**Nanoparticle Application: Silica Nanoparticles and Blood Coagulation**

**Teacher’s Guide**

INTRODUCTION: In this presentation, you will explain specifically how nanoparticles function in one current bio-medical application, blood coagulation. You will not only address the role of surface area and size in the function of nanoparticles, but also give students insight into the thought process that scientists use as they design nanoparticles for a specific purpose. There are also embedded opportunities for mini assessments in the included “Quickie Quizzes.”

OBJECTIVES:

Students will-

* Use a graphic organizer to create useful, effective notes
* Describe the connection between specific aspects of nanoparticle structure and function
* Describe the connection between surface area, size and function of nanoparticles

TIME: 45 min

MATERIALS:

* 3.2 Student Note Sheet
* “Nanoparticle Applications” Powerpoint Presentation
* Internet access for videos

PRESENTATION NOTES:

**Slide 1:**

Teacher Notes: This presentation covers 1 novel application of nanotechnology, the use of nanoparticles to initiate blood coagulation in internal injuries following some form of trauma.

**Slide 2:**

Trauma causes enormous losses every year, both in terms of life and in money. For young people, trauma is the number 1 cause of death and remains a significant cause across all age groups. Therefore, it is a widespread problem for which a solution would be both a significant benefit to the public and a potential moneymaker for pharmaceutical companies. In fact, much of the research in this area is funded by the military, who have obvious vested interest in curbing the consequences of traumatic events.

**Slide 3:**

Currently, adequate solutions exist for surface wounds caused by trauma. Products such as QuikClot, developed at UCSB, can be applied to the site of a wound and use a clay, called Kaolinite, to speed clotting. This clay has high surface area, much like nanoparticles, and a negative charge on its surfaces. This negative charge, which we will talk more about later, is essential to initiating and speeding clotting.

Video: <https://www.youtube.com/watch?v=G_xhJuduBE0>

(Explanation of how QuikClot works)

QuikClot works well for external injuries, but is useless for internal bleeding. Medical personnel, from the military to civilian paramedics, are interested in the development of a similar product that speeds blood coagulation for internal injuries. Kaolin, the clay used in QuikClot, will not work for this type of application for 2 reasons. First, it initiates clotting immediately upon contact- it would clot as soon as it entered the body, not at the site of the wound. Secondly, after kaolin causes the clot, it remains in the body and causes inflammation. This inflammation can result in many health problems that make it impractical for use with internal injuries. We need an injectable substance that will remain inactive as it travels through the blood stream to the site of an injury, where it then becomes active and initiates clotting. After clotting, this material needs to be harmlessly expelled by the body so it does not cause further complications.

**Slide 4:**

To design this product, researchers must first understand the process by which blood clots naturally. This is called the “Coagulation Cascade” and involves a series of chemical reactions, each one causing the following reaction to start like dominos falling one by one.

Video 1: <https://www.youtube.com/watch?v=--bZUeb83uU>

(general overview of coagulation)

Video 2: <https://www.youtube.com/watch?v=cy3a__OOa2M>

(more in-depth) One or both of these videos could be used

The specifics of this series of reactions are not super important to understand at this point, but it is important to know that this whole process is dependent upon the presence of a negatively charged surface (remember Kaolin’s negative surface?) So where does this negative surface typically come from?

**Slide 5:**

Blood platelets, which travel through our blood stream all the time, have this all-important negative surface that causes the Coagulation Cascade to happen. Under normal conditions, this negative surface is enough to initiate clotting. However, following a traumatic event, a person’s body may in a state of shock, making it more difficult for this process to start. The blood platelets alone may not be enough for clotting to occur.

**Slide 6:**

This is where nanoparticles come in. Nanoparticles are useful for many reasons, one of which being that they are, as you have learned, extremely small. Hopefully you have seen by now that extremely small things have extremely high surface area. We will talk more about how that surface area helps in just a moment.

Nanoparticles are also helpful because they are customizable- you can attach all kinds of molecules to a nanoparticle to design it for a specific purpose. For example, I could attach something to a nanoparticle that will make it glow under UV light, or attach a molecule that will help it recognize a specific protein in the body. For this reason, nanoparticles are being explored for a whole host of biomedical uses, some of which you may chose to investigate later.

