduated cylinder or pipets
- Stirring rods or magnetic stirrers
- 2 mL centrifuge tubes for blood samples

Simulated blood and urine stock solution

Dissolve 1 glucose tablet* (4 g of carbs) in 1 L of warm deionized or distilled water. The stock concentration will be 400 mg/dL. The concentration may be lower, so check the stock to make sure the glucose concentration is greater than 200 mg/dL and add more glucose if needed. The

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following dilutions are based on the stock solution being 400 mg/dL, so adjust the dilutions as needed.

**The glucose tablets can be purchased at a drug store, such as Walgreens or CVS. Use only glucose otherwise the activity may not work. The dilutions will be different depending on the glucose concentration.*

Fasting Urine and Blood

Normal "blood" and "urine" (100-120 mg/dL)

1. Mix 20 mL of the stock solution with 60 mL deionized or distilled water (1:4 dilution)
2. Place 40 mL of the solution in a beaker and add 2 drops of red food coloring. Label the container as **P1B1**.
3. Place the remaining 40 mL of the solution in another beaker and set it aside for the next dilution.
4. Add 2 drops of yellow food coloring to 40 mL of deionized water. Label the container as **P1U1**.

Hypoglycemic "blood" and "urine" (40-80 mg/dL)

1. Mix 40 mL of the solution from the previous dilution (step 3) with 40 mL of the deionized or distilled water (1:2 dilution)
2. Place the solution in a beaker and add 4 drops of red food coloring. Label the container as **P2B1**.
3. Place 40 mL of deionized water in another beaker and add 2 drops of yellow food coloring. Label the container as **P2U1**.

Hyperglycemic "blood" and "urine" (>200 mg/dL)

1. Place 50 mL of the stock solution in a beaker and add 2 drops of red food coloring. Label the container as **P3B1**.
2. Place 50 mL of the stock solution in a second beaker and add 2 drops of yellow food coloring. Label the container as **P3U1**.

Post-meal blood samples

Normal "blood" and "urine" (100-120 mg/dL)

1. Same as the fasting protocol
2. Label blood and urine samples as **P1B2** and **P1U2**, respectively.

Hypoglycemic "blood" and "urine" (40-80 mg/dL)

1. Same as the fasting protocol
2. Label blood and urine samples as **P2B2** and **P2U2**, respectively.

Hyperglycemic "blood" and "urine" (>200 mg/dL)

1. Dissolve a glucose tablet in 500mL of the stock solution. Make sure the stock is warm to ensure the glucose will dissolve.
2. Place 250 mL of the solution in beaker and label **P3B2**. Add 3 drops of red food color.
3. Place 250 mL of the solution in beaker and label **P3U2**. Add 3 drops of yellow food color.

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Place 2 mL of each blood sample in a labeled microcentrifuge tube or vial and give each group a tube of each sample. Place 3 mL of the urine samples in labeled beakers and distribute to each group.

Teacher Background:

The teacher needs a basic understanding of diabetes, role of hormones in biological processes, sensors, and nanotechnology (see resources section). In addition, the educator needs knowledge of principles of electrochemistry, specifically oxidation and reduction, which is the foundation of the blood glucose monitor. Also, the instructor should read the glucose monitor manual; it provides specific operating instructions of the device.

Teaching Strategies:

Use a hook, such as a game, to begin the lesson. For example, you may use the attached Jeopardy game based on an introductory presentation to **"engage"** the students. Introductory PowerPoints can be found in the NNIN lesson on Consumer products (http://www.nnin.org/nnin_k12nanotechproducts.html) or at Peter's PowerPoint Station (http://science.pppst.com/nanoscience.html); as well as video resources at NiseNet (http://www.nisenet.org/catalog/tools-guides/intro-to-nano) and at the University of Wisconsin MRSEC (http://mrsec.wisc.edu/Edetc/cineplex/videos/index.html) Also, a brief lecture on nanotechnology, diabetes, and biosensors can provide background information that will increase students understanding of the concepts. Afterwards, student should use the glucose monitors and urine testing strips to measure the glucose levels of synthetic blood and urine samples, respectively. Furthermore, students should "**explain**" their results, analyze the data, and answer the questions associated with the activity. Finally, students could "**explore**" glucose monitors by blogging about them online at the blog site in the resource section.

