Abstract

The use of metallic nanoparticles has gained importance as one of the therapeutic options to treat infections in recent years. Here, the stable copper nanoparticles (CuNPs) were synthesized using thiosalicylic acid as stabilizing agent and their antimicrobial activities against various Gram-negative bacteria was assessed. The CuNPs synthesized had a size range of 5-11 nm with an absorption maximum at 570 nm and face-centred cubic (FCC) crystal structure. The bacterial cells in both planktonic as well as sessile forms were susceptible to the CuNPs. Further, the nanoparticles were found cytotoxic to murine macrophage (RAW264.7) cell-line below 60 μg/ml. However, the expression of the oxidative stress defence gene *ahpC* revealed the possibility of ROS generation upon the treatment with CuNPs. Interestingly, localization of FtsZ and FtsI were destabilized in the presence of CuNPs that in turn inhibit bacterial cell division. Overall, we summarize that the CuNPs were synthesized by chemical reduction method and has the ability to kill bacteria by arresting cell division and/or ROS generation. In addition, in this work the antimicrobial potential of silver nanoparticles (AgNPs) was also assessed. Silver nanoparticles (AgNPs) are used as an antimicrobial agent since ages. However, it is unknown whether AgNPs can exert any inhibitory effect over the bacterial cells carrying metallo-beta-lactamases (MBLs). Here, using biosurfactin stabilized AgNPs, having a size range of 5-25 nm, we have established its antimicrobial effect against NDMs possessing cells. Antimicrobial effectiveness of AgNPs was assessed on *E. coli* cells harbouring NDM genes and its clinical isolates, which showed that the cells expressing NDM become susceptible to AgNPs. When sub-inhibitory concentration of AgNPs was combined with various groups of beta-lactams antibiotics, a synergistic increase in sensitivity was observed. Purified NDM enzymes were also inhibited by AgNPs, which was revealed by the inabilities of NDMs in hydrolyzing nitrocefin (a chromogenic cephalosporin) in presence of AgNPs. Further, the results obtained from biochemical analysis indicate that the Ag^{+} ions might possibly bind to the sulfhydryl (SH) group of cystine in NDMs to inactivate these enzymes. Nonetheless, these AgNPs have the ability to exert antimicrobial activity without affecting the RAW 264.7 and HCT15 host cell viability when the same was used at a moderate concentration (<40 μg/ml). In summary, thiol-stabilized CuNPs and biosurfactin-stabilized AgNPs might serve as good candidates for inhibiting bacterial population, either individually or in combination with other antibiotics.

Keywords: Copper-nanoparticles, HR-TEM, bactericidal, Cell division inhibition, DNA degradation, AgNPs, Nitrocefin, toxicity to NDM, synergistic effect.