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ARTICLE TYPE

AuNPs based selective colorimetric sensor for cysteine at wide pH range: Investigation of capping molecule structure on the colorimetric sensing and catalytic properties

V. Vinod Kumar and Savarimuthu Philip Anthony*

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Gold nanoparticles (AuNPs) stabilized with different surfactants, SDS, PEG, PVA, PVP, PSS and T-80, were synthesized and explored for cysteine colorimetric sensing and catalytic properties. The sensing and catalysis studies revealed an interesting trend that AuNPs surface covered with linear molecules, SDS and PEG, did not show any colorimetric sensing and exhibited least catalytic effect. Whereas moderately improved sensing and catalysis was observed with AuNPs covered with smaller functional group substituted PVA and PVP. Interestingly, selective and robust colour change for cysteine (10^{-7} M) in aqueous solution as well as strongest catalysis was observed with AuNPs covered with bulky functional groups substituted PSS and highly branched T-80. These differences could be attributed to the surface accessibility effect of AuNPs for analytes. HR-TEM analysis of T-80-AuNPs with cysteine clearly showed the formation of smaller aggregates of AuNPs. Importantly, T-80-AuNPs showed selective sensing of cysteine across wide *pH* range (2.0 – 10.0). PSS-AuNPs showed selective colorimetric sensing only in the *pH* range of 6.0 to 10. These studies suggest that surface capping molecule structure plays a very significant role on both colorimetric sensing and catalysis of AuNPs.

Introduction

In recent years, there is a strong interest to exploit the AuNPs unique optical and catalytic properties for developing efficient colorimetric sensor and catalyst as well as gaining more insight on the mechanism.[1,2] Colorimetric sensors offered several advantages such as simple, cost effective and allow onsite monitoring of analytes.[3-5] AuNPs based colorimetric sensor received significant attention because of its strong surface plasmon resonance and distance dependent optical properties.[6,7] Further, AuNPs posses stronger extinction coefficients compared to the organic dyes that makes them very suitable for colorimetric sensing systems.[8,9] The interaction of NPs with analytes induce a rapid visible color change due to the coupling of interparticle surface plasmon,[10-14] that provides a practical platform for the colorimetric detections.

Cysteine is an essential amino acid to the human body and can be found as a component of many proteins. Cysteine plays a crucial role in a variety of main cellular functions including protein folding, detoxification, metabolism and redox process.[15,16] It also act as the physiological regulator in various diseases such as heart disease, rheumatoid arthritis, and AIDS.[17,18] Cysteine deficiency causes many syndromes, such as hair depigmentation, oedema, liver damage, skin lesions and lethargy loss of muscle and fat.[19,20] Thus, development of suitable approaches for selective detection of cysteine in various samples has attracted considerable interest in recent years. A variety of detection techniques including high performance liquid chromatography,[11] chemiluminescence,[22] electrochemistry,[23] optical spectroscopy,[24] and capillary zone electrophoresis[25] have been developed for the determination of cysteine. However, most of these techniques are complicated, require expensive instrumentation and not suitable for routine analysis. Noble metal nanoparticles such as Ag and Au are employed for sensing sulfur containing amino acids by utilizing their thiophilic nature.[26,27] For example, oligonucleotide-functionalized Au NPs assays were developed for highly sensitive and selective colorimetric detection for cysteine.[28] Water soluble quaternized cellulose based AuNPs was recently fabricated for selective sensing of cysteine.[29] Citrate stabilized AuNPs were recently demonstrated for the selective sensing of cysteine that self-assemble NPs by supramolecular interactions with aspartic acid.[30] In most cases, Au NPs are modified with oligonucleotide- or thiol-containing organic molecules to indicate color or light intensity change. These assays own some advantages, but they are still cost-consuming and require targeted structural modification. And also cysteine sensing at wide *pH* range has never been explored.