You can show your students the YouTube videos developed by RET at Vanderbilt University. These can be found at: http://www.youtube.com/user/tcbnf1?feature=watch

Instructional Procedure:

A warm up can be used to grab the attention of the class. For instance, during the development of the lab the teacher used a game about nanotechnology, stop after fifteen minutes so that you can have some questions to ask in your summary. A link to the game is with this lesson on the NNIN website. Afterwards, a brief lecture (15 min) on nanotechnology, diabetes, and blood glucose monitors would be helpful-the notes will provide background information on biosensors. PowerPoint slides on biosensors can be found on the NNIN website along with this activity.

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The students need about 45 minutes to complete the activities, including a teacher lead demonstration of the proper use of the monitor and handling the test strips. Even after demonstrating the students will need to be given additional guidance in small groups on the proper operation of the blood glucose monitor. After the students have completed the lab, they will graph their data and answer the review questions. Once the students have finished the lab, they can blog about their discoveries on the Blood Glucose Monitor blog, the address can found in the resource section. Finally, the lesson can be summarized by having students answer the remaining questions on the game, the summary should take about 15 minutes.

Cleanup:

- Discard all used test strips into the trash can and placed the unused strips back into the test vial. Use water, soap, and a paper towel to clean up the work area.
- Clean off the microscope slides, rinse them off with soap and water. Place them on a paper towel so that they can dry.
- Remove any strips that remain in the glucose monitor and return the glucose monitor and check strips to their kits.
- Test materials ….

Resources

- Booker, R., & Boysen, E. (2005). *Nanotechnology for Dummies*. Indianapolis: Wiley Publishing, Inc.
- *American Diabetes Association* leads the fight against the deadly consequences of diabetes and fight for those affected -http://www.diabetes.org/
- *The OneTouch Ultra Mini:* A simple way to check your blood sugar- http://www.lifescan.com/
- *Oxidation/Reduction:* The website provides a background of the oxidation and reduction of oxygen- http://hyperphysics.phy-astr.gsu.edu/hbase/chemical/oxred.html
- *Glucose:* The site defines glucose and provides specific attributes of the sugar. http://www.medterms.com/script/main/art.asp?articlekey=3608
- *Glucose Test* The website describes the purpose of the glucose test: http://www.labtestsonline.org/understanding/analytes/glucose/test.html
- *Who wants to be a Nano Millionaire Game* .The game can be downloaded from the *NINN website.*
- *Enzyme Kinetics and The Rate of Biological Process*. The website provides an abstract about the kinetics of enzymes http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2147248/
- *The Electrochemical Society (ECS)* ECS was founded in 1902 as an international nonprofit, educational organization concerned with a broad range of phenomena relating to electrochemical and solid-state science and technology. http://www.electrochem.org/
- *The Blood Glucose Monitor Blog*. Students can blog about what they learned from the activity. http://thebloodglucosemonitor.edublogs.org/
- *PowerPoint Notes*: *Biosensors* The slides can be downloaded the from the NNIN website along with activity.

Guided Dialog Before Begin the lab, review the meaning of these terms

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- **Reactants:** *The starting substance in a chemical reaction.*
- **Products:** *A substance formed during a chemical reaction.*
- **Oxidation:** *The loss of electrons from the atoms of a substance: increases an atom's oxidation number***.**
- **Reduction***: The gain of electrons by the atoms of a substance; decreases an atom's oxidation number.*
- **Enzyme:** *A biological catalyst that speeds up chemical reactions by lowering the activation energy*.
- **Glucose:** *Glucose (Glc), a monosaccharide (or simple sugar) also known as blood sugar, or corn sugar, is a very important- product of photosynthesis*
- **Insulin:** *A protein that is used by the cells to transport glucose from the bloodstream for metabolism*

