Develop LSRP-based nobel metal nanomaterials for early detection of Alzheimer's amyloid-beta aggregation

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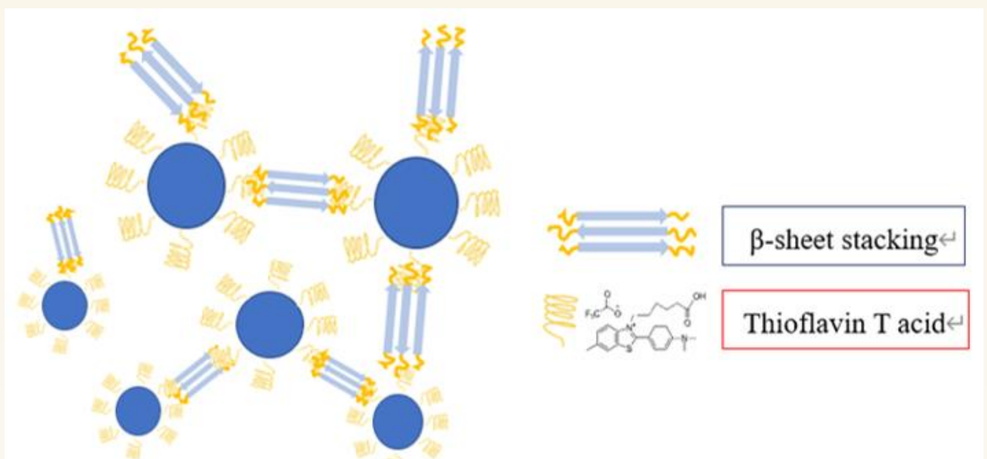
Abstract

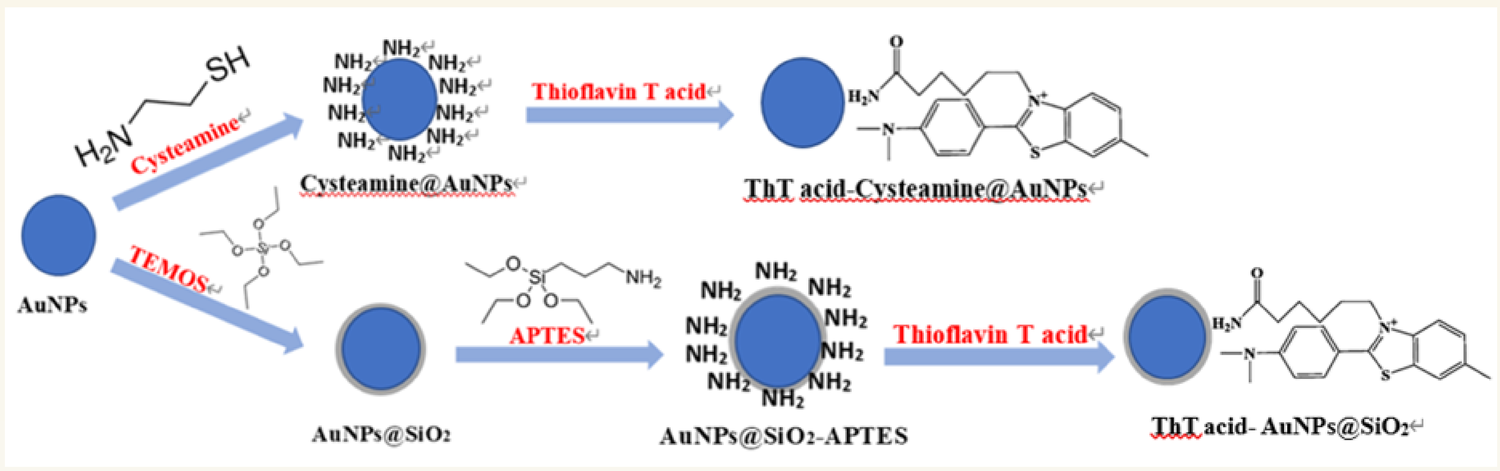
Progressive amyloid-β fibrillar aggregates have long been considered to be the pathogenesis of Alzheimer's disease (AD). At this phase, Aβ fibrillization has already caused irreversible memory damage which severely limits the outcome of most therapist methods for AD. Therefore, it is widely believed that early stage detection of AD is the key to find the ultimate cure for AD. Thioflavin T (ThT) is a fluorescent probe frequently used to monitor the fibrillization process, but not oligomer formation. Therefore, we come up with a concept to fabricate ThT acid carrying Au nanoparticles (ThT acid@Au NPs) to make them as LSPR-based (localized surface plasmon resonance, LSPR) sensing probe to achieve monitoring of β-sheet structure in Aβ peptide aggregation. In this report, we synthesized ThT acid-conjugated Au NPs and further manipulated the amount of ThT acid molecule onto Au NPs. Consequently, the ThT acid molecule are inert to β-sheet strucrure of Aβ and caused aggregation of Au NPs before Aβ irreversible fibrillization. Through continuously incubation between ThT acid@Au NPs and Aβ peptide, a new absorption response starts to develop near 640 nm, which can be explained by Au NPs clustering that red shift the corresponding LSPR response during the oligomerization phase. Meanwhile, the ThT-acid fluorescence assay is simultaneously for Aβ fibrillation under the same condition. We believe that the concept of ThT acid@Au NPs should provide a revolution way for early detection of Aβ aggregation.

