

Unmodified Gold Nanoparticles as Potential Diagnostic Agents for Colorimetric Detection of Pathogenic Infections

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Short Communication

Global outbreaks of infections have called for the development of rapid and sensitive in vitro diagnostic methods. Highly virulent and transmissible diseases are responsible for the increased rate of morbidities and fatalities worldwide. An infectious spread is best contained by early diagnosis, disease-load monitoring, and contact tracing. Ordinary diagnostic methods are expensive, laborious, time-consuming, and have slow data output. Simple, cost-effective, and rapid technologies for disease identification and monitoring have become significant for restraining disease spread. For high throughput sample analysis and shorter turnover time, several molecular diagnostic methods have been developed in the past few years. Rapid colorimetric diagnostic tools have proven their reliability to detect biomarkers present in the specimen through visual identification of color change of an indicator [1].

Attributed to their unique properties and ability to interact with biomolecules on a one-to-one basis, various nanoparticles show great promise to meet the rigorous demands of the clinical laboratory for diagnosing several pathogenic infections. Their high sensitivity and cost-effectiveness have enabled them to be used in the point-of-care diagnosis of diseases. Gold nanoparticles (GNPs, 2-50nm diameter) are popularly utilized for theranostic purposes. These metallic nanoparticles can emit intense absorption upon electromagnetic irradiation. They exhibit a unique phenomenon known as Surface Plasmon Resonance (SPR), which is responsible for their intense red color. GNPs possess a negative surface charge due to the absorption of citrate ions during their synthesis. Further addition of salt shields their surface charge leading to their aggregation. Aggregated GNPs show a red-to-blue color shift which forms the basis of a detection method. GNPs could be conjugated with different types of biomolecules such as antibodies, antigens, and enzymes, as probes, electrochemical labels, and optical signal transduction for disease diagnosis. This property has allowed the use of AuNPs in simple and rapid colorimetric assays for clinical diagnosis offering higher sensitivity and specificity than current detection techniques [2,3].

Several methods have been established which use genomic amplification followed by incubation with modified AuNPs for colorimetric observation. They mostly consist of the following steps: (i) extraction of nucleic acid from infected clinical sample, (ii) amplification using a nucleic acid amplification technique, (iii) preparation of modified AuNPs (hybridized with sequence-specific probes or ssDNA probes complementary to template) for attachment to the template, (iv) incubation of amplicons and AuNP-probe mixture in presence of salt and finally (v) observation of results [3-5]. Since, the main features of a rapid test are the simplicity and affordability, though, modifications and hybridizations of gold nanoparticles increase the time-consumption, complexity of fabrication, and hence, cost. Therefore, several approaches have been developed to employ unmodified gold nanoparticles for analyte identification. For instance, asymmetric PCR was used to generate long genomic ssDNA amplicons that wrapped around unmodified gold nanoparticles preventing their aggregation in high salt concentration, the red color of gold colloid remains unchanged [6]. In another study, a paper-based colorimetric test was developed for sensitive and specific diagnosis of tuberculosis using unmodified gold-nanoparticles and single-stranded detection oligos for smartphone-based data read-out [7].

In a recent study [8], a portable device was designed for point-of-care testing of SARS-CoV-2 by in-situ production of GNPs in the presence of amplicons during the loop-mediated isothermal amplification process. The presence of target DNA captures the GNPs which can be visually identified with a detection limit in femtograms. A method based on the use of protein-nanopore in conjunction with unmodified GNPs for sequence-specific detection was reported for biosensing with a label-free process and shorter turnover time [9].

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An amplification-free colorimetric strategy has also been investigated developed for rapid DNA detection based on manipulation of the plasmonic signal depending upon the capture of GNP clusters by the surface of magnetic microbeads [10]. This method showed increased sensitivity of as low as 15 attomoles of target DNA by simple visual detection. Several biosensing strategies using aptamers, antigens, enzymes, and other analyte-triggered aggregation methods utilizing unmodified GNPs have been explored by several researchers to detect the different biomolecules [11].

Conclusion

The future of molecular diagnostics relies on innovative techniques to make disease diagnosis rapid, robust, simple, affordable, and sensitive. GNPs play a significant role in fabricating user-friendly, easy-to-read colorimetric methods for the detection of several disease biomarkers with the naked eye. They could be coupled with several strategies such as lateral flow assays, immunochromatographic chips, and micro/nanofluidic detection methods to obtain rapid and sensitive detection using minimal reagent/sample volumes. Approaches have been made that use unmodified GNPs to reduce steps, duration, and complexity of the assay. This has proved that unsubstituted GNPs could be deployed for colorimetric solutions for theranostic purposes.

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