Journal Name

ARTICLE

Supporting Information

Adsorption/Desorption of Doxorubicin on Citrate-Capped Gold Nanoparticles: Insights into Engineering Potent Chemotherapeutic Delivery Systems

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Supporting Data:

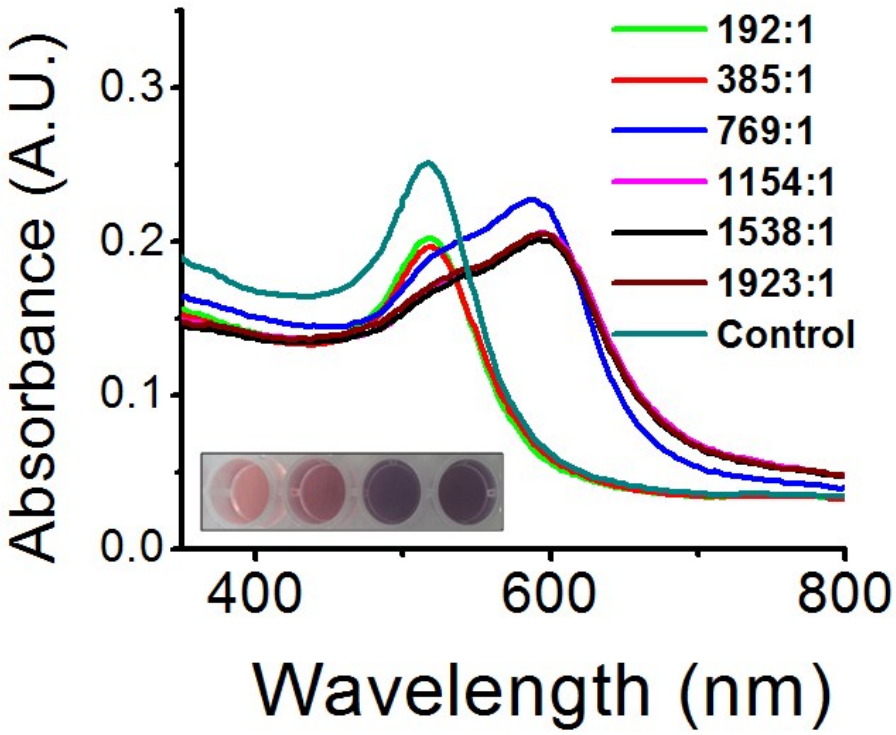


Figure S1. AuNP absorbance spectra upon addition of increasing [DOX] (Inset: AuNP color change upon addition of DOX, DOX:AuNP molar concentration ratio from right to left: 0, 385, 769, 1538)