AuNPs application in catalysis is another exciting area of research.[2,31] AuNPs immobilized on the polymer and solid matrixes were synthesized and studied their catalytic activities.[32] Particularly, redox reactions like CO oxidation[33] and hydrogenation of various compounds[34] were used to test the AuNPs catalytic capability. AuNPs with well defined size and shape were synthesized and explored the catalytic properties to gain more insight on the catalytic performances. Smaller the

particles size showed increasing catalytic activities.[35] Fenger *et al.* reported highest activity for 13 nm sized AuNPs.[36] AuNPs with sphere morphology showed stronger catalytic activity compared with prism and nanorods.[37] Herein, we report the synthesize of AuNPs stabilized with six different capping ligands, SDS, PEG, PVA, PVP, T-80 and PSS and investigation of cysteine amino acid colorimetric sensing and catalytic properties. AuNPs stabilized with linear capping molecules such as SDS and PEG exhibited lowest catalytic effect and no colorimetric sensing. Capping ligands with small branched functionality such as PVA and PVP stabilized AuNPs showed slightly improved catalytic effects and colorimetric sensing. In contrast, T-80 and PSS which are having bulky side group functionality showed robust sensing of cysteine with fastest reduction rate of 4-nitrophenol. Importantly, T-80-AuNPs showed selective colorimetric sensing of cysteine across wide *pH* range (2.0 – 10) whereas PSS-AuNPs exhibited selective sensing in the *pH* range of 6.0 to 10.0.

Materials and methods

Sodium dodecyl sulfate (SDS), poly(ethylene glycol) (PEG), poly(vinyl alcohol) (PVA), poly(vinyl pyrrolidone) (PVP), sodium salt of poly(styrene sulfonate) (PSS), polysorbate-80 (T-80), $HAuCl_4$, ascorbic acid, 4-nitrophenol and amino acids were obtained from Sigma-Aldrich and used as-received. Mill-Q water was used for the preparation of AuNPs with all stabilizing agents. All the amino acid solutions used for the experiments were prepared by mixing the requisite amount of amino acid in Mill-Q water.

General preparation of SDS, PEG, PVA, PVP, PSS and T-80-AuNPs

10 ml aqueous solution containing 0.1 mM $HAuCl_4$ and 1.0 mM of SDS (0.5 wt % in the cases of other polymeric capping agents) was taken in a 25 ml beaker and stirred at 60-70 °C. The addition of 1 ml of 1.0 mM ascorbic acid turned immediately the yellow solution into wine-red colloid dispersion. The solution was allowed to stir at 60-70 °C for another 30 min. The reactions were repeated at least three times to confirm the reproducibility of AuNPs formation. The characterization of the synthesized AuNPs was carried out after allowing the solution to stand at room temperature for more than one week.

Characterization

The UV-visible measurement of the AuNPs stabilized with six different ligands was analyzed in a Perkin Elmer model UV–Vis double beam spectrophotometer from 250 to 800 nm, at the resolution of 1 nm. The purified powders of PSS-AuNPs and cysteine added AuNPs were subjected to FT-IR spectroscopy measurement. These measurements were carried out on a Perkin–Elmer Spectrum-One instrument in the diffuse reflectance mode at a resolution of 4 cm^{-1} in KBr pellets.

The size and morphology of AuNPs were investigated using high resolution transmission electron microscopy (HR-TEM). Samples for TEM measurements were prepared by placing a drop of NPs solution on the graphite grid and drying it in vacuum. Transmission electron micrographs were taken using JEOL JEM-2100F operated at an accelerated voltage of 200 kV and an ultra high-resolution pole piece.

Zeta potential measurements were carried out using a Zetasizer ver.6.20. The aqueous suspension of silver nanoparticles was taken in a cuvette. Zeta potential is measured by the principle of Electrophoretic mobility created by applying an electric field across the dispersion media.

