Synthesis and Characterization of Lipid Coated Nanoparticles as Drug Delivery Vehicles

Chris W. Munjar, Brian D. Gilbert
Linfield College Department of Chemistry, McMinnville, OR

Introduction

Background: Nanoparticles have been an area of active research for several decades due to their interesting physical and chemical properties[2]. They have found widespread use in several sectors such as chemical sensing, imaging, and photovoltaics[1]. One important application is their potential use as drug delivery vehicles[2]. Surface modifications have been shown to allow for targeted binding with specific cell types that increases the therapeutic dose at the site of interest[4]. The ability to tailor the shape and core composition of nanoparticles affords a wealth of possible combinations for investigation. Nanoparticles functionalized separately with luminol, with lipids, and poly(allylamine hydrochloride) (PAH) have been found to have many advantages such as detection through Raman spectroscopy, immune system evasion, and increased stability, respectively[3,5].

Goals: In this research, nanoparticles are being layered with all three components to capitalize on each of these benefits. An important goal of nanoparticle synthesis is to achieve particles that are monodisperse in size. This is often difficult to achieve due to their tendency to aggregate, resulting in a relatively small number of nanoparticles of useable size. Moreover, aggregation can lead to difficulties in analytical determinations of successful surface modifications. Results herein suggest that monodispersity was successfully maintained for both metal nanoparticles after functionalization with PAH and lipids.

Materials and Methods

Citrate Capped Nanoparticle Synthesis

- Sodium tri-citrate (1.0-2.5 mL, 1%) was mixed with chloroauric acid (1.5 mL, 0.01 mM) and DI H_20 (50 mL) upon boiling and was refluxed for 30 min.
- Silver nitrate (25 mL, 1 mM) was mixed with DI H_20 (25ml) followed by sodium tri-citrate (2.5 mL, 1%) upon boiling and was refluxed for 30 min.
- Each separate mixture was cooled on ice to generate gold nanoparticles (AuNPs) and silver nanoparticles (AgNPs).

Poly(allylamine hydrochloride) (PAH) coating

- Sample aliquots (1.0 mL) were centrifuged and the pellets collected and resuspended (1.0 mL DI H_20 each).
- Particles were stored overnight at room temperature after addition of 100 μL sodium chloride (0.1 M) and 200 μL PAH (10 mg/mL).

Lipid Coating

- PAH coated nanoparticle aliquots were centrifuged and the pellets resuspended in HEPES (0.5 mL, 20 mM, pH 7.19).
- A 1:1 weight ratio of 1-palmitoyl-2-oleoyl-sn-glycero-3-phospho-L-serine (POPS) and lysophosphatidylcholine (LPC) solution (0.5 mL) was added to each 0.5 mL PAH coated sample and allowed to incubate overnight.
- Lipid-coated samples were centrifuged and the pellet was resuspended in HEPES buffer (1 mL, 20 mM).

Sample Analysis

- Samples were analyzed after coating and purification through a Shimadzu 2600 UV-vis spectrophotometer, a Malvern LM10 HS NanoSight particle sizer, and will be analyzed through Raman spectroscopy after coating and purification with luminol.

Results

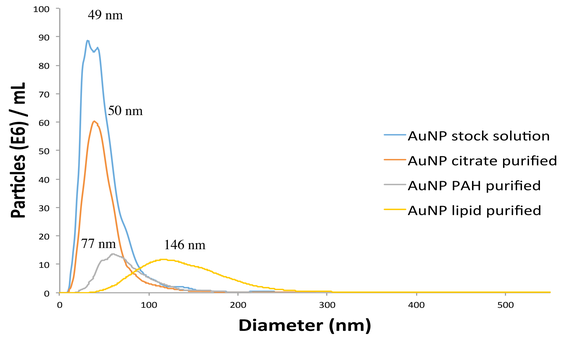

Figure 1. Distribution of diameter sizes (nm) in a gold nanoparticle sample made from 1.00 mL tri-sodium citrate after each surface modification.

