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Review Article

Utility of Nanoparticles as an Anti-Microbial Agent: A Breakthrough to Manage Anti-Microbial Resistant Bugs -

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ABSTRACT

In the epoch of advancement in science and technology, provision of many good therapeutic options even for fatal infections are helping to reduce the morbidity and mortality rates. But besides only the promising effects to treat infections, many of them are now adopting a resistance pattern. In view of this emerging scenario, around the Globe this burning issue of Anti Microbial Resistance (AMR) or antibiotic resistance, is becoming a great concern. The ordinarily used anti- microbials are now trailing their efficacy even to treat minor infections. Many etiologies are contributing to such waning consequence. Therefore researches around the Globe are devoting their efforts to ascertain those etiologies along with rectification measures. Nano technology is a new field, which to some extent is giving the promising results to successfully fight this burning issue of AMR. The presence of nanoparticles, their worthwhile delivery inside the cells, potent anti microbial effects and much reduced side effects has given hope to the clinicians. Therefore the objectives of current review article was to identify the significance for using various nanoparticles against resistant bugs. After a thorough literature review, it is concluded that usage of nanoparticles as anti microbial can be a break through to manage resistant bugs having fatal outcomes.

Keywords: Antimicrobial activity; Bacteria; Non metal nanoparticles; Metal nanoparticle; Nanotechnology; Anti-microbial resistance

INTRODUCTION

The Anti Microbial Resistance (AMR) is defined as the loss of effectiveness of anti-microbial against specific microbe. The increased emergence of AMR even for treating minor infections has been a serious concerns globally. Besides the desired effects of anti-microbial, their relentless use has resulted in the development of antibiotic bacterial resistance over time. Antibiotic forbearance in these bacteria is evolved through efflux pumps and biofilms formation. Therefore further advanced and emerging form of science i.e nanotechnology, has proven to be the scientific breakthrough in recent years for combating AMR. The comparison amongst the bioactive compounds with metal nanoparticles, showed their wide range of applications and sophisticated compatibility as nanocarriers. The published evidence supported their efficacious use as antibacterial, antifungal, antiviral, and antiparasitic agents [1].

Erstwhile deliberating the usefulness of nanoparticles, basis of AMR needs to be clarified in view of certain etiologies and correlations. The highlighted ones includes intrinsic resistance, genetic changes, DNA transfer pathologies or acquired resistance. The first category of intrinsic resistance involves the changes in microbial structural components. The notorious example can be given by taking penicillin group of antibiotics. They are the cell wall synthesis inhibitor. Therefore cannot be effective against wall less microbes or the ones having bets lactamases in their cell walls. The second group comprises of genetic changes in bacterium i.e alteration in protein synthesis. The extended spectrum beta lactamase producing Escherichia coli (ESBL), Enterococci, Klebsiella species, and Haemophilus influenza are few examples. They are found resistant to beta-lactams, tetracyclines, sulfonamides, trimethoprim, cefoxitin, and quinolones. The third group comprises of resistant pattern emergence due to disorders of bacterial transformation, conjugation and transduction. The examples can be Methicillin Resistance Staphylococcus Aureus (MRSA), Vancomycin-Resistant Staphylococcus Aureus (VRSA) Vancomycin-Resistant Enterococci (VRE). The fourth category involves acquired resistance. In this case bacterial resistance can be attained via genetic mutations. The example can be given form rifampicin which is one of the first line Anti Tuberculous Therapy (ATT) [2].

For combating issues linked to AMR, Antibiotic Stewardship (ASS) was recognized and came into recognition in 1996. The objectives of ASS were to provide guidance regarding jurisdictive use of antibiotics. These strategies were reinforced by Infectious Disease Society of America (IDSA) in association with the Society of Healthcare Epidemiology of America (SHEA). These infection control guidelines will ultimately be helpful in developing antimicrobial stewardship based upon results of culture and sensitivity of local settings [3,4].

Despite the utmost efforts, around the Globe, overwhelming situation is on the rise. Therefore, availability of nanoparticles to manage infectious diseases brought a hope and break through to combat infections with resistant bugs. The availability of such new therapeutic options, had proven to be cost effective, less side effects, and less drug interactions [5]. Nanoparticles (NPs) are increasingly used as therapeutic management option against bacterial infections as an alternative option to antibiotics. Their successful results were observed when used as antibacterial coatings for implantable devices, medicinal materials to prevent infection along with wound healing. The specific properties enhance antibiotic delivery to manage infections. A huge endless debate is still non conclusive amongst the scientist around the Globe regarding their mode of action for antibacterial effects. However, few narrated that oxidative stress induction, release of metal ion and non-oxidative mechanisms could be the reason. It was further elaborated that chances for NPs resistance are minimum because of these multiple simultaneous mechanisms of action against microbes. This is the main comparable difference with commonly used antibiotics which can easily develop resistance due to multiple simultaneous gene mutations in same bacterial cell [6].

