Optimization of Gold Nanoparticles as a Multifunctional Drug Delivery System for Chemotherapy

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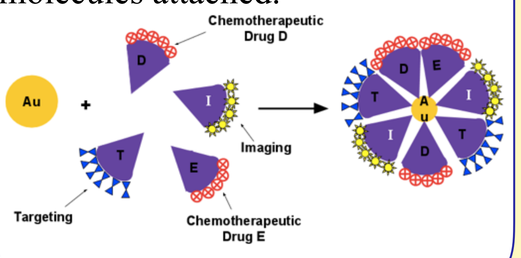
Abstract

The development of a gold nanoparticle (GNP) cored dendron as a drug deliver system can help people advance towards a better treatment of chemotherapy. The problem with the current application of the medicine is that it affects the whole human body, not just the tumor area. With the information collected in this research, we aim to eliminate the preexisting problem of excessive drug toxicity in the body and enhance targeting efficiency. By using these nanoparticles, we have found a way to get the drug into the body with enhanced permeability and retention (EPR) effect which provides passive targeting. Furthermore, through active targeting, the nanocarriers are able to attach to the cell and release the drug into the nucleus.

Introduction

The design of this drug is a GNP core coupled with spacers and dendrons around the surface that have multifunctional uses on their termini. The dendron is a first generation poly(propylene imine) (PPI) dendron with a phenolic focal point, and the spacer is a tetraethylene glycol (TEG) molecule that is connected at that focal point of the PPI dendron. With this model, we have multiple branches around the core that are made in a very limited amount of steps, and we can organize the distribution of different functions on the molecule connected to each branch. This makes the targeting to the tumor more efficient, makes multimodal imaging easier, and increases the amount of drug molecules attached.



Methods

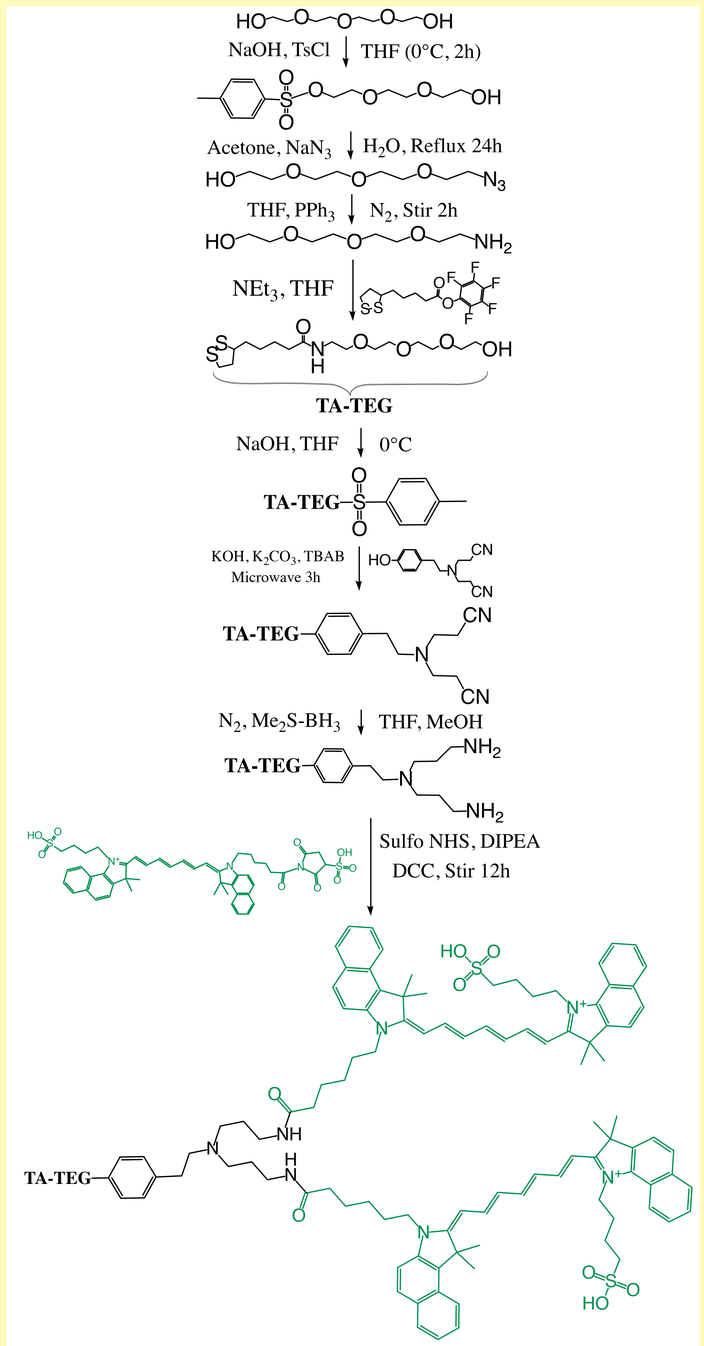


Figure 1. (Above) Fractions from the size exclusion of the first generation dendron with indocyanine green (ICG) dye.

Figure 2. (Right) Size exclusion of dendron-ICG in LH-20 with pure methanol.

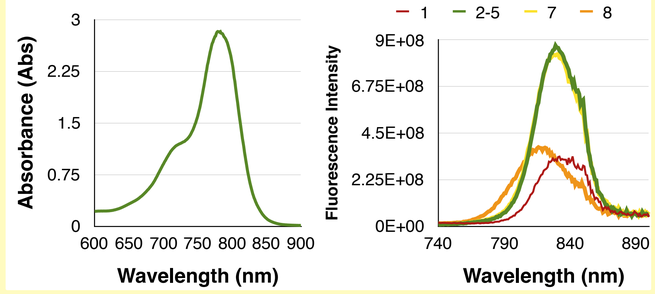


Figure 3. (Above, left) Ultraviolet-visible (UV-Vis) spectrophotometry of the ICG.