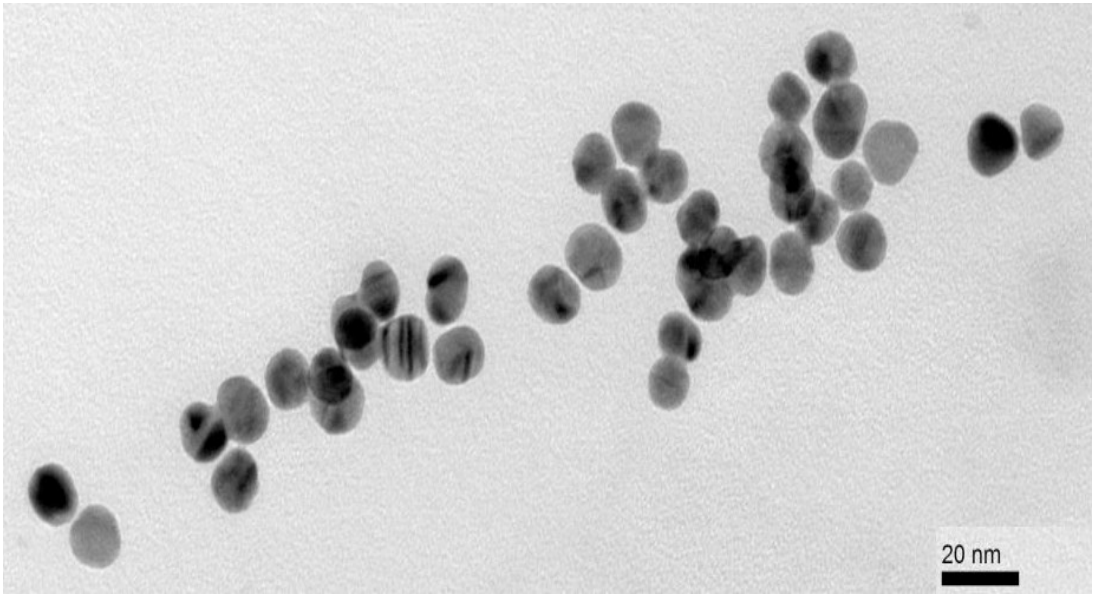


Figure S2. TEM micrograph of ~13 nm citrate-capped AuNP used in this work (Scale bar: 20 nm).

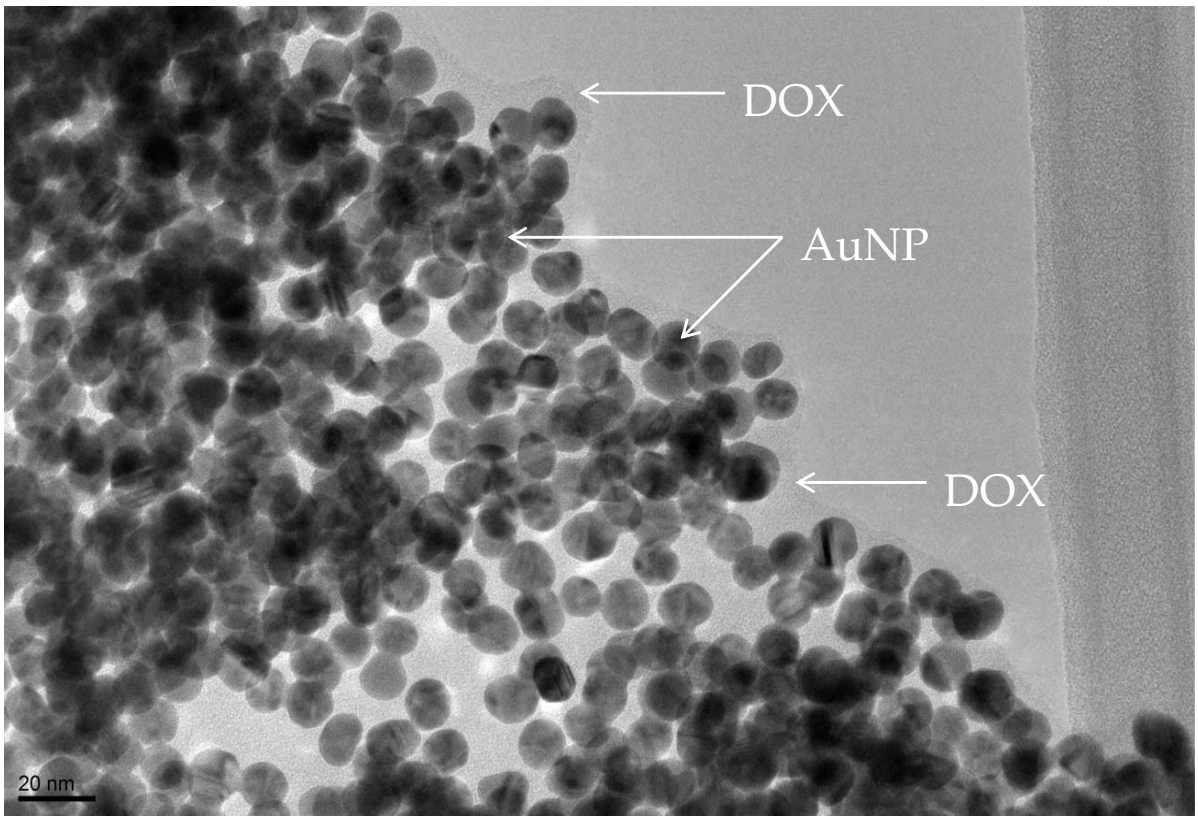


Figure S3. TEM micrograph of DOX-AuNP conjugates. DOX:AuNP molar concentration ratio = 307:1 (Scale bar: 20 nm).