Goals

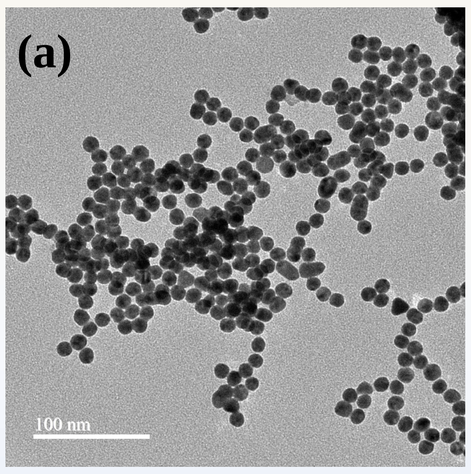


Methods

The experimental processes of ThT acid-Cysteamine@AuNPs/ThT acid-AuNPs@SiO_2



Results



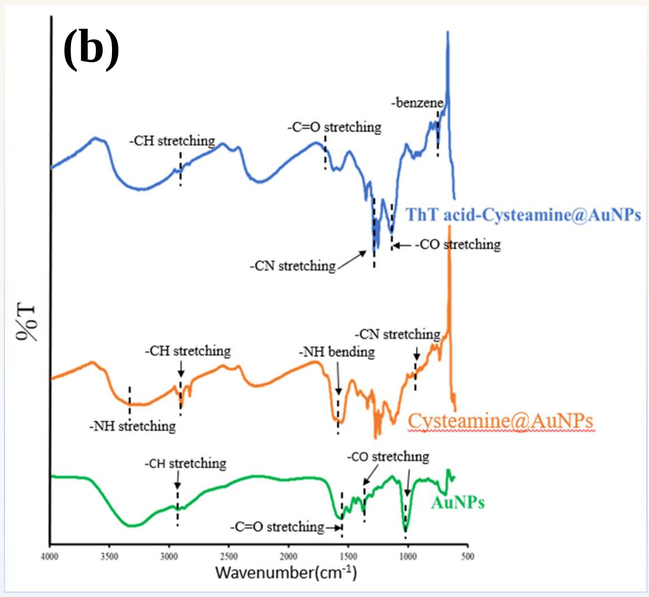


Figure 1. (a) TEM image and (b) FTIR of modify cysteamine on Au NPs; AuNPs (green line), Cysteamine@AuNPs (orange line), ThT acid-Cysteamine@AuNPs (blue line).