Catalytic reaction

A standard catalytic test reaction was carried out in 2.0 mL quartz cuvette. 2 mL aqueous solution of 0.1 mM p-nitrophenol was mixed with 1 mL of 0.1M $NaBH_4$ solution. The reaction was started with the addition of 50 µL of the AuNPs prepared using above mentioned procedure. Only 10 µL of the PSS-AuNPs was added in the case of nitrobenzene reduction since 50 µL addition complete the reduction immediately. The reaction was magnetically stirred vigorously to avoid diffusion limitation. Immediately after catalyst addition, time dependent absorption spectra were collected at 3 min intervals for at least 30 min at room temperatures. The background subtraction was done with deionized water as the reference. All spectra were corrected with the average value around 800 nm due to interferences during the catalytic reaction caused by the evolving gas bubbles (hydrogen release).

Result and Discussion

Addition of ascorbic acid into Au^{3+} aqueous solution in presence of stabilizing agent resulted in the formation of stable AuNPs with wine red colour. The clear and transparent wine red colour, which is due to the strong surface plasmon resonance (SPR) vibration,[38] confirms good dispersion of AuNPs. The absorption studies of AuNPs capped with different ligands exhibited typical SPR absorption in the range of 520 to 530 nm (Fig. 1). The size, morphology and crystallinity of the samples were analyzed using HR-TEM that clearly showed the formation of spherical crystalline polydispersed AuNPs in the size range of 3 to 15 nm (Fig. 2). Various morphologies including spheres and triangular prisms were observed in SDS-AuNPs (Fig. 2a, S1). From the Zeta potential measurements, it can be confirmed that both SDS and PSS stabilize AuNPs better than other ligands (Table S1). All other capping molecules (PEG, PVA, PVP, T-80) exhibited similar stabilization for AuNPs.

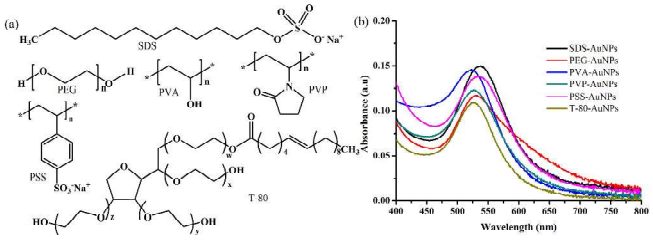


Fig.1. (a) Structure of capping ligands and (b) absorption spectra of AuNPs in different capping ligands.

AuNPs are known to form strong interaction with thiol groups due to its thiophilic nature.[26,27] The property has been utilized for selective colorimetric sensing of thiol functionalized amino acids which shows colour change from wine red to blue. The synthesized AuNPs were also investigated for colorimetric sensing of different amino acids, (glycine (Gly), alanine (Ala),

Serine (Ser), Valine (Val), Leucine (Leu), phenylalanine (Phe), tryptophan (Trp), histidine (His), cysteine (Cys), methionine (Met), tyrosine (Tyr) and glutathione (GSH)) in aqueous solution by monitoring the colour and absorption change. It is noted that Cys, Met and smallest tripeptide GSH are all having thiol functionality. SDS- and PEG-AuNPs did not show any significant change in absorption as well as colour with the addition of different amino acids even at higher concentration (10^{-2} M) except small decrease of absorption intensity without altering λ_{max} (Fig. S2). However, PVA-, PVP-, T-80 and PSS-AuNPs showed selective colorimetric changes from wine red to blue upon the addition of cysteine amino acid (Fig. 3, 4). Addition of other amino acids including methionine and glutathione did not show any colour change. The absorption studies of PVA- and PVP-AuNPs with cysteine has also confirmed the red shifting of λ_{max} (Fig. 3). The minimum detectable concentration of cysteine was determined by adding different volume of 10^{-6} M amino acid into PVA- and PVP-AuNPs (Fig. S3). The AuNPs absorption λ_{max} was completely red shifted by the addition of 280 µl (for PVA-AgNPs) and 340 µl (for PVP-AgNPs). It is noted that AuNPs absorption λ_{max} was red shifted by 6 and 18 nm with cysteine for PVA- and PVP-AuNPs, respectively.