Figure S4. Figure S4.TEM micrograph of DOX-AuNP conjugates. DOX:AuNP molar concentration ratio = 307:1 (Scale bar: 200 nm).

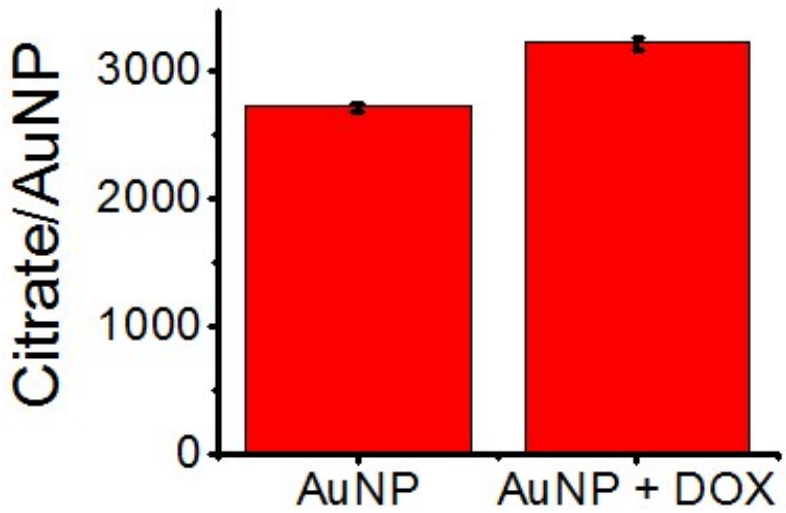


Figure S5. Citrate displaced per AuNP quantified via DOX fluorescence signal measured in supernatant solution (p<0.5).

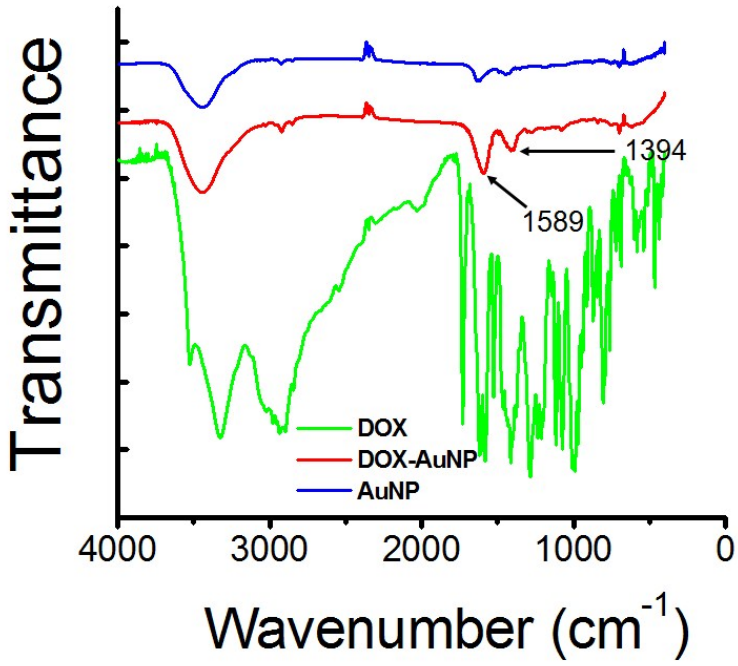


Figure S6. FTIR spectra of DOX-AuNP conjugate and AuNP.

