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Various novel strategies for functionalization of gold and silver nanoparticles to hinder drug-resistant bacteria and cancer cells

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ABSTRACT

A higher reactivity of nanomaterials specifically inorganic nanoparticles (NPs) compared to their counterparts, is caused by their unique physicochemical properties in the nanoscale such as large surface area to volume ratio and aspect ratio. In the case of metal and metal oxide NPs, gold (Au) and silver (Ag) NPs have been known to have appropriate therapeutic activities particularly anticancer and antimicrobial effects against a wide range of multidrug-resistant bacteria and cancer cells. However, low biocompatibility, bioavailability, and biodegradability in antibacterial and anticancer doses of these NPs are main hindrances to obtain an efficient safe formulation. For optimizing the micro and nano formulations, functionalization of the surface of Ag and Au NPs by biocompatible organic or inorganic materials has been applied in recent investigations. Therefore, in this review, various novel strategies to functionalize Au and Ag NPs particularly to hinder drug-resistant cancer cells and bacteria, have been discussed. In the term of an effective anticancer formulation, side effects of chemotherapeutic agents may be attenuated via employing multifunctional micro and nano agents composed of anticancer drugs, biocompatible materials and Au or Ag NPs.

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Introduction

Finding an effective formulation to hinder drug-resistant microbial pathogeneses and cancers is a critical issue because of the low efficiency and adverse side effects of conventional drugs [1-6]. For example, antibiotic-resistant bacteria and cancer cells can bypass the antibiotics and chemotherapeutic drugs by several mechanisms such as overexpression of efflux pumps [7]. In recent years, nanotechnology have presented novel technologies for fabrication of nanomaterials in the scale of 1-100 nm, which may be applied in various medical sections, particularly for overcoming drug-resistant bacterial and cancer cells [8, 9]. Top-down and bottom-up approaches are two main ways for synthesis of zero-dimension (nanoparticles (NPs), nanospheres and fullerenes), and one- dimension (nanotubes, nanofibers and nanorods), and two-dimension nanomaterials (nanoplates and nanofilms) [10-12]. NPs without any bulk scale in three dimensions are interesting nanomaterials to passive and active targeting bacteria and cancer tissues. In an active targeting way, organic or inorganic NPs can be functionalized by a specific ligand to target related receptors of cell membrane (Figure 1) [13, 14]. Metal or metal oxide nanoparticles, specifically gold (Au) and silver (Ag) NPs can be modified by adding various therapeutic agents directly or indirectly by photoreactive, heterobifunctional, and homobifunctional crosslinking reagents [15]. Here, recent advances and challenges about antibacterial

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and anticancer activity of Au and Ag NPs are discussed to better understand of therapeutic applications of these NPs. In addition to antibacterial and anticancer activities of Au and Ag NPs, biocompatibility and bioavailability of these NPs have been covered in this review to obtain effective approaches of their formulations in physiological conditions based on micro and nano aspects.

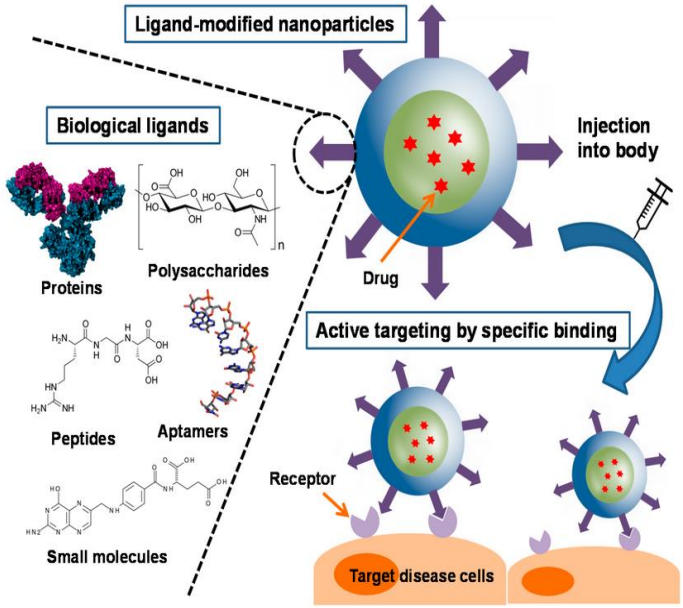

Fig. 1. schimatic illustration of active targeting of NPs by biological ligands [16].

AuNPs

Antibacterial activity

Gram-negative and Gram-positive bacteria have different cell wall and membrane structure, which should be considered for formulation of efficient functionalized metallic NPs [17-20]. Bacterial cell envelope with glycolipids has a high affinity to bind the boronic acid group of phenylboronic acid (Figure 2a) [21]. By this knowledge, AuNPs were modified with thiol- and amine-tethered phenylboronic acids due to binding with lipoteichoic acid (LTA) and lipopolysaccharide (LPS) of Gram-positive and Gram-negative bacteria, respectively. Moreover, different ratios of amine- and thiol-tethered phenylboronic acids or the density of surface coating of the AuNPs showed different antibacterial activities. In this regard, there was a broad antibacterial spectrum for uniform density of both acids [22]. Natural compounds related to plants, fungi, and bacteria have been used to produce and modify NPs [23]. For example, *Acalypha indica* aqueous leaf extract having phytochemicals of sildenafil citrate, geniposidic acid, 3,5-dimethylphenol, palmitic acid, borneol, 2-hexyl-1-octanol, and α-terpinyl acetate were exploited to synthetize AuNPs spherical shape of AuNPs with 20 nm of size (Figure 2b). Coating cotton with photosynthesized AuNPs exhibited antibacterial activity as inhibition zone diameter of 31 and 26 mm against *Staphylococcus epidermidis* and *Escherichia coli*, respectively [24]. At neutral pH, bacterial envelope with a negative charge density resulted from carboxyl and phosphate groups in the lipopolysaccharides and peptidoglycan has more affinity to bind positive charge particles via electrostatic interaction [25] (Figures 3A and B). Therefore, functionalization of NPs by positive materials such as chitosan ore their derivatives may increase interaction of NPs with cell wall and membrane of bacteria followed by interruption of these hindrances [26]. Using different levels of the chitosan charge as amine protonation in a formulation can lead to dissimilar interaction between formulation and lipid membrane of bacteria, wherein the high charge density of chitosan displayed dispersion of chitosan on the lipid bilayer because the strong electrostatic interactions. In contrast, chitosan by a low density of positive charge can penetrate into the membrane with major perturbations in the structure of the lipid membrane (Figure 3C) [27].

