## Surpassing Antibiotic Resistance through Synergistic Effects of Polyethyleneimine-Silver Nanoparticle Complex Coated Mesoporous Silica Trio-Nanoconstructs

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**Abstract :** Antibiotic resistance in bacteria has become an emergency situation clinically. To improve the efficacy of antibiotics in resistant strains, advancement of nanoparticles is inevitable than ever. Herewith, we demonstrate a design by immobilizing tetracycline (TET) in copper substituted mesoporous silica nanoparticles (Cu-MSNs) through a pH-sensitive coordination link, enabling its release in the acidic environment. Subsequently, MSNs are coated with silver nanoparticles stabilized polyethyleneimine (PEI-SNP) to act against drug-resistant (MDR) bacterial strains. Silver ions released from SNP are capable of sensitizing the resistant strains and facilitate the generation of free radicals capable of damaging the cell components. In addition, copper ions in the framework are also capable of generating free radicals through Fenton-like reaction. Furthermore, the nanoparticles are well-characterized physically, and various antibacterial efficacious tests against isolated multidrug resistant bacterial strain were highly commendable. However, this formulation has no significant toxic effect on normal mammalian fibroblast cells accounting its high biocompatibility. These MSN trio-hybrids, i.e., SNP, tetracycline, and copper ions result in synergistic effects, and their advancement could bypass resistance and allow synergism for effective treatment of antibiotic clinically.

**Keywords :** antibiotic resistance, copper, mesoporous silica nanoparticles, Ph-sensitive release, polyethyleneimine, silver, tetracycline

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**Conference Title :** ICN 2017 : International Conference on Nanotechnology **Conference Location :** Singapore, Singapore **Conference Dates :** July 04-05, 2017