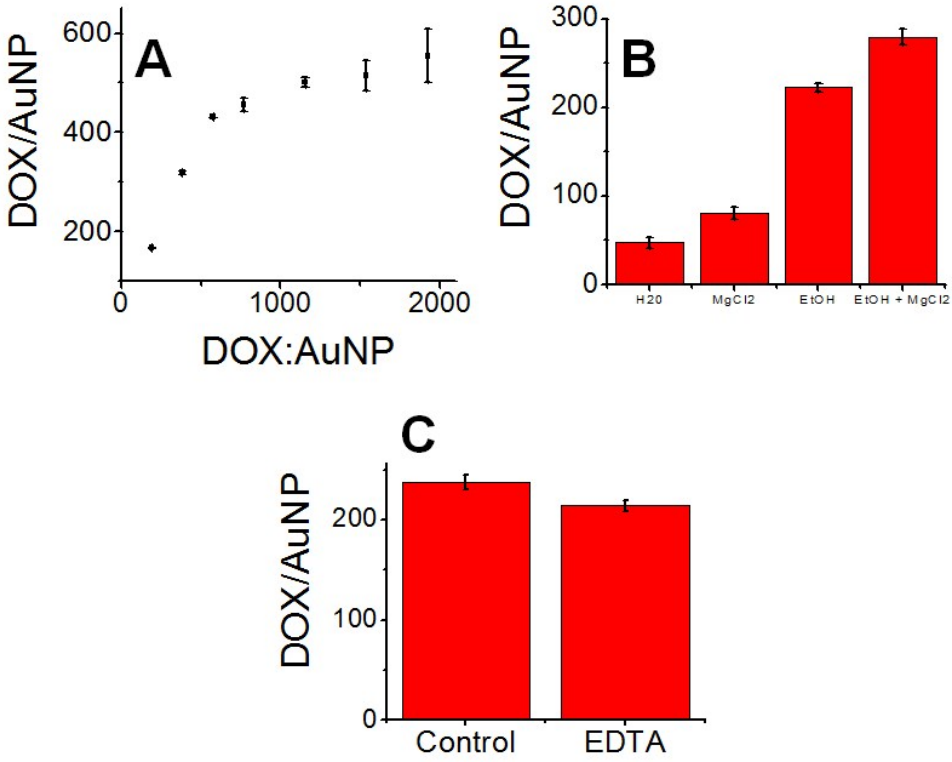


Figure S7. (A)Original DOX-AuNP loading isotherm including standard error bars. (B) Desorption of DOX from AuNP surface after treatment with $MgCl_2$ ([62.5 mM]), EtOH (31.25% v/v) and EtOH-$MgCl_2$. DOX:AuNP ratio = 317:1. (C) Adsorption of DOX to AuNP surface after EDTA ([3.84 μM]) treatment of AuNP. DOX:AuNP ratio = 308:1.

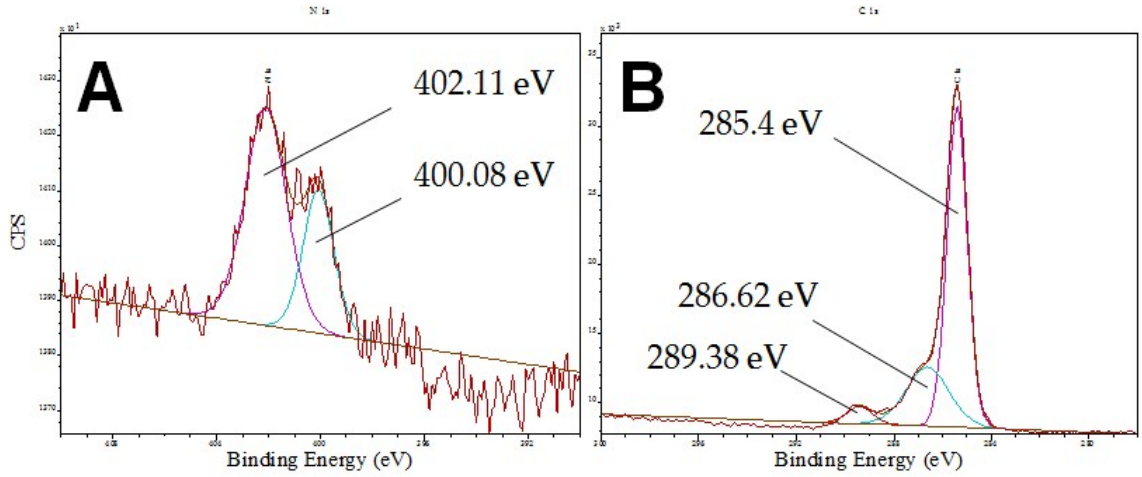


Figure S8. XPS N 1s (A) and C 1s (B) deconvoluted spectra for DOX-AuNP conjugate solutions.