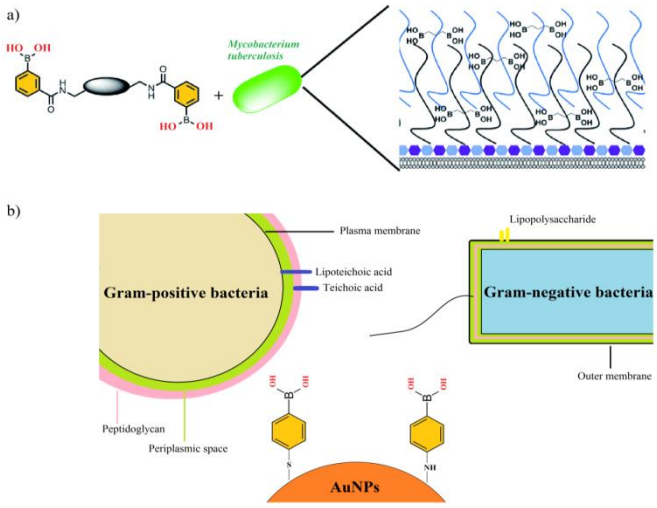

Fig. 2. a) Multimeric boronic acid to target cell-envelope glycans of *Mycobacterium tuberculosis* [21]. b) functionalization of the AuNPs by amine- and thiol-tethered phenylboronic acids to target Gram-positive and Gram-negative bacteria [22].

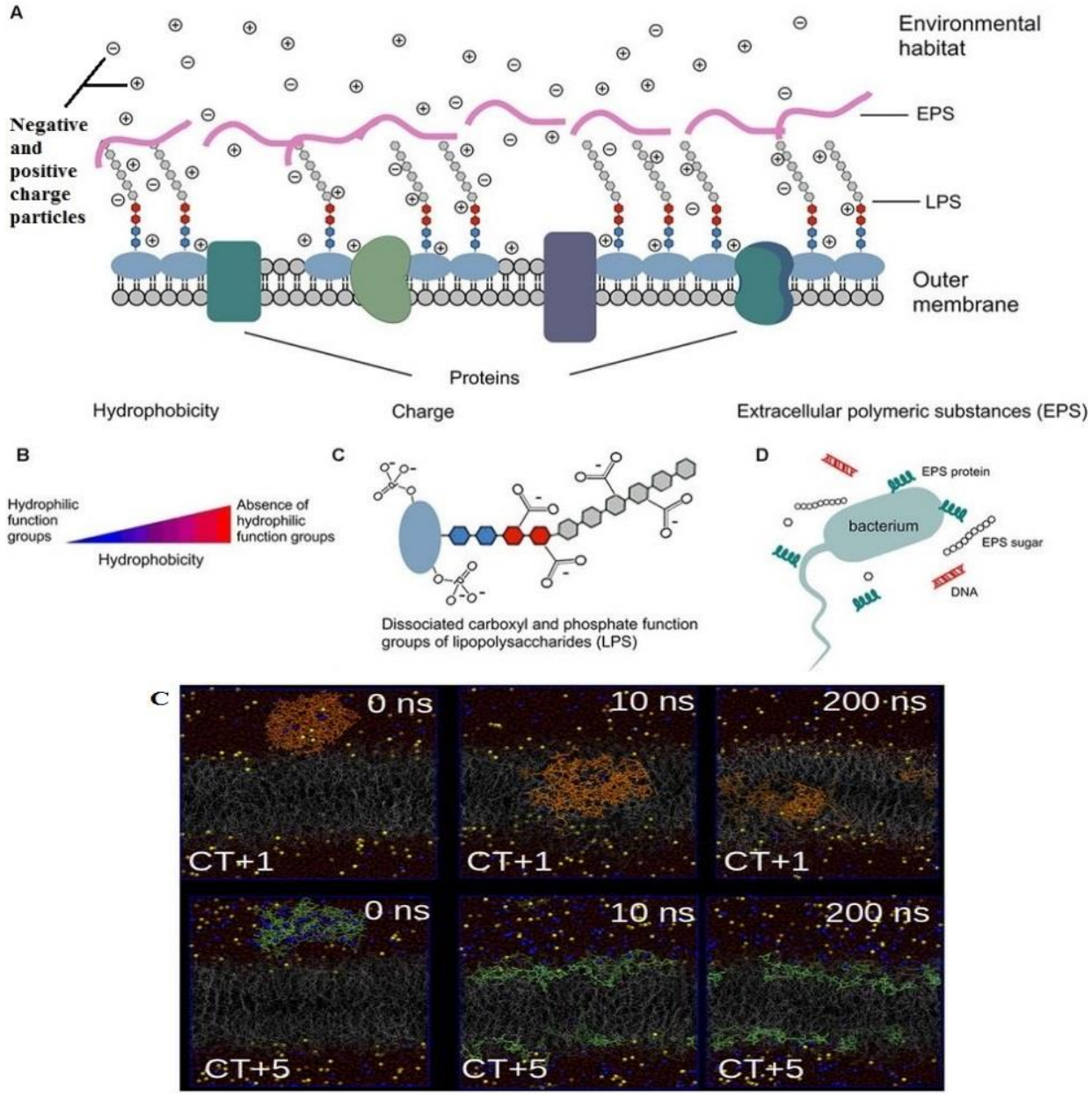

Fig. 3. A and B) interaction of positive charge particles with bacterial membrane having negative charge resulting from lipopolysaccharide and teichoic acid related to Gram-negative and Gram-positive bacteria, respectively [25]. C) Simulation for interaction of two chitosan models including CT+5 (with charge +5) and CT+1 (with charge +1) with lipid bilayer. Permission under the terms of the Creative Commons Attribution License (CC BY) [27].

Anticancer activity

As mentioned in the introduction section, natural compounds extracted from primary and secondary metabolites of living organisms can contribute indirectly or directly in formation and surface functionalization of metal NPs. Curcumin as a phenolic compound obtained from *Curcuma longa* plant species has various therapeutic properties desirable for novel micro- and nano-formulations due to growth inhibition of both cancer cells and microbial pathogens. In addition, this metabolite can act as reducing and stabilizing agent for directly synthesis of Au and Ag NPs [23]. For the case of AuNPs, curcumin and isonicotinic acid hydrazide (INH) were employed to reduce Au^{+3} ions and modify surface of AuNPs to produce AuNPs-curcumin-INH with hydrodynamic radius and polydispersity index of 53.4 nm and 3.1, respectively. Dose-dependent anticancer activity was indicated for AuNPs-curcumin-INH at 1 µg/mL towards K-2 cancer cells at 5 µg/mL with low toxicity against TIG-120 fibroblasts. Reactive

oxygen species (ROS) generation by this formulation at low-dose can activate cell signaling, but at high-dose, dysfunction of biological macromolecules is expected via oxidative stress [28]. AuNPs were stabilized and functionalized by thiol-functionalized repeat units of polyamidoamine (AGMA1-SH) and Trastuzumab monoclonal antibody to target HER2-positive breast cancer cells. These nanoformulations with 5 nm and a high positive charge exhibited the higher cellular uptake and cytotoxicity compared to the smaller formulations by 2.5 and 3.5 nm (Figure 4) [29].

