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**Stimuli-Responsive Drug Delivery Systems using Gold Nanoparticles and Phospholipid Vesicles**

Thomas Solon, Cody Davidson, Matthew Stonaker, Taylor Ledford, Connor LeRoy, Christopher L. Kitchens

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**abstract**

In the near future, new pharmaceutical therapeutics will evolve to contain complicated protein molecules, gene therapies, etc., which must be transported in extremely specific environments such as a specific pH level or sodium concentration. The problem is that throughout the body, there are many different environments that a drug could pass through. For example, gastric acid can have pH levels as low as 1 where blood is around 7.4. This is a problem because as the drugs pass through these harsh environments they may become rendered useless. Furthermore, these new therapeutics are not compatible with conventional drug delivery mechanisms and new strategies for drug delivery are required. To solve these problems, Gold nanoparticles (GNPs) are being used to transport these drugs. The vesicles encapsulate the drug of choice and protect it from the harsh environments of the body. Gold nanoparticles can be designed to either be embedded in the lipid bilayer of the vesicles, or decorate the vesicle exterior. When radiation is applied, the nanoparticles are excited and cause a disruption in the vesicle structure, leading to the release of the drug into the body. Our research is centered around how the stability of lip vesicles changes based on the size, surface chemistry, and distribution of the nanoparticles.

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**results**

**Histories for 50% Fractionation**

- **Hydrophilic GNP:**
  - **Hydrodynamic diameter (nm):**
    - Citrate: 10.00
    - Choline: 10.71
    - EDC: 10.57
  - **Polydispersity index (PDI):**
    - 0.564
    - 0.828
    - 0.685
  - **Zeta (mV):**
    - -0.2
    - -0.6
    - -0.7
  - **Conformed Through UV-Vis:**
    - Yes

- **Hydrophobic GNP:**
  - **Hydrodynamic diameter (nm):**
    - Citrate: 10.62
    - Choline: 10.52
    - EDC: 10.22
  - **Polydispersity index (PDI):**
    - 3.84
    - 4.98
    - 5.32
  - **Zeta (mV):**
    - -0.3
    - -0.3
    - -0.3
  - **Conformed Through UV-Vis:**
    - Yes

**Future Goals:**

- To determine nanoparticle effects on drug delivery when exterioy bound to lipid vesicles as well as determining the effect of the particles on fluorescent dye—quenching or enhancement
- The variations in surface chemistry can either produce a quenching or enhancement effect on the fluorescence emitted. Once these effects are analyzed and a control curve is obtained, the measurement of the leakage rate of dye will be determined.
- The development of nanoparticle-lipid vesicle assembly will provide a new mechanism for drug delivery for patients that can provide site specific targeting upon thermal stimulation.
- This targeting system can be utilized to release the desired medication to specific sites within the body, thus, replacing the current technique of full body chemical treatment such as chemotherapy.

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In the near future, new pharmaceutical therapeutics will evolve to contain complicated protein molecules, gene therapies, etc., which must be transported in extremely specific environments such as a specific pH level or sodium concentration. The problem is that throughout the body, there are many different environments that a drug could pass through. For example, gastric acid can have pH levels as low as 1 where blood is around 7.4. This is a problem because as the drugs pass through these harsh environments they may become rendered useless. Furthermore, these new therapeutics are not compatible with conventional drug delivery mechanisms and new strategies for drug delivery are required. To solve these problems, Gold nanoparticles (GNPs) are being used to transport these drugs. The vesicles encapsulate the drug of choice and protect it from the harsh environments of the body. Gold nanoparticles can be designed to either be embedded in the lipid bilayer of the vesicles, or decorate the vesicle exterior. When radiation is applied, the nanoparticles are excited and cause a disruption in the vesicle structure, leading to the release of the drug into the body. Our research is centered around how the stability of lip vesicles changes based on the size, surface chemistry, and distribution of the nanoparticles.

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**research goals**

1. Perform various gold nanoparticle syntheses and analyze the varying size, surface chemistry, and hydrophilicity the nanoparticles to determine their effects on drug delivery.
2. Measure the leakage rate of fluorescent dye from lipid-nanoparticle vesicles to stimulate simultaneous responsive drug delivery.
3. Tailor nanoparticle surface chemistry to increase stability and bioavailability, decrease macrophage uptake, and enable site-specific targeting.

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**introduction**

**Hydrophilic GNP:**
- **Citrate(-)**
- **Carboxymethyl cellulose, CMC(-)**
- **Polyethylene imine, PEI(+)**
- **Polyethylene glycol, PEG(0)**
- **Dipalmitoylphosphatidylcholine, DPPC**
- **Carboxymethyl cellulose, CMC(-)**
- **Dipalmitoylphosphatidylcholine, DPPC**

**Gold Nanoparticles (GNPs):**
- **Citrate(-)**
- **Carboxymethyl cellulose, CMC(-)**
- **Polyethylene imine, PEI(+)**
- **Polyethylene glycol, PEG(0)**
- **Dipalmitoylphosphatidylcholine, DPPC**

**Hypothesis:**
- Size and hydrophilicity will increase rate of fluorescent dye release.
- GNP will cause enhancement of fluorescent dye

**Experimental- Instrumentation**
- **Instruments for Characterization**
  - Dynamic Light Scattering (DLS)
  - Ultraviolet Visible Spectroscopy (UV/Vis)
  - Approximate size, distribution, stability, surface chemistry
  - Transmission Electron Microscope (TEM)
  - Core GNP diameter, visual placement
  - Synergy H1 Plate Reader
  - Fluorescence intensity of dye

**medical implications**

The vesicles will help the medicine inside travel through the harsh conditions that they will have to endure while inside the body. The vesicles can be tracked in the blood stream and then leaked into the body when thermal radiation is applied. The vesicles must be stable enough to endure the temperature of the body without rupturing, but must also break under temperatures that the human body can easily tolerate. If this can be achieved, then the patient will be put under the least amount of stress and the medicine will be delivered most efficiently.