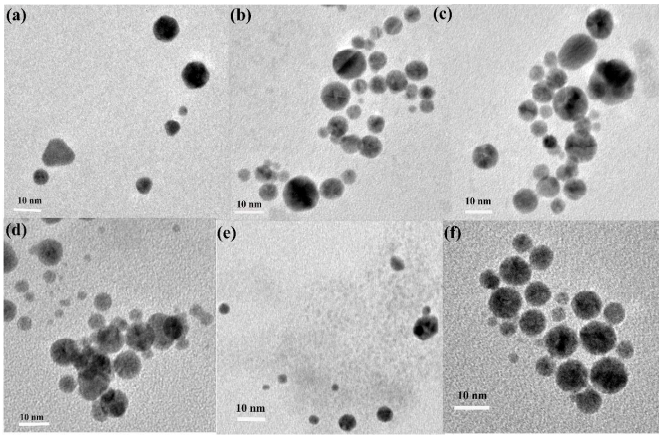


Fig. 2. HR-TEM images of (a) SDS-AuNPs, (b) PEG-AuNPs, (c) PVA-AuNPs, (d) PVP-AuNPs, (e) PSS-AuNPs and (f) T-80-AuNPs

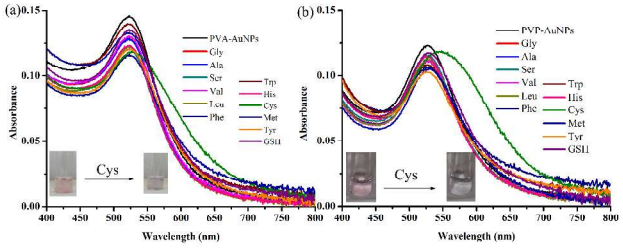


Fig. 3. Cysteine colorimetric sensing studies of (a) PVA-AuNPs and (b) PVP-AuNPs. Digital images of colour change are shown in the inset.

Interestingly, PSS- and T-80- AuNPs showed strong red shifting of absorption with robust sensing of cysteine compared to PVA- and PVP-AuNPs. Particularly, PSS-AuNPs exhibited strongest absorption red shift with cysteine (535 to 610 nm). T-80-AuNPs absorption red shifted from 525 to 560 nm with cysteine. Concentration dependent studies of T-80-AuNPs with cysteine showed a clear red shift of absorption even at 80 µl addition (10^{-7} M) which was completed by 120 µl addition (Fig. 5). Similarly PSS-AuNPs absorption has been red shifted from 535 nm to 610 nm at 60 µl addition itself. The red shifting was completed at 80 µl addition of cysteine. Further additions of cysteine did not show any significant shift in the λ_{max} rather it only reduced the absorption intensity. The reduction of absorption intensity was due to the formation and settling down of smaller AuNPs aggregates with cysteine. The effect of coexisting of other amino acids on the selective colorimetric sensing of cysteine by PSS- and T-80-AuNPs was also studied (Fig. S4). The absorbance change of AuNPs toward cysteine in presence of other amino acids including methionine and glutathione do not interfere the cysteine binding with AuNPs probes as well as subsequent change of absorption, indicating that other amino acids presence had negligible interfering effect on cysteine sensing.

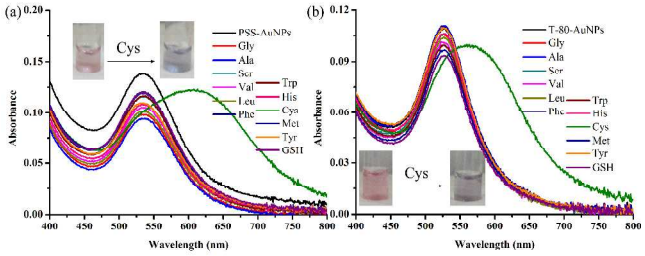


Fig. 4. Cysteine colorimetric sensing studies of (a) PSS-AuNPs and (b) T-80-AuNPs. Digital images of colour change are shown in the inset.