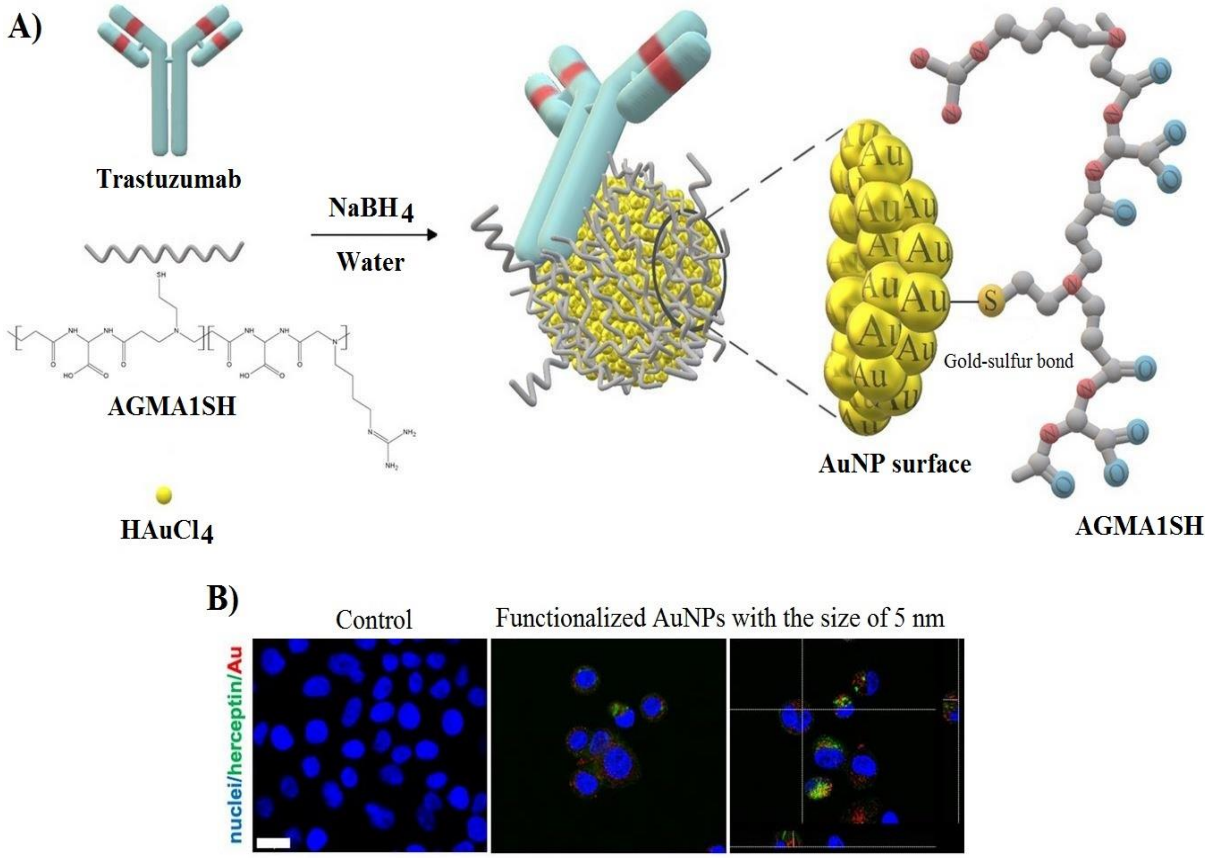

Fig. 4. A) Functionalization steps of AuNPs by polyamidoamine of AGMA1-SH and Trastuzumab monoclonal antibody. B) High cellular uptake of functionalized AuNPs with 5 nm size (copyright under the terms of the Creative Commons Attribution License (CC BY) [29].

AgNPs

Antibacterial activity

Naringenin ($C_{15}H_{12}O_5$), a heterocyclic flavonoid extracted from citrus has various therapeutic activities such as anticancer activities, antioxidant, and antibacterial activity against different antibiotic-resistant bacteria [30, 31]. This metabolite is known to hold the reducing and stabilizing role in formation of metal NPs. Reduced graphene oxide (RGO) (by carbonyl and hydroxyl functional groups of naringenin) was decorated by naringenin-AgNPs to prepare nanocomposites of naringenin-AgNPs-RGO. These nanocomposites exhibited antibacterial effects on a wide range of Gram-negative and Gram-positive bacteria involving *E. coli*, *Vibrio cholera*, *Staphylococcus epidermidis*, *Salmonella typhi*, *Rhodococcus rhodochrous*, *Proteus mirabilis*, and *S. aureus* [32]. As another herbal compound, catechol ($C_6H_6O_2$) was conjugated to chitosan polymer as reducing and stabilizing agent in AgNPs (a size range of 44.2 -48.9 nm with the spherical morphology) formation in one-pot reaction (Figure 5A). As shown in Figure 5B, bactericidal effects were observed as a change in the permeability of bacterial membrane at very low concentrations of 25 µg/mL and 14 µg/mL against *S. aureus* and *E. coli*, respectively [33]. In addition to plant metabolites such as flavonoids, terpenoids, saponins, and alkaloids [34-39], secondary metabolites of bacteria and fungi are suitable sources to