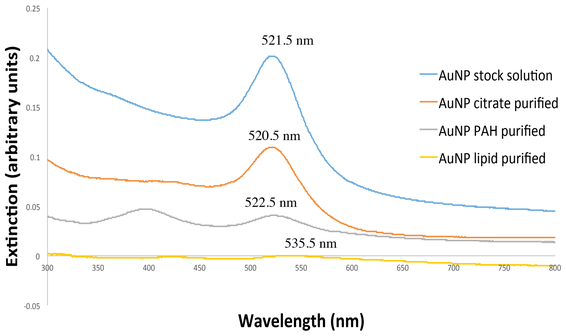

Figure 2. Extinction spectra after each gold nanoparticle (generated from 1.00 mL tri-sodium citrate) surface modification.

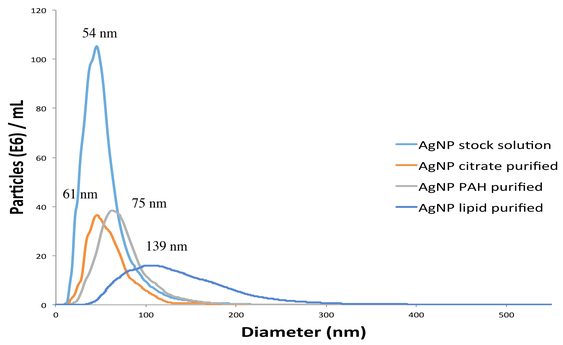

Figure 3. Distribution of diameter sizes (nm) in a silver nanoparticle sample made from 2.50 mL tri-sodium citrate after each surface modification.

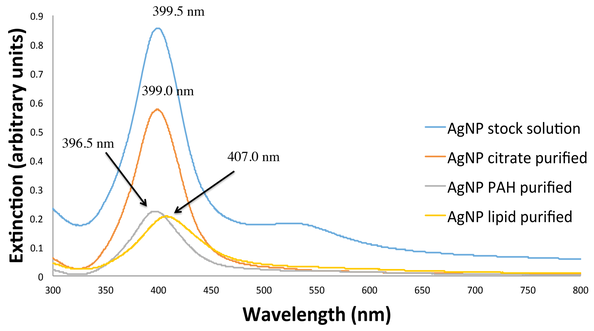

Figure 4. Extinction spectra after each silver nanoparticle (generated from 2.50 mL tri-sodium citrate) surface modification.

Discussion

Size Results: In general, size increases were detected upon each additional surface modification. Relative monodispersity was also maintained with each successive modification. Both nanoparticle solutions underwent approximately 60 nm increase in mean diameter upon functionalization with lipids.

Optical Results: Both solutions underwent an approximately 11 nm red shift upon functionalization with lipids, and maximum extinction was typically observed to increase with each modification, suggesting successful coating.

Conclusion

- The data collected suggests the successful synthesis and modification of gold and silver nanoparticles with LPC and POPS lipids.
- This work is significant because it demonstrates that a variety of different nanoparticles consisting of different cores can be functionalized and could potentially be further functionalized for use as drug delivery vehicles.

Future Work

- Further functionalization with luminol, a Surface Enhanced Raman Scattering tag molecule, will be investigated next.
- If monodispersity with luminol is maintained, the particles will be introduced into cell cultures to monitor for cellular uptake.
- Lipid coated gold-silver alloy nanoparticles will be investigated as well, since current efforts have maintained monodispersity up until PAH coating.

References

1. Alex, S. and Tiwari, A. *Journal of nanoscience and nanotechnology*. **2015**, 15, 1869-1894.
2. Giljohann, D, et al. *Angew. Chemie. Int. Ed.* **2010**, 49, 3280-3294.
3. Syed, et al. *Analyst*. **2013**, 138, 5600.
4. Wang, J.; Byrne, J.; Napier, M. and DeSimone, J. *Small*. **2011**, 1, 1919-1931.
5. Yang, J. and Murphy, C. *Langmuir*, **2012**, 28, 5404-5416.

Acknowledgments

We would like to thank Victoria Wood, Madison Gladding, Allison Smith, and the Linfield College Chemistry Department for their consultation and insight during the course of this research.