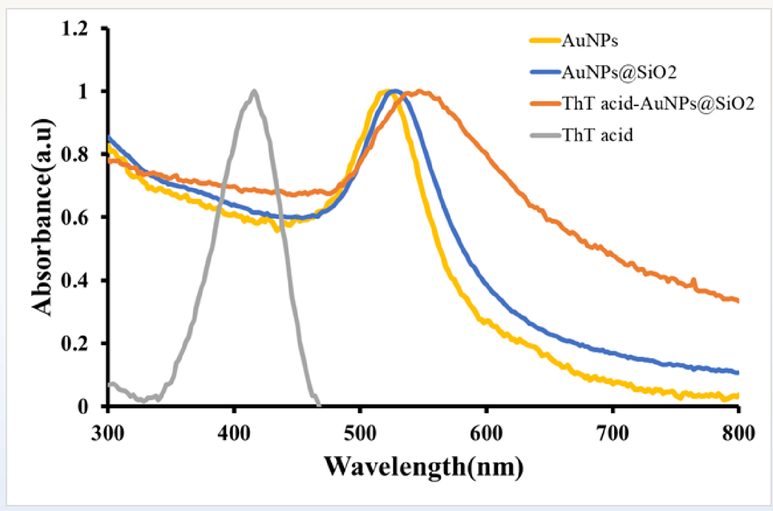


Figure 2. (a) UV-VIS spectrum of AuNPs (yellow line), AuNPs@SiO_2 (blue line), ThT acid-AuNPs@SiO_2 (orange line) and ThT acid (gray line).

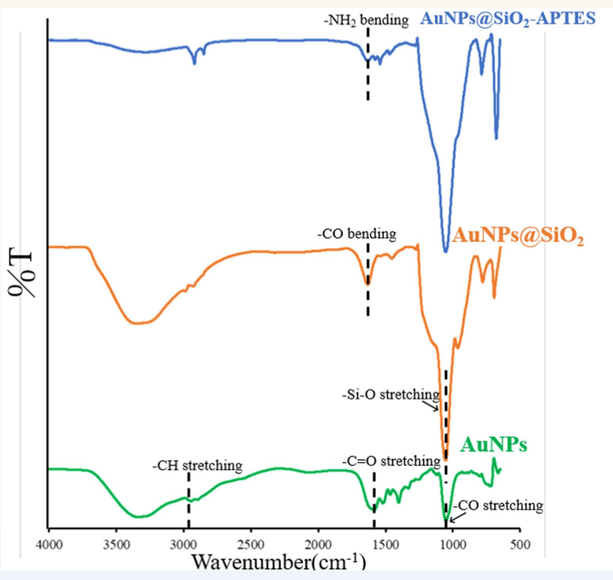


Figure 3. FTIR spectra of AuNPs (green line), AuNPs@SiO_2 (orange line), AuNPs@SiO_2-APTES (blue line).

Conclusion

In this report, we attempted to synthesize Au NPs with several surface modification such as cysteamine and ThT acid through surface chemistry process to form ThT acid- cysteamine@AuNPs. After that, the structure characterization and optical properties analysis of cysteamine@AuNPs and ThT acid-cysteamine@AuNPs were done by a series of equipment. However, the cysteamine@AuNPs were not very stable and easier aggregation in experimental process. Hence, we change the surface functionalization method to Au and SiO_2 core-shell nanostructure and further modified the ThT acid molecule onto Au@SiO_2 NPs surface. Finally, we successfully synthesized and finished materials characterization of ThT acid-Au@SiO_2 by UV-VIS and FT-IR measurement.

Future work

In the future, we will plan to finish the Aβ sensing experiments including the observation Aβ fibrillization time, LSPR band shift, SERS and Rayleigh scattering analysis within Aβ peptides and ThT acid-Au@SiO_2 incubation. We believe that the ThT acid@Au NP can be a Rayleigh scattering enhancer to boost optical intensity during short-term β sheet of Aβ generation. It can provide a revolution way for early detection of Aβ aggregation platform of Alzheimer disease in the early stage.

References

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