biosynthesize AgNPs (Figure 6) [40-42]. For example, alternant polymer with molecular formula $C_{72}H1_{22}O_{61}$ was applied for stabilizing spherical and aggregated AgNPs by a size range of 50–100 nm. These NPs showed antibacterial activity against *S. aureus*, *Yersinia enterocolitica*, *Bacillus cereus*, *E. coli*, *Salmonella typhimurium* with the inhibition diameters of 19, 18, 9, 12, and 20 mm, respectively at concentration 250 µg/mL. The hydroxyl groups (O-H), stretching of C-O, C-O-C, and symmetric CH_3 bending were indicated as main functional groups for formation of AgNPs-alternant [43]. AgNPs in spherical shape with the size of ~33 nm were synthesized by a supernatant of *Bacillus* sp. HAI4 medium , which showed antibacterial effect on *E. coli* and *S. aureus* [44]. Moxifloxacin, a fluoroquinolone antibiotic was used to modify Ag_2ONPs (by crystallite size of 53.26 and 50.87 nm for cubic and hexagonal phase) to synergize antibacterial activity, which *E. coli* and *Pseudomonas aeruginosa* displayed more sensitivity compared to *Bacillus subtilis* and *S. aureus* upon these NPs [45]. Another antibiotic, penicillin G was used to coat $Ag@SiO_2$ triangular NPs in a core-shell structure, which showed minimum bactericidal and bacteriostatic concentrations of 350 and 130 ppm, respectively against methicillin-resistant *S. aureus* [46]. Thiobarbituric acid and11-mercaptoundecanoic acid residues were employed to functionalize the surface of AgNPs as TBA-AgNPs and MUA-AgNPs, respectively. TBA-AgNPs and MUA-AgNPs exhibited values of 0.78- 0.078 µg/mL and 0.66-0.066 µg/mL compared to bare AgNPs (0.9-0.09 µg/mL) against *Salmonella typhimurium* TA98 for minimum bactericidal concentrations (MBC) and minimum inhibitory concentrations (MIC), sequentially [47].

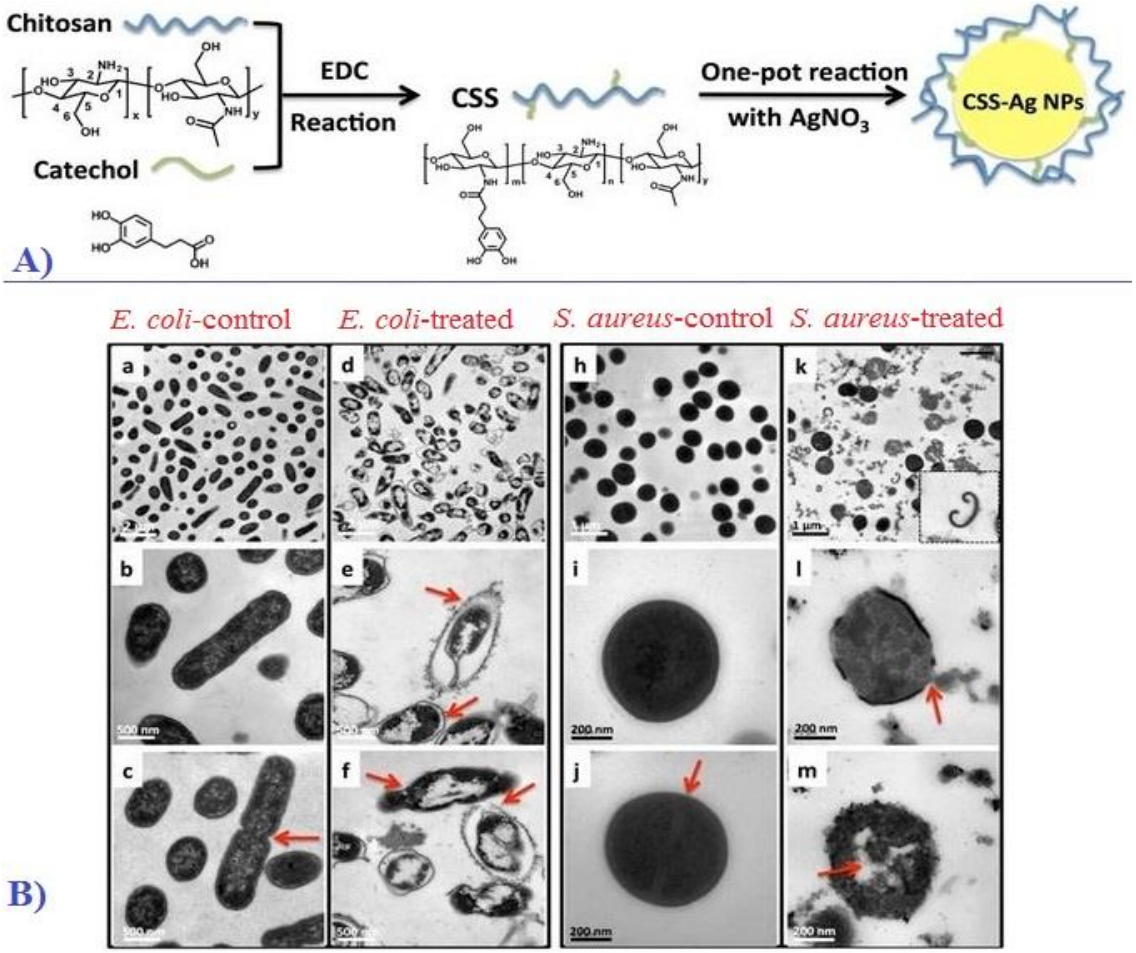

Fig. 5. A) Surface functionalization of AgNPs with chitosan and catechol by one-pot synthesis; B) TEM images presenting control and treated *E. coli* and *S. aureus* under AgNPs stress by a change in bacterial membrane permeability (a copyright under the license of http://creativecommons.org/licenses/by/4.0/.) [33].