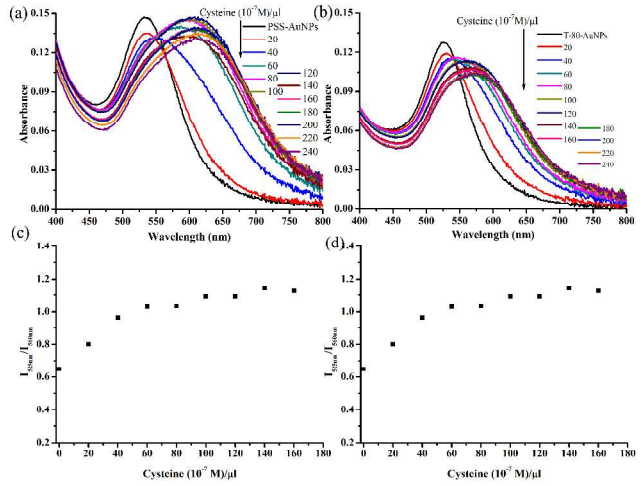


Fig. 5. Cysteine concentration dependent studies of (a, c) PSS-AuNPs and (b, d) T-80-AuNPs.

The selective sensing of cysteine by T-80- and PSS-AuNPs was also explored at different *pH* (Fig. 6). The *pH* of T-80- and PSS-AuNPs was tuned by adding dilute HNO_3/NaOH solution. Absorption studies of both T-80-and PSS-AuNPs at different *pH* did not show any significant variation and confirms the good stability of AuNPs (Fig. S5). Interestingly, AuNPs stabilized with nonionic ligand, T-80, exhibited selective colorimetric sensing of cysteine across wide *pH* range from 2.0 to 10.0. But PSS-AuNPs showed cysteine sensing only in the pH range of 6.0 to 10.0. It is noted that T-80-AuNPs exhibited strongest red shifting of absorption with cysteine at acidic condition whereas PSS-AuNPs

showed at basic condition.

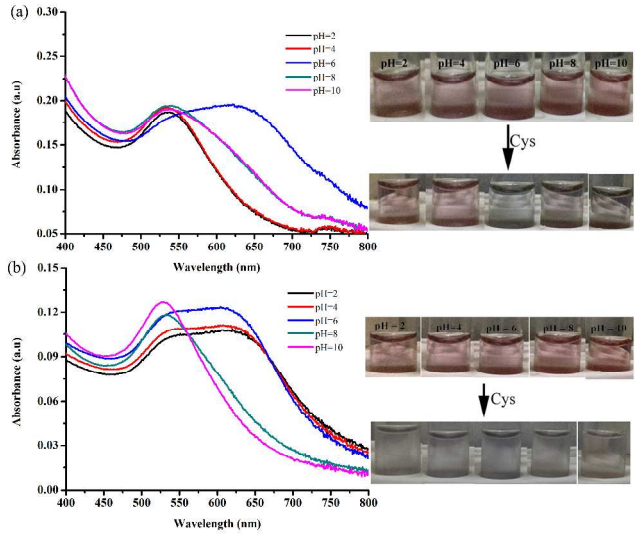
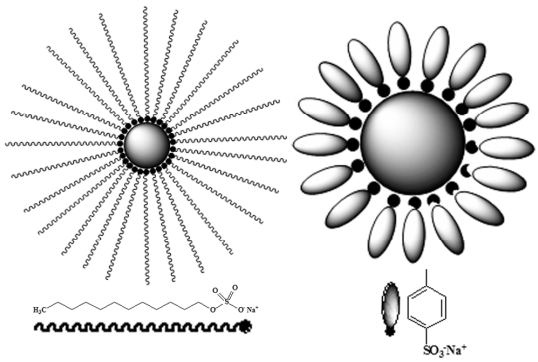


Fig. 6. *pH* dependent cysteine colorimetric sensing of (a) PSS-AuNPs and (b) T-80-AuNPs. The insets show the digital images of cysteine sensing.

