Preface

The evolution of multi-drug resistance (MDR) in pathogenic microorganisms, especially fungi and bacteria, has led to the clinical challenge of unmanageable infections. Multi-drug resistant (MDR) microorganisms, particularly bacteria, pose a global health challenge, with dramatic increases in morbidity and mortality rates among infected individuals; MDR microorganisms are associated with significant clinical consequences in a broad group of patients, including those admitted to the ICU, those undergoing surgery, organ transplantation recipients, and cancer patients. Annually, the United States records at least 2.8 million annual cases of MDR bacterial or fungal infections; the deaths of more than 35,000 patients per year are attributed to these infections. In addition, the global surveillance system of the World Health Organization highlighted antimicrobial drug resistance among microorganisms (AMR) as a global health crisis. The estimated average financial burden of treating an AMR infection is around US $ 50,000 per patient or around ~US $20 billion. Engineered (surface-modified or decorated) nanoparticles have the potential to counter the MDR challenge by serving as a clinical alternative for treating a broad spectrum of infections, particularly those caused by MDR microorganisms. Several studies have revealed that the smaller-sized (~10 nm) nanoparticles have a greater antimicrobial effect than larger-sized particles. This phenomenon is because smaller nanoparticles can directly pass through bacterial cell membranes via water channels. Direct cellular entry may lead to membrane damage. Similarly, smaller nanoparticles can also achieve the disruption of mature biofilms. Smaller-sized nanoparticles can pass through the water channels in the core of the biofilm matrix. The biocidal activity of metal nanoparticles

also depends on their shape. Different shapes of nanoparticles such as triangular, rod-shaped, and spherical shapes have shown noticeable alterations in the cell membrane architecture. For example, triangular silver nanoplates with a basal lattice plane were more biocidal than spherical and rod-shaped silver nanoparticles. The variation can explain the morphology-dependent biocidal activity of the Ag nanoparticles in Ag ion release kinetics. Therefore, it may be possible to control the biocidal activity of silver nanoparticles by controlling their shape. Metal nanoparticles' surface charge (zeta potential) may also affect their antimicrobial activity. An increase in zeta potential forms the strong electrostatic interaction between nanoparticles and negatively charged bacterial cell walls leading to cell membrane disruption and membrane depolarization. The surface charge of nanoparticles can be tuned by capping or doping active molecules to increase the possibility of electrostatic interactions between the nanoparticles and the biofilm. The present study describes the nano-geometry-controlled rapid synthesis of metal nanoparticles by using 3-APTMS and variable molecular weights of Polyethyleneimine with organic reducing agents (such as cyclohexanone, 3-GPTMS & Formaldehyde) and its qualitative interaction dynamic with microbial cell surface along with associated antimicrobial mechanisms. The synthetic protocol has attempted to use microwave irradiation to fasten the reduction reaction in the presence of capping/stabilizing agents (3-APTMS and Polyethyleneimine) to control the nano-geometry of silver, gold, and palladium nanoparticles. Further, the addition of ethylene glycol diacetate prevents the evaporation of base solvent during irradiation and prevents agglomeration of nanoparticles. Furthermore, the application of 1-vinyl 2 pyrrolidone helps in the reduction and stabilization process and controls the dispersibility in various solvents.

The capping with Polyethyleneimine provides an opportunity to load antibiotics on gold nanoparticles and is explored as a nanoparticle-mediated drug delivery platform against MDR pathogens. This work has been organized into seven chapters with a Summary where the influential role of PEI, 3-APTMS/3-GPTMS has been investigated and discussed from different perspectives in an elementary means. Chapter (1) 'General Introduction' incorporates reviews of the present status of the subject, including the outcome of earlier studies performed on the antimicrobial activity and associated mechanism of metal nanoparticles. Chapter (2) includes the microwave-assisted rapid synthetic strategy of different types of silver gold and palladium nanoparticles by using 3-APTMS and 3-GPTMS and reducing agents cyclohexanone, 3-GPTMS, and Formaldehyde and their characterization by using different instruments. Chapter (3) included the synthesis of three different types of silver nanoparticles depending on the molecular weight of Polyethyleneimine and their qualitative interaction dynamics with bacterial cell surface using Fluorescence spectroscopy. Chapter (4) included microwave-assisted rapid synthesis of silver nanoparticles using Polyethyleneimine as a capping/stabilizing agent and their qualitative interaction dynamics with fungal cell surface using fluorescence spectroscopy. Chapter (5) included microwave-assisted rapid synthesis of silver nanoparticles using Polyethyleneimine as a capping/stabilizing agent and their antifungal activity against COVID-19-associated mucormycosis fungus *R. arrhizus*. Chapters (6&7) included the rapid synthesis of vancomycin-loaded gold nanoparticles using Polyethyleneimine as a stabilizing agent and their application in heavy metal sensing and exploration as drug delivery platforms against gram-negative and fungal cells. The outputs of this thesis work have been published in

different journals such as Journal of Material Research, 35, 2405–2415 (2020); Nano Life, 10 (3), 2050002 (2020); Nanomaterials, 12(13), 2235, (2022); Frontiers in Microbiology, 14, 1131122, (2023) and Frontiers in Chemistry, 11, 1238631, (2023).