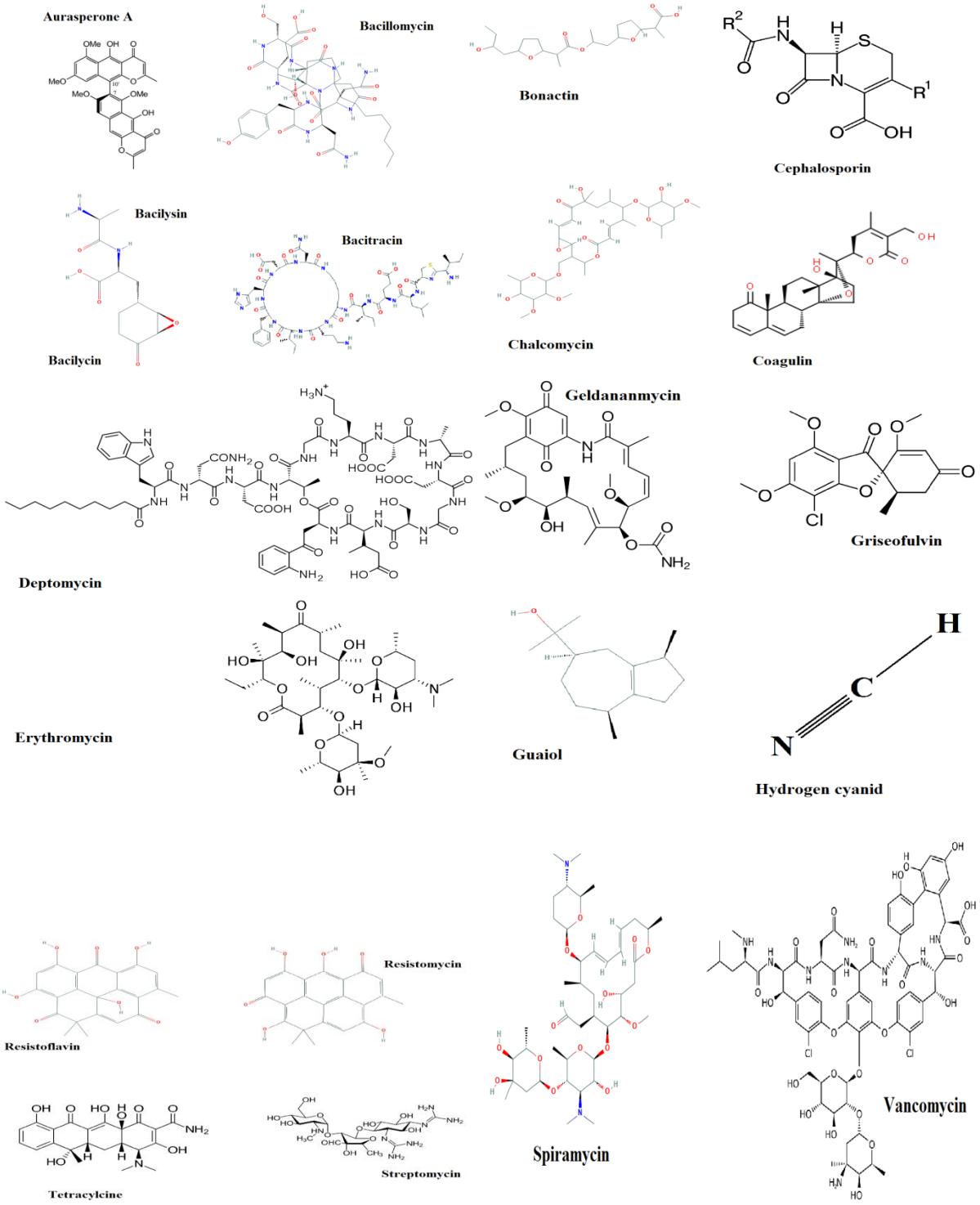

Fig. 6. Chemical structures of important secondary metabolites with antimicrobial activity in relation to bacterial and fungal sources (https://pubchem.ncbi.nlm.nih.gov/).

Anticancer activity

Inhibition of cell proliferation and activation of apoptosis may be caused by AgNPs via p53 mediated signaling pathways, cellular block in the S-phase and induction of G1 arrest [48, 49]. Preparing a novel formulation with the ability of precise targeting of cancer cells for reducing side effects of conventional chemotherapy and drug resistance is a vital affair. Multifunctional nanoformulations composed of paclitaxel (PTX), AgNPs coated with polydopamine (PDA), and tumor-targeting peptide NR1 were used as NR1/AgNP-decorated PTX nanocrystals to target cancer cells, increase cellular uptake efficiency, and activate pro-apoptotic P53 and

caspase 3 [50]. In a similar study, coated AgNPs with NeutrAvidin-PEG(5K)-thiols were more functionalized with biotinylated targeting peptide (RPARPAR) and monomethyl auristatin (MMAE) as a cytotoxic drug (Figure 7A). After the uptake of formulation by peptide-mediated endocytosis, MMAE was released under the degradation of the AgNPs via a lysosomal protease cathepsin B. Cellular uptake for these NPs was 85% relative to MMAE–AgNPs and MMAE with 5 and 20% values [51]. The endocytosis and passive diffusion are main pathways for penetration AgNPs into mammalian cells. Cell-penetrating peptides (CPPs) as small cationic peptides with 5–30 amino acids are majorly exploited to transport a plethora of micro and nanocarriers across cell membranes. Modified AgNPs with CPPs showed prominent anticancer activity against MCF-7 cells at concentration 16 µg/mL [52]. Enhanced entrance of siRNA into mammalian cells is possible by modification of surface of the AgNPs followed by loading siRNA on the AgNPs. In this manner, carbosilane dendron was used to surface modification of the AgNPs and formation the stable complex with siRNA (anti-Bcl-xl siRNAs). Efficient cellular uptake without increased anticancer activity were observed for this nanoformulation (Figure 7B) [53].