The mechanism of selective sensing of cysteine by AuNPs is believed due to the thiophilic interaction of sulfur that leads to the AuNPs aggregates formation. The formation of aggregates changes the AuNPs colour from wine red to blue. HR-TEM studies of T-80-AuNPs with cysteine clearly demonstrate the formation of AuNPs aggregates (Fig. S6a). PVP-AuNPs with cysteine also exhibited the formation of AuNPs aggregation but lesser extent compared to T-80-AuNPs (Fig. S6b). But SDS-AuNPs with cysteine did not show any significant aggregation and support the observation of no colour and spectral changes (Fig. S6c). Theoretical and experimental studies has shown that the plasmon oscillations of metal nanoparticles couple to each other when they are brought in proximity and exhibited different colour.[39,40] The comparison of selective cysteine colorimetric sensing of AuNPs with six different capping ligands, SDS, PEG, PVA, PVP, T-80 and PSS revealed a very interesting trend. The linearly structured SDS and PEG capped AuNPs did not show any colorimetric sensing. However, substitution of bulky functional groups in the capping ligands, AuNPs with T-80 and PSS showed robust colorimetric sensing of cysteine. AuNPs with PVA and PVP in which smaller functional groups are attached showed moderate colorimetric sensing and catalytic properties. Thus, the difference in the colorimetric sensing of AuNPs with SDS, PEG, PVA, PVP, PSS and T-80 might be attributed to the structural and shape differences of capping molecules. The diffusion of cysteine molecules to the NPs surface could be critically important step for colorimetric sensing. It is noted that except SDS, all samples showed polydispersed spherical sized AuNPs. Hence the role of size or shape on the colorimetric sensing differences can be excluded. Zeta potential measurements showed that PSS stabilizes AuNPs better than PEG yet exhibited robust sensing of cysteine and exclude the effect of stabilization from different capping molecules (Table S1). The above results indicate that linear capping molecules (SDS and PEG) provided better packing around AuNPs and hence cysteine molecules might not be able reach the AuNPs surface. Whereas, substitution of bulky functionality (PSS, T-80) provided easy access for cysteine to the AuNPs surface and exhibited robust sensing (Scheme-1). Further to confirm the surface accessibility differences, catalysis of AuNPs stabilized with six different capping ligands were also studied.

Nitro group reduction by $NaBH_4$ in presence of AuNPs that also has industrial relevance in the preparation of aniline and paracetamol is a standard reaction to test the catalytic capability of nanoparticles.[41] The conversion of 4-nitrophenol to 4-aminophenol and nitrobenzene to aniline by AuNPs were explored using a standard UV-Vis setup. A strong yellow coloured 4-nitrophenolate has formed by the addition $NaBH_4$ into 4-nitrophenol. Absorption spectrum showed strong band (λ_{max}) at 400 nm. Time dependent absorption spectra were recorded to monitor the reaction progress after adding AuNPs to the reaction solution. The solution was stirred after the addition of AuNPs to make uniform distribution immediately. The intensity of absorption correlates the concentration of the 4-nitrophenolate. Fig. 7 shows the time-dependent evolution of absorption spectra of the reaction catalysed by PSS-AuNPs. The intensity of 4-nitrophenolate absorption band at 400 nm disappeared completely within 30 min and indicates the successful reduction of 4-nitrophenol to 4-aminophenol. Similarly nitrobenzene was reduced to aniline within 30 min by PSS-AuNPs. The appearance of new peak at 230 nm was taken as the indication of aniline formation. Further to confirm the catalytic activity of AuNPs, the same reaction was performed in the absence of PSS-AuNPs catalysis. This solution remains unchanged even for a week, thus indicating that 4-nitrophenol was not reduced without the catalyst. Since $NaBH_4$ was taken excess (1000:1) with respect to 4-nitrophenol, this reaction can be handled under pseudo-first order condition.



Scheme-1. Schematic representation of SDS and PSS packing around AuNPs.

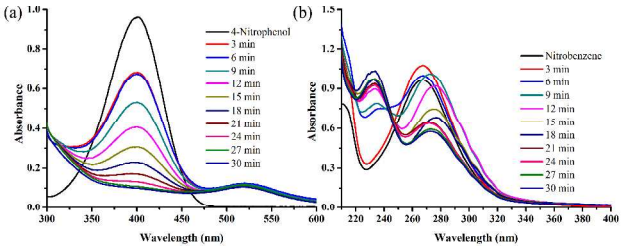


Fig. 7. Catalytic reduction studies PSS-AuNPs (a) 4-nitrophenol and (b) nitrobenzene.