Figure 4. (Above, right) Fluorescence analysis of fractions 1, 2-5, 7, and 8

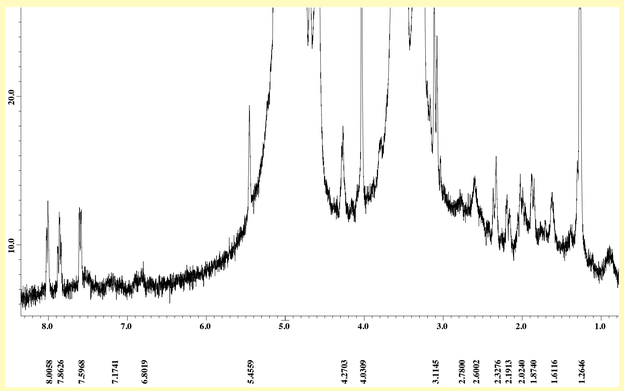


Figure 5. (Above) Proton nuclear resonance (^1H NMR) spectra of the ICG dye coupled with the dendron in MeOD was obtained using a JEOL ECX 400 MHz NMR spectrometer (X axis: Parts Per Million-1H / Y axis: Thousands).

Scheme 1. (Left) Synthetic path of the spacer, coupling of dendron, and coupling of ICG.

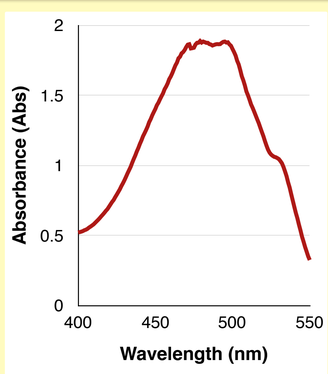
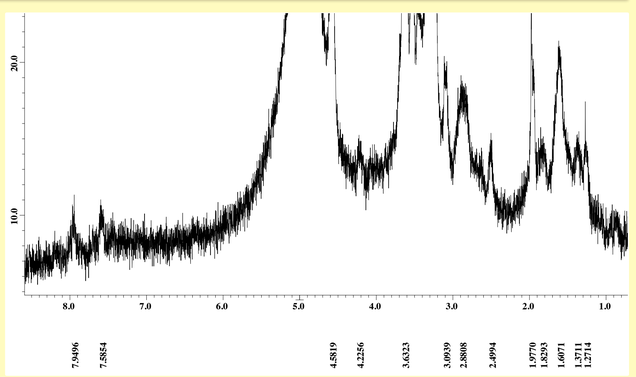


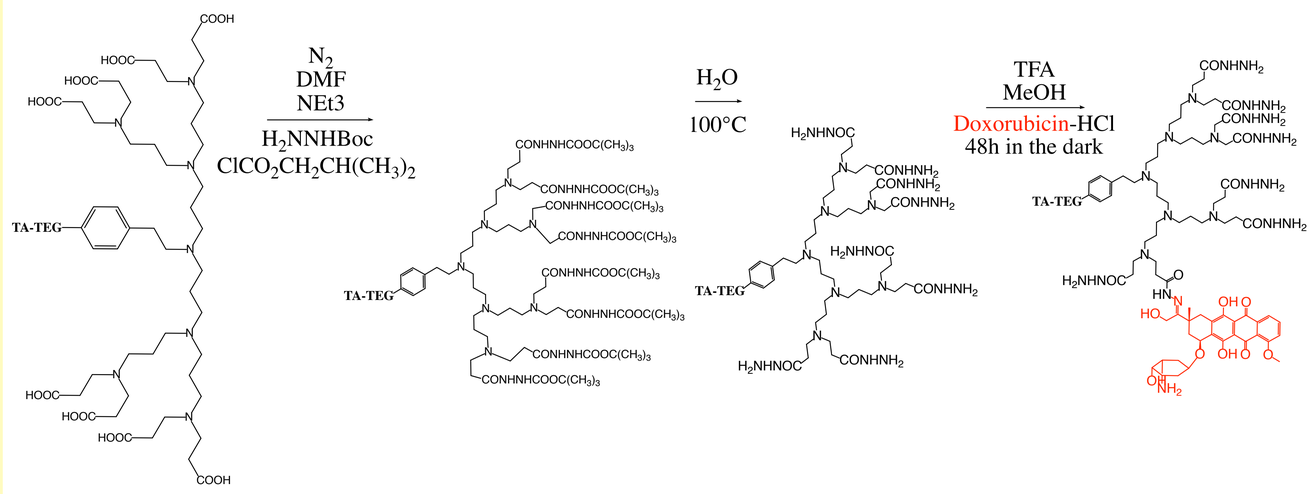
Figure 8. (Above) Doxorubicin and the dendron.

Figure 7. (Left) UV-Vis of dendron and doxorubicin.

Figure 6. (Right) ^1H NMR of the dendron and the Doxorubicin drug.

Scheme 2. (Below) Coupling of the third generation dendron to the drug Doxorubicin.





Results

In this study, we have functionalized the first generation dendron with near infrared fluorescence marker. We have also attached Doxorubicin to a third generation dendron.

Conclusion

With this ideal drug, we are able to have a multifunctional drug delivery system that releases into the body with decreased drug toxicity.

Future

Future studies include being able to attach molecules to all eight branches in the third generation PPI.

Acknowledgments

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