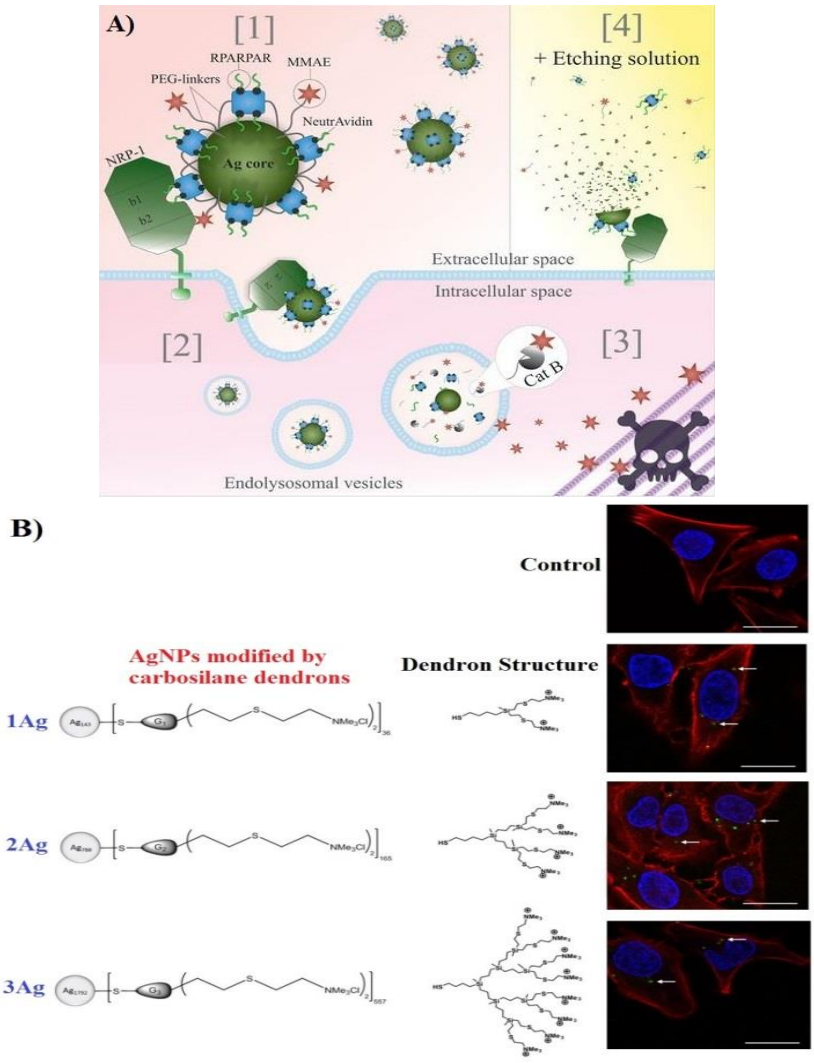

Fig. 7. A: 1) Decorated AgNPs were functionalized with RPARPAR and MMAE; 2) peptide-mediated endocytosis of NPs; 3) release of MMAE under the degradation of the AgNPs via a lysosomal protease cathepsin B 4) Etching solution including thiosulfate and hexacyanoferrate can be employed to remove the AgNPs in extracellular space. copyright under the terms of the Creative Commons CC BY license [51]. B: Modification of AgNPs by dendron:siRNA; 1Ag, 2Ag, and 3Ag show the complexes of dendron:siRNA by molar ratios of 55:1, 12.5:1, and 7.5:1, respectively [53] (Copyright under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/).

Conclusions

Secondary and primary metabolites related to living organisms encompassing medicinal plants, bacteria, fungi, and lichens are known to hold various therapeutic potentials desirable to functionalize the surface of metal and metal oxide NPs specifically Au and AgNPs. Production of ROS by Au and Ag NPs at high doses can damage the biological macromolecules such as nucleic acids, proteins, and enzymes, but low cytotoxicity and activation of cell signaling may be resulted at low doses. In the case of anticancer activity, side effects of chemotherapy may be decreased by using multifunctional agents composed of anticancer drugs, biocompatible materials and Au or Ag NPs due to obtain precise tumor-targeting and reverse drug resistance. Therefore, according to this review, functionalized Au and Ag NPs can be the appropriate alternative for loading antibacterial and anticancer agents. However, more studies are needed to evaluate biocompatibility and bioavailability of effective antibacterial and anticancer doses in physiological conditions.

Study Highlights

- Surface functionalization of Ag and Au NPs by secondary metabolites of plants, bacteria, fungi, and lichens can be a safe method.
- Production of ROS by Au and Ag NPs at high doses can damage the biological macromolecules such as nucleic acids, proteins, and enzymes.
- At low doses of Au and Ag NPs, there are low cytotoxicity and activation of cell signaling.
- Effective antibacterial and anticancer activities of these NPs in low doses can be possible using the surface functionalization by the natural compounds.

Abbreviations

AGMA1-SH: Thiol-functionalized repeat units of polyamidoamine
CPPs: Cell-penetrating peptides
INH: Isonicotinic acid hydrazide
LPS: Lipopolysaccharide
LTA: Lipoteichoic acid
MBC: Minimum bactericidal concentrations
MIC: Minimum inhibitory concentrations
MMAE: Monomethyl auristatin
NPs: Nanoparticles
PDA: Polydopamine
PTX: Paclitaxel
RGO: Reduced graphene oxide
ROS: Reactive oxygen species

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Conflict of interest

The authors declare that they have no conflict of interest for this study.

Ethical approval

This article does not contain any studies with animals or human participants.

Authors' contribution

MA: conceptualization, preparing the first draft, and revising; RK, RC, HDMC, and IRADM: revising of the manuscript.

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References

1. Alavi M, Rai M. Antisense RNA, the modified CRISPR-Cas9, and metal/metal oxide nanoparticles to inactivate pathogenic bacteria. Cellular, Molecular and Biomedical Reports. 2021:52-9. doi:https://doi.org/10.55705/cmbr.2021.142436.1014
2. Abbas-Al-Khafaji ZK, Aubais-aljelehawy Qh. Evaluation of antibiotic resistance and prevalence of multi-antibiotic resistant genes among Acinetobacter baumannii strains isolated from patients admitted to al-yarmouk hospital. Cellular, Molecular and Biomedical Reports. 2021:60-8. doi:https://doi.org/10.55705/cmbr.2021.142761.1015
3. Rahbar-Karbasdehi E, Rahbar-Karbasdehi F. Clinical challenges of stress cardiomyopathy during coronavirus 2019 epidemic. Cellular, Molecular and Biomedical Reports. 2021;1(2):88-90. doi:https://doi.org/10.55705/cmbr.2021.145790.1018
4. Muhammad I, Sale PM, Salisu MK, Muhammad TM, Abubakar B, Maidala AL, et al. Molecular analysis of Bio-makers of Chloroquine resistance in Plasmodium falciparum Isolate from Gombe Local Government Area, Gombe State, Nigeria. Cellular, Molecular and Biomedical Reports. 2022;2(1):42-55.