The structural difference of AuNPs capping ligands provided the opportunity to study the structure dependent catalytic activity of AuNPs. It is noted that AuNPs with six different capping ligands exhibited different cysteine colorimetric sensing. The comparison of catalysis of 4-nitrophenol to 4-aminophenol and nitrobenzene to aniline by AuNPs stabilized with six different ligands are shown in Fig. 8. AuNPs stabilized with SDS and PEG capping ligands exhibited least or almost negligible catalytic activity on the reduction of 4-nitrophenol and nitrobenzene. PVA and PVP stabilized AuNPs exhibited higher activity than SDS and PEG-AuNPs. However, T-80 and PSS stabilized AuNPs showed strongest catalytic activity in both reactions. Nitrobenzene was reduced into aniline within 15 min and further reactions did not show any absorption change at 230 nm. Whereas increasing absorption at 230 nm with time for PVA- and PVP-AuNPs suggest the incomplete reduction even after 30 min. Similarly, T-80- and PSS-AuNPs almost completely reduced 4-nitrophenol to 4-aminophenol within 30 min. PVA-AuNPs showed better activity than PVP-AuNPs and closer T-80 and PSS-AuNPs activity in 4-nitrohphenol reduction. Based on the catalytic activities, AuNPs capped with six different ligands were grouped into three categories. The least active SDS- and PEG-Au, moderate active PVA- and PVP-AuNPs and strongest active T-80- and PSS-AuNPs. The selective cysteine colorimetric sensing also showed similar trend; no sensing by SDS- and PEG-AuNPs, moderate sensing by PVA- and PVP-AuNPs and robust sensing by T-80- and PSS-AuNPs.

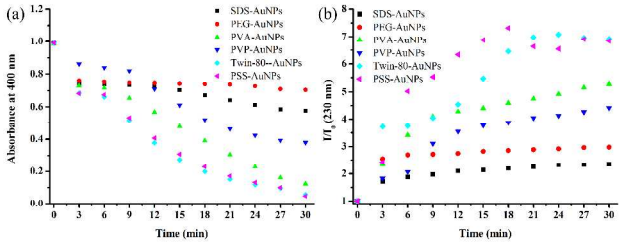


Fig. 8. Comparison of catalytic reduction of (a) 4-nitrophenol and (b) nitrobenzene with AuNPs capped with different ligands.

The structural comparison of six different capping ligands showed an interesting trend, from linear to bulky functional group substitution in the side chain. For colorimetric sensing as well as catalysis, the efficient interaction of analytes/reactant with AuNPs surface is very important and hence any hindrance is expected to reduce both sensing as well as catalytic activities. We assume that both colorimetric and catalytic differences of AuNPs might be due to the surface packing differences by capping ligands (Scheme-1). It appears that linearly structured SDS and PEG have formed denser packing, thus completely block the access of analyte/reactant to the AuNPs surface. The dense coverage of AuNPs surface by Lyzome protein showed lowest catalytic activity.[42] The smaller functional group substitution in PVA and PVP might be providing restricted access for analytes/reactants to the AuNPs surface in PVA and PVP capped AuNPs. However, T-80 and PSS with bulky functional group substitution might cover the AuNPs surface with more porous, thus provides easy access for analyte/reactant to the NPs surface and hence strongest activity in both sensing and catalysis. These results clearly indicate that capping ligands packing on the surface of AuNPs and structural shape could control both colorimetric and catalytic properties.