A published report by World Health Organization (WHO) described that AMR is amongst the most serious health hazards around the Globe. The frequency of resistant and mutated bacteria is increased to an alarming extent. Therefore discovery of effective antimicrobials is the need of time. The availability of nanoparticles and their role as antimicrobial agents added up a good hope to handle the worsening scenario from AMR. The nanoparticles can be metal and non metal. Amongst metal oxide nanoparticles, commonly used ones are silver, copper, gold, iron oxide, zinc oxide, and titanium oxide [7]. Due to certain physicochemical properties, they have good antimicrobial properties even at very low concentration. They have biocompatible nature against human cells and even serve as essential micronutrients required for vital functioning of the human body [8]. A systematic review by Bilal H in 2021 concluded, a very high incidence of AMR, along with gaps in health surveillance and monitoring system. His study analyzed the data of about a decade [9]. Another published report by Javaid N in 2021 highlighted same noteworthy mortality rates from AMR at various places in Pakistan. Easy accessibility and amplified use of broad-spectrum antimicrobials, for treating noninvasive infections, was amongst the main etiological factor. This has resulted in troublesome managing of such infections ultimately causing high mortality. Comparatively global statistics revealed 5.3 million deaths annually from AMR [10]. Contrary to all published evidence, only one published report by Gharpure in 2022, concluded non anti-microbial and non-cancerous properties of zinc oxide nanoparticles. Uncalcinated ZnO nanoparticles was found to have scrawny antibacterial actions [11]. Whereas calcinated ZnO nanoparticles exhibited a non-antibacterial effects. Besides this both calcinated and non calcinated ZnO was analyzed to have antifungal activity against different fungi (Aspergillus flavus, Penicillium species, Rhizoctonia solani and Fusarium oxysporum) and cytotoxicity against HCT-116 cancer cells. The variation for antimicrobial efficacy and biocompatibility of ZnO nanoparticles are dependent upon various parameters of microorganisms and human cells. The biosynthesized ZnO nanoparticles revealed nontoxic nature, which is promising alternative in biomedical applications [11].

A published review article for the year 2021, showed that Silver Nanoparticles (AgNPs) have an excellent in vivo and in vitro antimicrobial properties. The antibacterial spectrum cover of AgNPs includes many Gram-negative and Gram-positive bacteria, including the multidrug resistant strains. AgNPs exhibit synergistic effect against many bacteria i.e Escherichia coli and Staphylococcus aureus. This property along with decreased side effects make them rank in good repute to manage and prevent infections efficiently [12-14].

Another published review article highlighted the effectiveness of silver nanoparticles along with relatively less adverse effects [15]. They own broad spectrum of antibacterial, antifungal and antiviral properties. The rapid and efficacious penetration in a bacterial cell walls, increased cell membrane permeability eventually results in bacterial death. Their large surface area to volume ratio is the added ability besides their nanoscale size to kill a bacteria. Moreover they also aids to produce reactive oxygen species, which interrupt replication of Deoxyribonucleic Acid (DNA) by releasing silver ions. The review of literature narrated effective role in dentistry when used as antimicrobial agents. They can easily be incorporated in acrylic resins, which helps in fabrication of removable dentures in prosthetic management, irrigating solution, composite resin in restorative managements, and obturation material in endodontic management. They were also found useful when used as adhesive materials in orthodontic treatment, membrane for guided tissue regeneration in periodontal treatment, and titanium coating in dental implant treatment [16,17].

Another review article for the year 2021 also supported effective use of gold nanoparticles to manage resistant superbugs having resistant pattern. A good antibacterial activity was observed for 4,6-Diamino-2-Pyrimidine Thiol (DAPT)-Capped Gold Nanoparticles (AuDAPTs) [18]. It increases the Minimum Inhibitory Concentration (MIC) of Escherichia coli to 16-fold without developing cross-resistance to commercialized antibiotics. It was also observed that bactericidal activities of AuDAPTs were further enhanced upon reduction in their size without employing new chemicals. These good results even to treat Multi-Drug-Resistant (MDR) bacterial infections were comparable to traditional antibiotics or other nanomaterials [19,20].

In view of deteriorating scenario for increasing AMR, sooner the time will arise where non availability of anti-microbial will lead to disastrous outcomes. Therefore necessity for breakthrough is the need of time. Utility of nanoparticles are becoming promising to manage even the resistant bugs in much effective manner along with less side effects. The researchers, microbiologists, clinicians, pharmaceutical companies and bio-nanotechnologist should join hands to identify utility of nanoparticles as anti-microbial tools.

CONCLUSION

The usage of nanoparticles as anti-microbial agents can be a break through to manage resistant microbes (bacteria, virus or fungi) having fatal outcomes.

RECOMMENDATIONS

1. This review article is a guide map for the researchers, microbiologists, pharmaceutical companies and nanotechnologist to unite hand and work on various nanoparticles to identify their anti-microbial properties.
2. Since the literature review showed extreme deficiency of original articles, meta-analysis and randomized control trials, so they should be the targeted modalities for further work.
3. Effectiveness of both metallic and non metallic nanoparticles should be studied for their anti-microbial properties
4. Effectiveness of both metallic and non metallic nano particles should be studied for their effectiveness to treat the cases of anti-microbial resistance with carbapenams and colistin.
5. The anti-microbial properties for both metallic and non metallic nano partilces should be studied for bacterial, fungal, viral even the parasitic infections.

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