doi:https://doi.org/10.55705/cmbr.2022.335753.1033
5. Muhammad I, Abubakar B, Muhammad TM. Genetic resistance to human malaria. Cellular, Molecular and Biomedical Reports. 2022;2(2):116-28. doi:https://doi.org/10.55705/cmbr.2022.342533.1043
6. Mohammadi MR, Sabati H. When Successive Viral Mutations Prevent Definitive Treatment of COVID-19. Cellular, Molecular and Biomedical Reports. 2022;2(2):98-108. doi:https://doi.org/10.55705/cmbr.2022.339012.1040
7. Nanayakkara AK, Boucher HW, Fowler Jr VG, Jezek A, Outterson K, Greenberg DE. Antibiotic resistance in the patient with cancer: Escalating challenges and paths forward. CA: A Cancer Journal for Clinicians. 2021;71(6):488-504. doi:https://doi.org/10.3322/caac.21697
8. Khorsandi K, Hosseinzadeh R, Sadat Esfahani H, Keyvani-Ghamsari S, Ur Rahman S. Nanomaterials as drug delivery systems with antibacterial properties: current trends and future priorities. Expert Review of Anti-infective Therapy. 2021;19(10):1299-323. doi:https://doi.org/10.1080/14787210.2021.1908125
9. Alavi M, Rai M, Martinez F, Kahrizi D, Khan H, Rose Alencar de Menezes I, et al. The efficiency of metal, metal oxide, and metalloid nanoparticles against cancer cells and bacterial pathogens: different mechanisms of action. Cellular, Molecular and Biomedical Reports. 2022;2(1):10-21. doi:https://doi.org/10.55705/cmbr.2022.147090.1023
10. Paramasivam G, Palem VV, Sundaram T, Sundaram V, Kishore SC, Bellucci S. Nanomaterials: Synthesis and Applications in Theranostics. Nanomaterials. 2021;11(12). doi:https://doi.org/10.3390/nano11123228
11. Alavi M, Webster TJ. Recent progress and challenges for polymeric microsphere compared to nanosphere drug release systems: Is there a real difference? Bioorganic & Medicinal Chemistry. 2021;33:116028. doi:https://doi.org/10.1016/j.bmc.2021.116028
12. Alavi M, Nokhodchi A. Antimicrobial and wound healing activities of electrospun nanofibers based on functionalized carbohydrates and proteins. Cellulose. 2022;29(3):1331-47. doi:https://doi.org/10.1007/s10570-021-04412-6
13. Alavi M, Hamidi M. Passive and active targeting in cancer therapy by liposomes and lipid nanoparticles. Drug Metabolism and Personalized Therapy. 2019;34(1). doi:https://doi.org/10.1515/dmpt-2018-0032
14. Alavi M. Bacteria and fungi as major bio-sources to fabricate silver nanoparticles with antibacterial activities. Expert Review of Anti-infective Therapy. 2022:1-10. doi:https://doi.org/10.1080/14787210.2022.2045194
15. Fernández M, Orozco J. Advances in Functionalized Photosensitive Polymeric Nanocarriers. Polymers. 2021;13(15). doi:https://doi.org/10.3390/polym13152464
16. Yoo J, Park C, Yi G, Lee D, Koo H. Active Targeting Strategies Using Biological Ligands for Nanoparticle Drug Delivery Systems. Cancers. 2019;11(5):640. doi:https://doi.org/10.3390/cancers11050640
17. Vila Domínguez A, Ayerbe Algaba R, Miró Canturri A, Rodríguez Villodres Á, Smani Y. Antibacterial Activity of Colloidal Silver against Gram-Negative and Gram-Positive Bacteria. Antibiotics (Basel, Switzerland). 2020;9(1):36. doi:https://doi.org/10.3390/antibiotics9010036
18. Sathiyaraj S, Suriyakala G, Dhanesh Gandhi A, Babujanarthanam R, Almaary KS, Chen T-W, et al. Biosynthesis, characterization, and antibacterial activity of gold nanoparticles. Journal of Infection and Public Health. 2021;14(12):1842-7. doi:https://doi.org/10.1016/j.jiph.2021.10.007
19. Alavi M, Hamblin MR, Martinez F, Kennedy JF, Khan H. Synergistic combinations of metal, metal oxide, or metalloid nanoparticles plus antibiotics against resistant and non-resistant bacteria. Micro Nano Bio Aspects. 2022;1(1):1-9
20. Aubais aljelehawy Qh, Hadi Alshaibah LH, Abbas Al- Khafaji ZK. Evaluation of virulence factors among Staphylococcus aureus strains isolated from patients with urinary tract infection in Al-Najaf Al-Ashraf teaching hospital. Cellular, Molecular and Biomedical Reports. 2021;1(2):78-87. doi:https://doi.org/10.55705/cmbr.2021.144995.1017
21. Guy CS, Gibson MI, Fullam E. Targeting extracellular glycans: tuning multimeric boronic acids for pathogen-selective killing of Mycobacterium tuberculosis. Chemical Science. 2019;10(23):5935-42. doi:https://doi.org/10.1039/C9SC00415G
22. Wang L, Li S, Yin J, Yang J, Li Q, Zheng W, et al. The Density of Surface Coating Can Contribute to Different Antibacterial Activities of Gold Nanoparticles. Nano Letters. 2020;20(7):5036-42. doi:https://doi.org/10.1021/acs.nanolett.0c01196
23. Alavi M, Adulrahman NA, Haleem AA, Al-Râwanduzi ADH, Khusro A, Abdelgawad MA, et al. Nanoformulations of curcumin and quercetin with silver nanoparticles for inactivation of bacteria. Cellular and Molecular Biology. 2022;67(5):151-6. doi:https://doi.org/10.14715/cmb/2021.67.5.21
24. Boomi P, Ganesan R, Prabu Poorani G, Jegatheeswaran S, Balakumar C, Gurumallesh Prabu H, et al. Phyto-Engineered Gold Nanoparticles (AuNPs) with Potential Antibacterial, Antioxidant, and Wound Healing Activities Under in vitro and in vivo Conditions. International journal of