Conclusion

In summary, capping ligands that are known to have strong influence on the optical properties of noble metal NPs, were also played an important role in the colorimetric sensing and catalysis. AuNPs stabilized with linear molecular structures (SDS and PEG) displayed least catalytic and no cysteine colorimetric sensing. AuNPs stabilized with small functional group substituted ligands (PVA and PVP) exhibited moderate catalytic and sensing properties. Interestingly, selective and robust colour change for cysteine in aqueous solution and strongest catalysis were observed with AuNPs stabilized with bulky functional groups substituted PSS and highly branched T-80. The formation of polydispersed spherical AuNPs with all samples except SDS rule out the role of size and shape on the colorimetric and catalysis differences. Similarly Zeta potential measurement exclude the stabilization effect since better stabilized PSS-AuNPs showed stronger colorimetric and catalysis compared to PEG-AuNPs. HR-TEM analysis of T-80-AuNPs with cysteine clearly showed the formation of smaller aggregates of AuNPs. Further, pH dependent colorimetric sensor studies of T-80-AuNPs showed selective sensing of cysteine across wide pH range (2.0 – 10.0). PSS-AuNPs showed selective colorimetric sensing only in the pH range of 6.0 to 10. We believe that the present studies could be useful in choosing noble metals NPs surface capping ligands for developing efficient colorimetric sensor and catalysis.

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Notes and references

School of Chemical & Biotechnology, SASTRA University, Thanjavur-613401, Tamil Nadu, India. Fax: +914362264120; Tel: +914362264101; E-mail: philip@biotech.sastra.edu

† Electronic Supplementary Information (ESI) available: Cysteine colorimetric studies of SDS- and PEG-AuNPs, cysteine concentration dependent studies of PVA- and PVP-AuNPs, PSS-, T-80-AuNPs absorption at different pH and formation of smaller AuNPs aggregation due to selective cysteine interaction with PSS-AuNPs. See DOI: 10.1039/b000000x/

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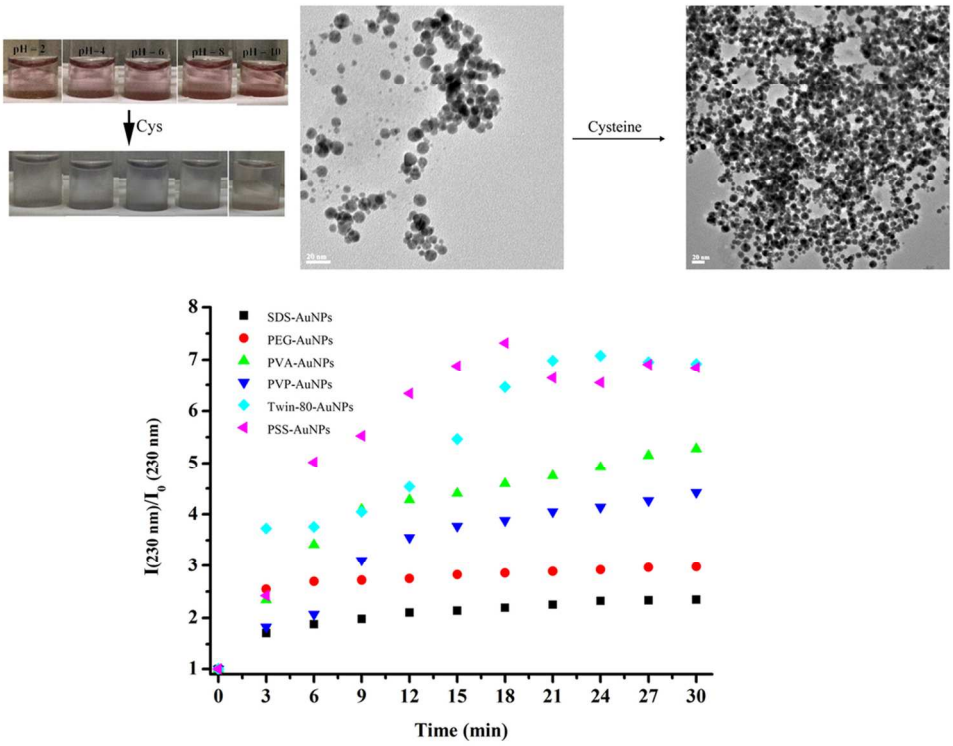

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