# Effect of trisodium citrate as an intermediate at metal nanoparticle/aminoglycoside antibiotic interface

Amritpal Kaur and Rajesh Kumar

Email ID: kamritpal59@gmail.com

## Abstract

For the efficient drug delivery/carrier system, silver and gold nanoparticles have been considered to be highly useful platform due to their well-studied synthesis, easy surface modification and biocompatibility and low toxicity [1]. These metal-antibiotic conjugates were reported to have encouraging applications against both Gram-positive and Gram-negative class of bacteria [2]. The spherical silver and gold nanoparticles (AgNPs/AuNPs) have been synthesized by chemical reduction method in the presence of trisodium citrate. The citrate anions stabilize metal nanoparticles through electrostatic mechanism [3, 4]. For the synthesis of AgNPs and AuNPs, trisodium citrate in the presence of reducing agent ($NaBH_4$), were mixed with silver nitrate ($AgNO_3$) and gold chloride ($AuCl_3$), respectively. 10 mM (2 mL) of trisodium citrate was added to 1 mM of $AgNO_3$ and $AuCl_3$. The solutions were left for 2 hours at room temperature under vigorous stirring for complete synthesis of citrate-AgNPs and citrate-AuNPs. Further, surfactant coated AgNPs and AuNPs have been functionalized with amikacin. antibiotic bound nanoparticles were prepared by stirring different concentrations (0.2 mM and 0.4 mM) of amikacin solution to constant volume of synthesized AgNPs/AuNPs (5 mL)) for 30 min followed by incubation for overnight at room temperature. Then, the resulting amikacin functionalized silver and gold nanoparticles (Amk@citrate-AgNPs/Amk@citrate-AuNPs) stored at low temperature in the dark. The role of trisodium citrate as a binder between drug and nanoparticle has been analyzed by using different analytical techniques such as UV-Visible absorption spectroscopy, and X-ray diffraction, DLS and FTIR. It has been observed that in case of AgNPs, citrate is not a good linker for amikacin to bind with nanoparticle surface as silver lost its SPR after the addition of amikacin. The reason is the formation of unstable compounds with AgNPs as citrate could not able to stabilize AgNPs completely (Fig.1(a)). However, Tween 20-AgNPs and PVP-AgNPs could be used as linker for amikacin due to their better stabilizing property than citrate. In case of AuNPs, citrate could be used as a linker between drug and nanoparticle surface. The XRD pattern has been recorded for bare and drug coated nanoparticles which also depicts the loading of amikacin on AuNPs with slight change in reflection lines (Fig. 1(b)). The measured Z-average size from dynamic light scattering before and after drug conjugation is another parameter that hints the binding of drug to gold nanoparticles surface. Fourier infrared transform spectroscopy results also infer the presence of hydrogen bond through secondary amide or amine group of amikacin and gold nanoparticles.

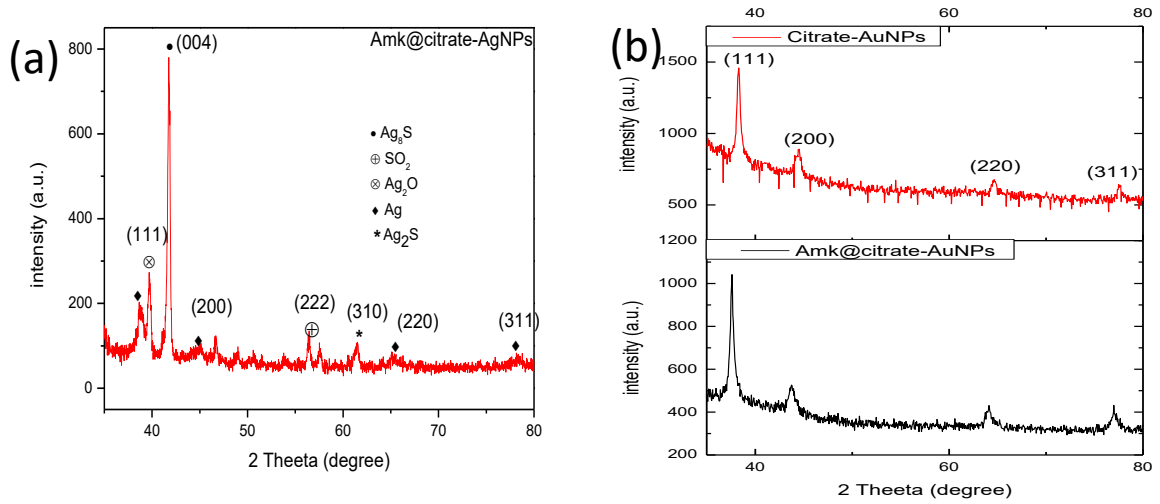


**Fig.1.** XRD pattern for (a) Amk@citrate-AgNPs and (b) citrate-AuNPs and Amk@citrate-AuNPs,

## References

[1] A. J. Huh, Y. J. Kwon, "Nanoantibiotics": a new paradigm for treating infectious diseases using nanomaterials in the antibiotics resistant era, *Journal of Controlled Release*, 156 (2011), 128-14.

[2] E. Ebrahimi, A. Jarrahpour, N. Heidari, V. Sinou, C. Latour, J. M. B, A. R. Zolghadr, E. Turos, Synthesis and antimalarial activity of new nanocopolymer β-lactams and molecular docking study of their monomers, *Med Chem Res*, 25 (2016), 247–262.

[3] F. Vetrone, F. Variola, P. Tambasco de Oliveira, S. F. Zalzal, J. H. Yi, J. Sam, K. F. Bombonato-Prado, A. Sarkissian, D. F. Perepichka, J. D. Wuest, F. Rosei, A. Nanci, Nanoscale Oxidative Patterning of Metallic Surfaces to Modulate Cell Activity and Fate, *Nano Lett.*, 9 (2009), 659-665.

[4] N. Doshi, S. Mitragotri, Designer Biomaterials for Nanomedicine, *Advanced functional materials*, 19 (2009), 3843-3854.