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Editorial

Use of biofabricated silver nanoparticles-conjugated with antibiotic against multidrug resistant pathogenic bacteria

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The discovery of penicillin at a time when there was no effective treatment for infections such as pneumonia, gonorrhea or rheumatic fever opened new avenues for treatment of life threatening infectious diseases. Penicillin heralded the dawn of the antibiotic age. The progress in antibiotics research has led to the commercial production of a wide array of antibiotics capable of treating most of the life threatening infectious diseases. Contrary to earlier scientific notions that these antibiotics will always be effective against the specific pathogens we are now observing a new phenomenon called multidrug resistance. Multidrug resistance (MDR) is defined as insensitivity or resistance of a microorganism to the administered antimicrobial medicines (which are structurally unrelated and have different molecular targets) despite earlier sensitivity to it (Tanwar et al. 2014). Nowadays, the huge amounts of antibiotics are used worldwide for human therapy, farm animals and even for fish in aquaculture resulting in the development of pathogenic bacteria resistant to multiple drugs. Antibiotic resistance amongst bacterial pathogens is a crisis that has been worsening over recent decades, resulting in serious and often fatal infections that cannot be treated by conventional means. Diseases caused by these drug resistant agents results in protracted illnesses, greater mortality rates and increased treatment costs. Improvements in existing drugs/ therapies and the development of novel treatments is need of the hour to deal with this escalating threat to human health. Microorganisms evolve and develop multidrug resistance by several mechanism for example in bacteria it occurs by the accumulation, on resistance (R) plasmids or transposons, of genes, with each coding for resistance to a specific agent, and/or by the action of multidrug efflux pumps, each of which can pump out more than one drug type. The phenomenon of multidrug resistance can be best studied in the case of drug vancomycin, a fermentation product from streptomycetes that has an unusual mode of action which instead of inhibiting an enzyme binds to a substrate, the lipid-linked disaccharidepentapeptide, a precursor of cell wall peptidoglycan and due to this mechanism it was assumed that it would be impossible for microorganisms to generate resistance against vancomycin. However, vancomycin resistance is now prevalent among enterococci, normal inhabitants of the human intestinal tract (Nikaido 2009). Enterococci are naturally resistant to β-lactams, aminoglycosides, macrolides and tetracycline these vancomycin-resistant strains of enterococci become prevalent in a hospital environment, colonize the patients, and cause infections that are difficult to treat.Different approaches are being considered by researchers worldwide to resolve the issue of multidrug resistance and to increase the efficiency of currently available antibiotics. Recent advances in nanobiotechnology have led to the exploration of the possibility of conjugating lipophilic and water-soluble antibiotics inside or on the surface of nanoparticles or carried via encapsulation (Abeylath & Turos 2008).Among all metal nanoparticles, gold nanoparticles (AuNPs) have been considered to be a highly useful platform for the efficient drug delivery/carrier system due to their facile and well-studied synthesis, easy surface functionalization and biocompatibility and less toxicity (Demurtas & Perry 2013). AuNPs have been reported to increase drug concentration at the infected site with the reduced toxicity of the drug (Pinto-Alphandary et al. 2000).Guzman (Guzman et al. 2012) had synthesized Ag nanoparticles via chemical route and studied their antimicrobial activities against E.coli, P. aeruginosa, and S. aureus bacteria as function of nanoparticle concentration and size. They observed a strong antimicrobial activity for a concentration of silver nanoparticles less than 7 ppm. In a recent work, the mechanism of antimicrobial activities of silver nanoparticles coated with

glutathione (GSH) was investigated on gram positive and gram negative bacterial strain in two ways firstly by dispersing the silver nanoparticles in solution and secondly by grafting on thiol functionalized glass surfaces. The antimicrobial activities of GSH coated nanoparticles dispersed in solution was found to be more intense as compared to the nanoparticle grafted on thiol functionalized glass surfaces due the penetration of Ag^{+} of the colloid into the cytoplasm of E-coli bacteria (Taglietti et al. 2012). The toxicological studies indicate that toxicity percentage inhabitation of chemically fabricated was much greater than the biofabricated nanoparticles synthesized from apple onion, garlic and followed by papaya and observed PI value indicated that the gut microbial community probiotic B. subtilis and E. coli was killed in higher percentage of CH-AgNPs as compared to Bio-AgNPs synthesized from apple, onion garlic and papaya (Tyagi et al. 2016).

To study whether multidrug resistant pathogenic bacteria can be effectively targeted with a novel nanoparticles antibiotics conjugated system we performed several sets of experiments.In the first set of experiments, antimicrobial activities of biofabricated silver nanoparticles against three pathogenic bacteria (Micrococcus luteus, Staphylococcus epidermidis and Aeromonas pneumonia) were analyzed.Our results indicated that biofabricated silver nanoparticles were less effective in killing these bacteria with a zone of inhibition 0.1 to 0.2 cm only. In the second set of experiments antimicrobial activity four different drugs ciprofloxacin, gentamycin, tetracycline and cholramphenicol were analyzed against all three pathogenic bacteria involved in our study. We observed that out of 4 drugs only ciprofloxacin showed 0.3 mm zone of inhibition against A. pneumonia and there was no zone of inhibition against Micrococcus luteus, Staphylococcus epidermidis by any of the drugs involved in our study. Our study confirmed the fact that Micrococcus luteus, Staphylococcus epidermidis and Aeromonas pneumonia have developed multidrug resistance. In our third set of the experiment we conjugated antibiotics with biofabricated silver nanoparticles and then their antimicrobial activity was analyzed against all three multidrug resistant pathogenic bacteria. To our surprise nanoparticles conjugated antibiotics effectively targeted multidrug resistant bacteria and exhibited a very good zone of inhibition range from 0.6 to 1.0 cm. This approach not only enhanced the antimicrobial effects of antibiotics but also reduced the need of high doses of antibiotics as nanoparticles effectively increase the bioavailability of the drug at the target site an example of which is well demonstrated in case of nanoparticles mediated cancer drug delivery system. The promising results shown in our study opens new therapeutic avenues for targeting diseases associated with multidrug resistant pathogenic strains.

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