Synthesis and Characterization of Chitosan Nanoparticles for Oral Delivery

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Introduction and Objective

- Oral delivery of drugs offers the highest patient compliance and ease of use.
- Chitosan (CS), a polysaccharide derived from the deacetylation of chitin, is known for its biocompatibility, nonreactivity, and mucoadhesivity. (Landriscina et al., 2015)
- In nanoparticle form, it can increase the bioavailability of therapeutic agents which may otherwise be limited by their low intestinal absorption and instability in the gastrointestinal (GI) tract. (Chen et al., 2013)

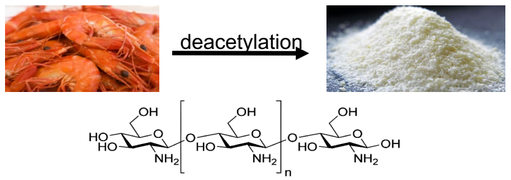


Figure 1. Derivation and chemical structure of chitosan. news.com.au, indiamart.com.

- We aim to test CS-NPs in various pH conditions representative of the GI tract for the development of a oral delivery nanocarrier.

Impact of Professor's Research

The Chung Lab uses nanomedicine and tissue engineering to address clinical limitations.

Research focus includes:

- Nanoparticles to target diseases such as atherosclerosis and autosomal dominant polycystic kidney disease (ADPKD),
- Improving contrast agents to enhance imaging techniques such as magnetic resonance imaging (MRI) and positron emission tomography (PET).

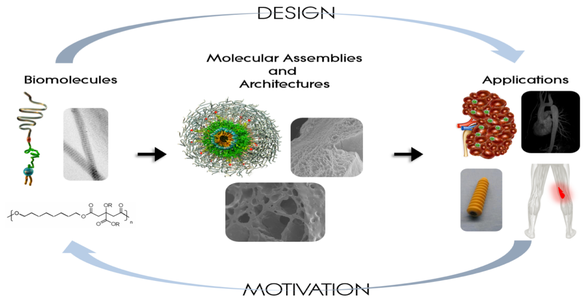


Figure 2. "Our Vision". chunglaboratory.com.

Techniques and Skills Learned

- **Dynamic Light Scattering (DLS):** a laser is directed at a sample housed in a cuvette. The correlation of the light scattering pattern is used to determine the size of the particles in the sample.

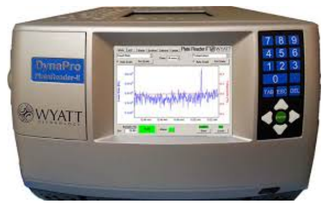


Figure 3. A DLS Instrument. USC School of Pharmacy Core Facilities.

- **Scanning Electron Microscopy (SEM):** a beam of electrons scans the surface of the sample. The position of the beam and its intensity is used to produce an image of the sample.
- **Transmission Electron Microscopy (TEM):** a beam of electrons are transmitted through a sample that is loaded onto a grid. The interaction is then measured and focused to display an image of the sample.

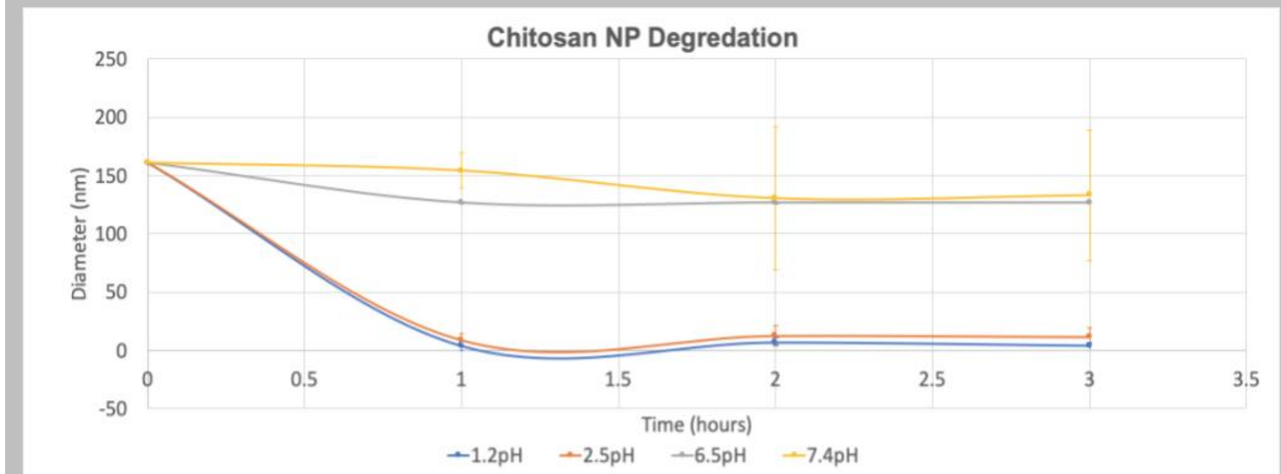
Figure 4. A Transmission Electron Microscope. Hitachi High Technologies America.

- **High-Performance Liquid Chromatography (HPLC):** samples are separated into its components and purified from waste products.
- **Matrix Assisted Laser Desorption/Ionization (MALDI):** a laser is directed at a sample crystalized in a matrix material, and the time of flight (TOF) is measured in order to calculate the mass of a substance.

Methods

- Chitosan Nanoparticles are formed using acetic acid, MilliQ H_20, Chitosan, a cross-linker (sodium tripolyphosphate (TPP) or polyglutamic acid, as well as a drug (metformin hydrochloride) to be loaded into the nanoparticle.
- Chitosan solution is added dropwise to the cross-linker solution and final solution is vortexed and sonicated.
- The solution is distributed in 5mL Eppendorf tubes and centrifuged for 30 minutes at 14,000 RPM at 14°C.
- After centrifuging, the solvent is poured out, and the nanoparticle pellet is preserved and washed with 20%, 60%, and 100% Ethanol.
- The completed solution is preserved in a -80°C freezer for 24 hours, then lyophilized for 8 hours until analysis in DLS.

Results



- The most dramatic size differences were seen after 1 hour elapsed, especially in low pH such as pH 1.2 and 2.5; noticeable degradation from 161 nm (diameter) to 9.20 nm was noticed under pH 2.5.

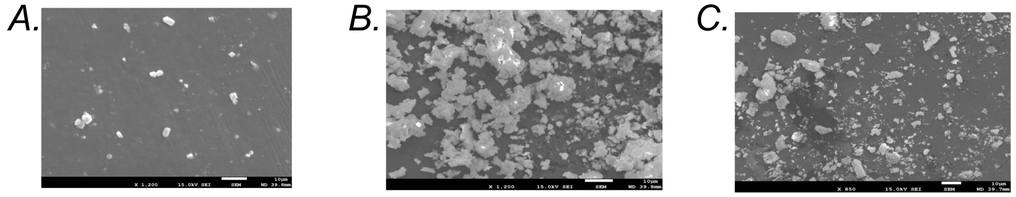


Figure 5. SEM Imaging of Chitosan after 2 hours under untreated conditions (A), 2.5pH (B), and 7.4pH (C). PC: Jiwoo You and Jonathan Wang.

- Clumping was more noticeable in lower pH (A), indicating further degradation, while CS-NPs at higher pH (C) preserved its shape better and less clumping was present, indicating less degradation.

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