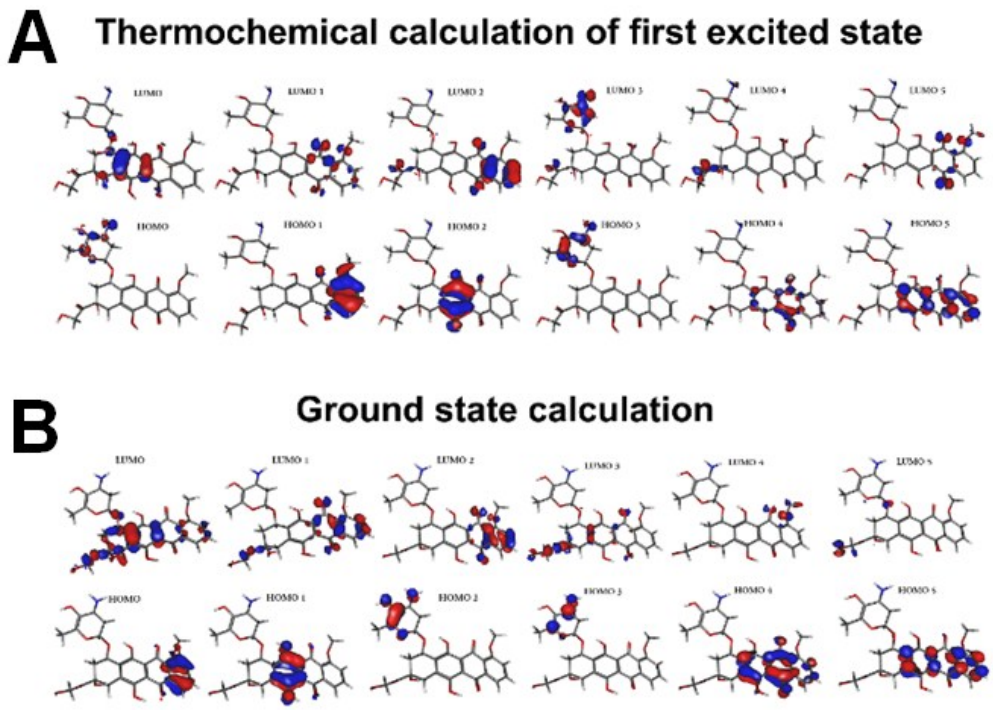


Figure S9. Molecular orbital (MO) of DOX showing localised electron sites in (A) first excited and (B) ground states. The first excited state is sampled between 200 - 400 °K at the PM7 level of theory in MOPAC2012 with PCM water. The first 6 energy level state of the alpha orbital are displayed. The ground state MO of the HOMO is located at the first benzene ring, which is the highly hydrophobic region of DOX. In contrast, the MO of LUMO is delocalised around the hydrophobic site of DOX. At HUMO 1, the -OH group is involved in MO while in HUMO 4 the carbonyl contributed to the delocalisation of the MO. In LUMO 1, the MO was delocalized from the ring 4 containing -OH to the ring 1. However, LUMO 4 MO does not involve a hydrophobic electronic site. This suggests a possible transition that involves either the carbonyl or the hydroxyl functional group. Regarding the particular transition of HOMO 1 to LUMO 1, the MO migrated from -OH site to C=O site. Moreover, the delocalisation of the MO of the hydrophobic site (ring 30) to the acceptor hydrophobic site at the rings 1 and 2. However, HOMO 4 showed a migration of MO from hydrophobic electronic transition to a localised highly electrophilic site. The HOMO 5 displayed the MO delocalised around the hydrophobic electronic sites in ring 1, 2 and 3 towards HOMO 5 localised electrophilic site. The main observation was the absence of MO in ring 5 ground state HOMO to LUMO 5. The thermochemistry calculation demonstrated the contribution of the ring 5 (ether) in the

electronic transition is an intra-thermochemistry reaction that involved the amine functional group. As for the ground state, the hydrophobic electronic transitions are partially delocalized.