Guided Dialog Before Begin the lab,ask the following the questions

- **Question#1:** *What is an enzyme?*
- **Question#2:** *What is the relationship between oxidation and reduction?*
- **Question#3**: [The teacher holds up an example of a Blood Glucose Monitor] *What is the name of the device that I am holding in my hand?* If the students can not answer the question, the teacher can provide solution if more than five people miss the question.
- **Question#4:** *What can you measure with a Blood Glucose Monitor?*
- **Question#5:** *Who uses this type of device?*
- **Question#6:** *What is diabetes and who is it treated?*

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Activity I: Blood Glucose Monitor and Urine Analysis

Instructor preparation

Test blood glucose monitor

1. Remove the plastic check strip that comes with your kit
2. Insert the check strip into the test port of the monitor with the dimple facing up.
3. The monitor should turn on and should prompt for blood collection
4. If the monitor does not work, take the strip out and rotate it 180 degrees.
5. If the instrument still does not work, call your teacher**.**

I. Test Monitor for accuracy

1. Insert the testing strip into the meter (make sure you are wearing gloves)
2. Using the blood glucose standard that is included with your monitor, take a measurement of the substance by placing a small drop on the testing strip
3. Wait 5 seconds for the measurement to display. Record the value.
4. Repeat two more times
5. Calculate the average blood glucose
6. Compare your value to the concentration shown on the bottle. If your value is in the range of the manufacturer's value, then proceed to Part II.
7. If your value is outside of the manufacturer specification, test a different vial of the standard and contact your teacher.

	Blood glucose measurements (mg/dl)			
Monitor Value	1	2	3	Ave
Kit blood				

II. Measuring blood and urine glucose concentration

Blood testing

a) One at time, place a sample of the patients' blood on the labeled microscope slide using the transfer pipet. ***Be careful not to mix the blood samples and wear gloves at all times.***

b) Touch the testing strip to the blood sample and remove when the meter beeps and is calculating the glucose concentration

c) Record the value of the glucose concentration for the patient and remove the testing strip. Discard each strip after use.

d) Install a new strip and repeat the experiment two more times for each blood sample.

Urine testing

a) Dip the testing strip into the urine sample. *Make sure to wear gloves at all times.*

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b) Determine the glucose concentration by matching the testing strip to the corresponding color on the strip bottle. Discard the used strip.
c) Test each sample three times using a new strip for each trial and record the results in the appropriate table.

Activity

You are a doctor who is administering physicals for three patients. You will use nanotechnology to determine if your patients have normal, high, or low glucose values. Patients with low glucose values are hypoglycemic and will be prescribed a high glucose diet to maintain normal glucose levels. Those who have high blood or urine glucose values may be diabetic and may require future insulin therapy. Test the patient’s fasting and post-meal samples to determine the status of their blood and urine glucose levels.

I. Pre-meal values

When the patients came to the doctor’s office and their blood and urine was collected to measure their fasting (pre-meal) glucose levels.

1. Determine the pre-meal blood and urine glucose values of the three patients.

Pre-meal Sample	Blood glucose measurements (mg/dl)			
Patient	1	2	3	Ave
1				
2				
3				
	Urine glucose measurements (mg/dL)			
Patient	1	2	3	Ave
1				
2				
3				

2. Calculate the average value for each patient.

II. Post-meal values

The patients were given a meal of carbohydrate-rich meal of rice, chicken, orange juice, and ice cream sundaes. Blood samples and urine were collected two hours after the meal.

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1. Determine the post-meal blood and urine glucose values of the three patients.

Post-meal Sample	Blood glucose measurements (mg/dl)			
Patient	1	2	3	Average
1				
2				
3				
	Urine glucose measurements (mg/dL)			
Patient	1	2	3	Average
1				
2				
3				

2. Calculate the average value for each patient and fill in the chart. How do the values compare to each other?

Analysis & Conclusion

1. Graph the pre- and post-meal data for the blood and urine glucose concentration for each patient. How do the values for the patients change after having a meal?