Lastly, nanoparticles can be biocompatible, depending on what they are made of, so they have the potential to cause fewer problems after the blood clotting has finished.

**Slide 7:**

For this application, researchers at UCSB have designed a nanoparticle with several important components. First, the key to the particle is silica, or SiO2. This molecule, it may or may not surprise you, is a component of many naturally occurring clays (remember that kaolin) and tends to carry a negative charge.

Secondly, there is a long stringy molecule called PEG (or polyethylene glycol). This molecule wraps around the silica and actually serves to cover up or hide the negative charge that silica carries. So while the PEG molecule is attached, no negative surface is exposed. This means that the particle will not react in the blood stream to cause clotting as long at the PEG molecule is attached.

Lastly, the particle contains a compound called APTES and a chain of things called a peptide. These will react with a naturally occurring enzyme (a molecule found at the wound site) to remove the PEG molecule once it reaches an internal injury, therefore “unleashing” the silica’s negative charge.

**Slide 8: Quickie Quiz 1**

**Slide 9: Quickie Quiz Answer**

**Slide 10: Quickie Quiz Explanation**

Remember that the negative surfaces are the key to kick-starting coagulation. As soon as these surfaces are exposed to the blood, they will begin to cause clotting. The purpose of the PEG molecule, a long stringy molecule, is to mask those surfaces so they do not come into contact with the blood until a reaction at the wound site removes PEG. So without this component, the particle would react too quickly to be functional.

**Slide 11: Quickie Quiz 2**

**Slide 12: Quickie Quiz 2 Explanation**

Once at the wound site, the SNP reacts with an enzyme found only at the site of internal bleeding. This enzyme binds with a specific peptide (basically a mini protein) on the SNP. This reaction removes the peptide and everything attached to it, including PEG. Once PEG is gone, the negative surfaces are exposed and free to start coagulation.

**Slide 13:**

You can see that every piece of the nanoparticle is attached for a very specific purpose so that it can ultimately help speed the process of blood coagulation. Once the PEG-less nanoparticle is present in the blood stream, it acts like a blood platelet, providing that essential negative surface to encourage blood coagulation.

**Slide 14:**

This is a video of SNP at work in some human blood plasma. Also in the plasma is a special chemical that glows under UV light when a clot starts to form- the more brightly it glows, or fluoresces, the larger the clot. This video takes place over the course of just a few minutes, and you can clearly see the plasma start to glow. This means that the nanoparticle is doing its job.

**Slide 15:**

So the particle works, but researchers are still working on the best way to deliver the nanoparticle. Testing is taking place on both a “patch” form and a solution form, in which the particle is suspended in a liquid. Let’s take a look at both of these while we revisit the idea of surface area.

**Slide 16:**

Remember that surface area is one of the key features of nanoparticles. Nanoparticles are extremely small and therefore have tons and tons of surface area. In this case, that means tons and tons of negative surfaces are available to kick start that blood coagulation cascade. The more surfaces are exposed to the blood stream, the more effectively this nanoparticle can cause blood to clot. When suspended in a liquid, all the surfaces of these particles are exposed. This means lots of negative surfaces. In a patch form, however, the surfaces are squished together, essentially forming a larger particle with the same volume as all these nanoparticles, but much less surface area. Which one do you think would cause blood to clot more quickly? In your notebooks, write a claim that answers this question, and support it with evidence and reasoning.

**Slide 17: Quickie Quiz 3**

**Slide 18: Quickie Quiz 3 Explanation**

Remember that surface area is one of the essential, unique characteristics that make nanoparticles so special and useful. More surface area means more exposed binding sites to cause a chemical reaction. In this case, particles in solution would have all surfaces exposed and available for reaction, while particles in a patch will only have the outer surfaces available. The inner particles will be hidden, thus making the surface area smaller than it would be if the particles were suspended. You’ll notice that in this picture, the suspended particles on the left have 72 available surfaces, while the patched particles on the right have only 26 available surfaces. This means that the SNP in solution will cause clotting more quickly than those in patch form.

**Slide 19:**

Now you have a pretty sophisticated knowledge of how nanoparticles can be used to help blood clot at the site of internal injuries, a very tricky dilemma. You also understand how surface area and size play key roles in the effectiveness of these nanoparticles in this application.

Lastly, I just want to thank some of the many people who helped inform me (and therefore you) about this exciting new application of nanotechnology.