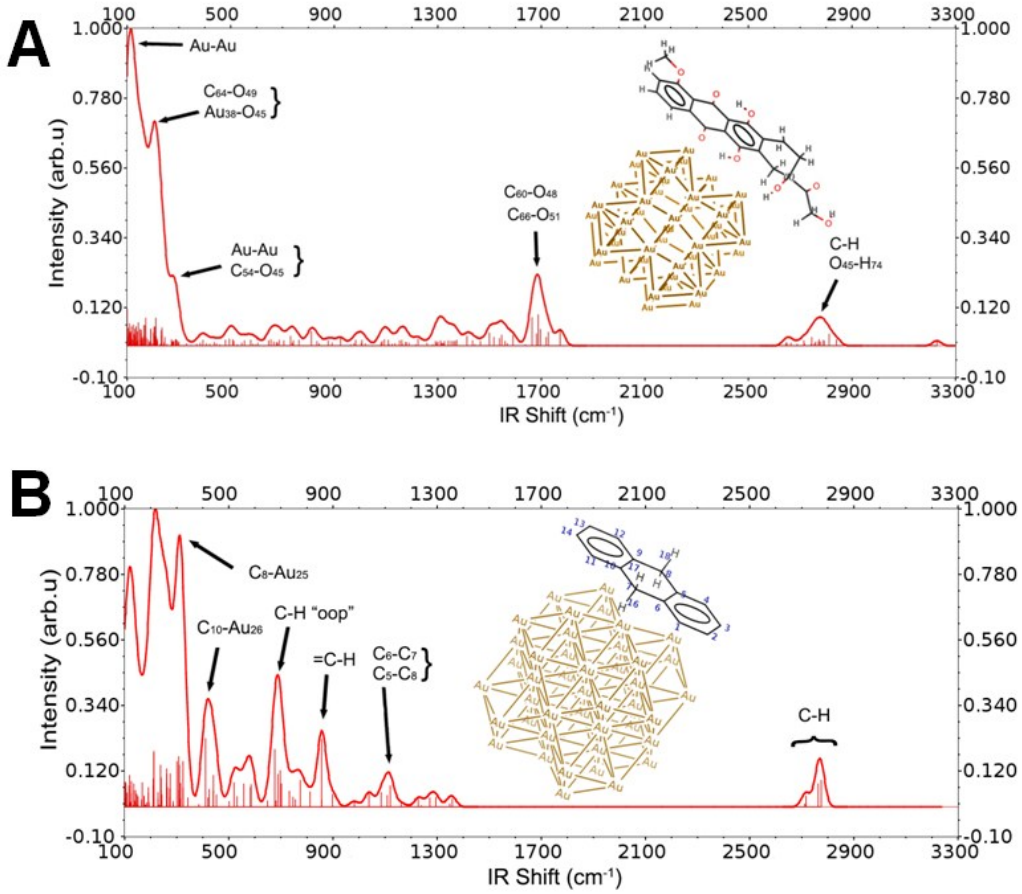


Figure S10. (A) Modelling of IR spectrum of DOX without ring 1 connected to amine moiety with a 0.5 nm AuNP. (B) Modelling of IR spectrum of the DOX-like anthracene with 0.5 nm AuNP.