2. Which patient was diabetic, normal, and hypoglycemic?

3. Why was it important to conduct a quality control test on the blood glucose monitor before you started taking data on the blood samples?

4. How did the blood glucose value change for the normal person after having a meal? Why?

5. Why is insulin important for the body?

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Activity II: Modeling the glucose concentration in the body due to the action of insulin

In this activity you will investigate the conservation of mass of glucose to further your understanding of the role of insulin on glucose metabolism.

The conservation of mass law states that mass is not gained or destroyed during chemical reactions. For example in the equation below, when oxygen and hydrogen are combined to form water, the number of oxygen and hydrogen atoms in the products must be equal the reactants.

$$O_2 + 2H_2 \rightarrow 2H_2O$$

Figure 1: Illustrating the conservation of mass in the formation of water. The number of oxygen and hydrogen atoms in the reactants and products are in the same.

In this activity you will build a model to illustrate the conservation in the presence (non-diabetes) and absence of insulin (diabetes). In order to build the model you must determine the following

I. Create a model to determine the accumulation of glucose in the blood for the following scenarios. Make sure you list all assumptions. Use the conservation of mass equation below to help create the model.

In – out= accumulation- consumption

In (I)=glucose coming into the blood
Out (O)=glucose leaving the blood
Accumulation (A)=amount of glucose building up in the blood
Consumption (C)-amount of glucose being used for chemical reactions
We will assume that C is 0 for the model.

Revised mass balance equation: I-O=A

A. To get started the model for a non-diabetic person is below

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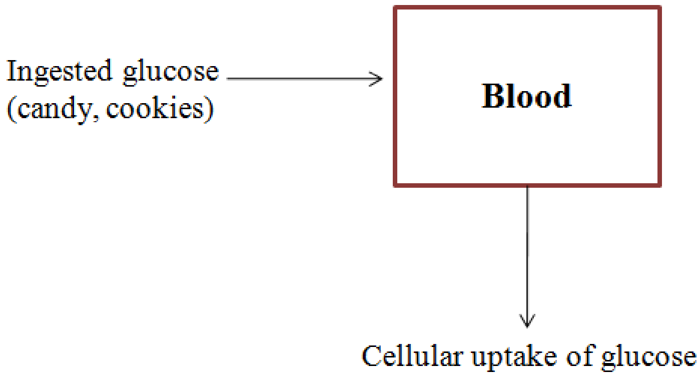

Model Equation

I – O= A

Based on previous results you will find that accumulation of glucose in the blood is zero since insulin is present, so the mass balance for the non-diabetic patient is below.

I = O

For example if 45 g of sugar is ingested, then we can roughly estimate that all 45 g will be taken up by the cells.

B. Create a model for someone who has untreated diabetes. List all assumptions. What is the conservation of mass equation for this person? Hint: The body does not like to accumulate large amounts of sugar in the blood.

Model picture

Model Equation

C. Create a model for someone who has untreated diabetes and non-functioning kidneys. List all assumptions. What is the conservation of mass equation for this person?

Model picture

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Model Equation

Questions

1. What is the source of the glucose input for the model?
2. What are the ways in which glucose can leave the blood?
3. Why do people with untreated diabetes drink a lot of water and urinate frequently?
4. How does lack of insulin affect the untreated diabetes model?

National Science Education Standards [Grade Level 9-12]

Content Standard 6

- Structure of atoms
- Structure and properties of Matter
- Understanding about science & technology

Georgia Performance Standards (GPS)

- SCSH2 Students will use safety practices for all classroom laboratory and field investigations.
- SCSH4 Students will use tools and instruments for measuring, and manipulating scientific equipment and materials.

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- SCSH5 Students will demonstrate the computation and estimation skills, necessary for analyzing data and developing reasonable scientific explanations.
- SC6 Students will understand the effects motion of atoms and molecules in chemical and physical process.
- S7L2e (7th grade Life Sciences); S8P1,5 (8th grade Physical Science); SPS1,10 (Physical Science); SB1 (Biology); SC2,3,7 (Chemistry); SP5 (Physics)

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