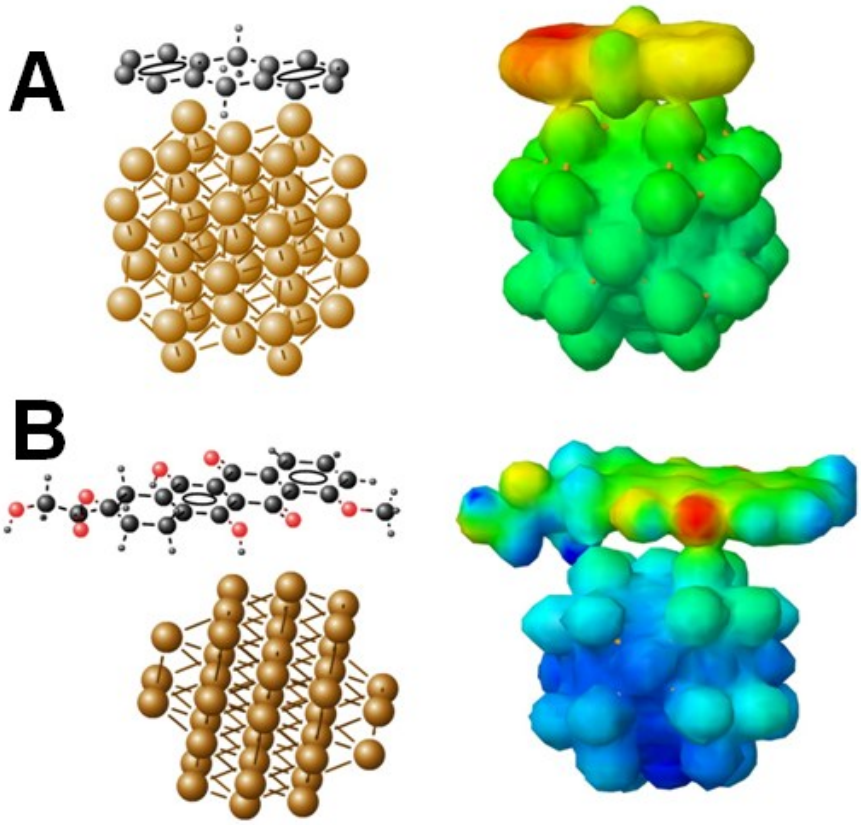
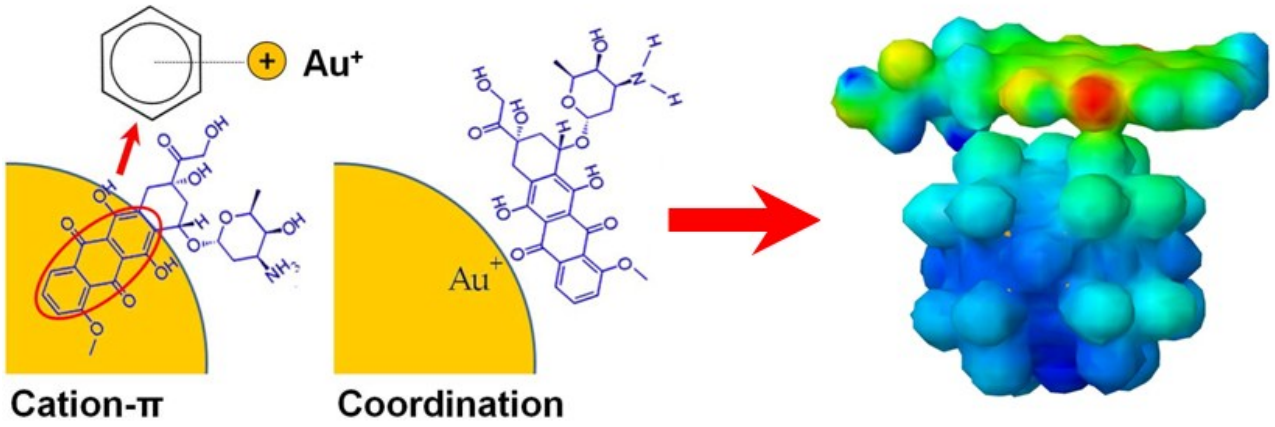


Figure S11. Calculation of electrostatic potential of the surface at PM7 level of theory: (A) DOX-like anthracene-AuNP, and (B) DOX without ring 1 AuNP. The potential energy surface of the last 1ns of 12 ns MD demonstrated DOX bent and formed an Au-N bond (Model 1). Further QM calculation of DOX alone with high level of theory in gas phase as well as with continuum water (B3LYP/6-31G(d)) had depicted a bent formation. Increasing the theory level did not change the bend. This highlights the hypothesis that the bent formation between ring 5 containing N and the ring 1 to 4 may be due to the π - σ attraction that dominated the edge to face interaction.[47] Therefore, the bending of ring 5 is likely to be independent of the presence of AuNP. To refine the interaction mechanism between DOX – AuNP, we further analysed two models, model 2 was DOX lacking ring 5, which provided insight of the carbonyl interaction with theAuNP surface.

Graphical Abstract Only



Experimental and theoretical studies substantiate Doxorubicin adsorption onto citrate-capped gold nanoparticles is mainly governed by cationic-π and carbonyl coordination chemistry.