nanomedicine. 2020;15:7553-68. doi:https://doi.org/10.2147/IJN.S257499
25. Liang X, Liao C, Thompson ML, Soupir ML, Jarboe LR, Dixon PM. E. coli Surface Properties Differ between Stream Water and Sediment Environments. Frontiers in microbiology. 2016;7(1732). doi:https://doi.org/10.3389/fmicb.2016.01732
26. Alavi M, Rai M. Chapter 11 - Antibacterial and wound healing activities of micro/nanocarriers based on carboxymethyl and quaternized chitosan derivatives. In: Rai M, dos Santos CA, editors. Biopolymer-Based Nano Films: Elsevier; 2021. p. 191-201. doi:https://doi.org/10.1016/B978-0-12-823381-8.00009-0
27. Fuster MG, Montalbán MG, Carissimi G, Lima B, Feresin GE, Cano M, et al. Antibacterial Effect of Chitosan-Gold Nanoparticles and Computational Modeling of the Interaction between Chitosan and a Lipid Bilayer Model. Nanomaterials (Basel, Switzerland). 2020;10(12):2340. doi:https://doi.org/10.3390/nano10122340
28. Umapathi A, Pn N, Madhyastha H, Singh M, Madhyastha R, Maruyama M, et al. Curcumin and isonicotinic acid hydrazide functionalized gold nanoparticles for selective anticancer action. Colloids and Surfaces A: Physicochemical and Engineering Aspects. 2020;607:125484. doi:https://doi.org/10.1016/j.colsurfa.2020.125484
29. Bloise N, Massironi A, Della Pina C, Alongi J, Siciliani S, Manfredi A, et al. Extra-Small Gold Nanospheres Decorated With a Thiol Functionalized Biodegradable and Biocompatible Linear Polyamidoamine as Nanovectors of Anticancer Molecules. Frontiers in Bioengineering and Biotechnology. 2020;8. doi:https://doi.org/10.3389/fbioe.2020.00132
30. Arafah A, Rehman MU, Mir TM, Wali AF, Ali R, Qamar W, et al. Multi-Therapeutic Potential of Naringenin (4',5,7-Trihydroxyflavonone): Experimental Evidence and Mechanisms. Plants (Basel, Switzerland). 2020;9(12):1784. doi:https://doi.org/10.3390/plants9121784
31. Al-Khayri JM, Sahana GR, Nagella P, Joseph BV, Alessa FM, Al-Mssallem MQ. Flavonoids as Potential Anti-Inflammatory Molecules: A Review. Molecules. 2022;27(9):2901. doi:https://doi.org/10.3390/molecules27092901
32. Shanmuganathan R, Sathishkumar G, Brindhadevi K, Pugazhendhi A. Fabrication of naringenin functionalized-Ag/RGO nanocomposites for potential bactericidal effects. Journal of Materials Research and Technology. 2020;9(4):7013-9. doi:https://doi.org/10.1016/j.jmrt.2020.03.118
33. Huang X, Bao X, Liu Y, Wang Z, Hu Q. Catechol-Functional Chitosan/Silver Nanoparticle Composite as a Highly Effective Antibacterial Agent with Species-Specific Mechanisms. Scientific Reports. 2017;7(1):1860. doi:https://doi.org/10.1038/s41598-017-02008-4
34. Ahmadi S, Ahmadi G, Ahmadi H. A review on antifungal and antibacterial activities of some medicinal plants. Micro Nano Bio Aspects. 2022;1(1):10-7
35. Mirzaei AR, Shakoory-Moghadam V. Bioinformatics analysis and pharmacological effect of Stevia rebaudiana in the prevention of type-2 diabetes. Cellular, Molecular and Biomedical Reports. 2022;2(2):64-73. doi:https://doi.org/10.55705/cmbr.2022.336232.1035
36. Doosti-Moghaddam M, Miri HR, Ghahghaei A, Haginegd MR, Saboori H. Effect of unripe fruit extract of Momordica charantia on total cholesterol, total triglyceride and blood lipoproteins in the blood of rats with hyperlipidemia. Cellular, Molecular and Biomedical Reports. 2022;2(2):74-86. doi:https://doi.org/10.55705/cmbr.2022.338806.1038
37. Ahmadi S. Antibacterial and antifungal activities of medicinal plant species and endophytes. Cellular, Molecular and Biomedical Reports. 2022;2(2):109-15. doi:https://doi.org/10.55705/cmbr.2022.340532.1042
38. Alavi M, Karimi N. Effect of the simulated dust storm stress on the chlorophyll a fluorescence, Chlorophyll content, Flavonoids and phenol compounds in medicinal plant Thymus vulgaris L. JOURNAL OF PLANT PROCESS AND FUNCTION. 2015;4(13):17-23. doi:http://jispp.iut.ac.ir/article-1-185-en.html
39. Alavi M, Karimi N. Biosynthesis of Ag and Cu NPs by secondary metabolites of usnic acid and thymol with biological macromolecules aggregation and antibacterial activities against multi drug resistant (MDR) bacteria. International Journal of Biological Macromolecules. 2019;128:893-901. doi:https://doi.org/10.1016/j.ijbiomac.2019.01.177
40. Mojtaba Taran MR, Mehran Alavi. Characterization of Ag nanoparticles biosynthesized by Bacillus sp. HAI4 in different conditions and their antibacterial effects: ssue: 11; 2016. 094-9 p
41. Alavi M, Rai M. Topical delivery of growth factors and metal/metal oxide nanoparticles to infected wounds by polymeric nanoparticles: an overview. Expert Review of Anti-infective Therapy. 2020;18(10):1021-32. doi:https://doi.org/10.1080/14787210.2020.1782740
42. Mistry H, Thakor R, Patil C, Trivedi J, Bariya H. Biogenically proficient synthesis and characterization of silver nanoparticles employing marine procured fungi Aspergillus brunneoviolaceus along with their antibacterial and antioxidative potency. Biotechnology

Letters. 2021;43(1):307-16. doi:https://doi.org/10.1007/s10529-020-03008-7
43. Yilmaz MT, İspirli H, Taylan O, Dertli E. Synthesis and characterisation of alternan-stabilised silver nanoparticles and determination of their antibacterial and antifungal activities against foodborne pathogens and fungi. LWT. 2020;128:109497. doi:https://doi.org/10.1016/j.lwt.2020.109497
44. Taran M, Rad M, Alavi M. Characterization of Ag nanoparticles biosynthesized by Bacillus sp. HAI4 in different conditions and their antibacterial effects. J Appl Pharm Sci. 2016;6(11):094-9. doi:https://doi.org/10.7324/JAPS.2016.601115
45. Haq S, Rehman W, Waseem M, Meynen V, Awan SU, Saeed S, et al. Fabrication of pure and moxifloxacin functionalized silver oxide nanoparticles for photocatalytic and antimicrobial activity. Journal of Photochemistry and Photobiology B: Biology. 2018;186:116-24. doi:https://doi.org/10.1016/j.jphotobiol.2018.07.011
46. Malekzadeh M, Yeung KL, Halali M, Chang Q. Preparation and antibacterial behaviour of nanostructured Ag@SiO2–penicillin with silver nanoplates. New Journal of Chemistry. 2019;43(42):16612-20. doi:https://doi.org/10.1039/C9NJ03727F
47. Borowik A, Butowska K, Konkel K, Banasiuk R, Derewonko N, Wyrzykowski D, et al. The Impact of Surface Functionalization on the Biophysical Properties of Silver Nanoparticles. Nanomaterials. 2019;9(7):973. doi:https://doi.org/10.3390/nano9070973
48. Varunkumar K, Anusha C, Saranya T, Ramalingam V, Raja S, Ravikumar V. Avicennia marina engineered nanoparticles induce apoptosis in adenocarcinoma lung cancer cell line through p53 mediated signaling pathways. Process Biochemistry. 2020;94:349-58. doi:https://doi.org/10.1016/j.procbio.2020.04.034
49. Almanghadim HG, Nourollahzadeh Z, Khademi NS, Tezerjani MD, Sehrig FZ, Estelami N, et al. Application of nanoparticles in cancer therapy with an emphasis on cell cycle. Cell Biology International. 2021;45(10):1989-98. doi:https://doi.org/10.1002/cbin.11658
50. Muhammad N, Zhao H, Song W, Gu M, Li Q, Liu Y, et al. Silver nanoparticles functionalized Paclitaxel nanocrystals enhance overall anti-cancer effect on human cancer cells. Nanotechnology. 2020;32(8):085105. doi:https://doi.org/10.1088/1361-6528/abcacb
51. Tobi A, Willmore A-MA, Kilk K, Sidorenko V, Braun GB, Soomets U, et al. Silver Nanocarriers Targeted with a CendR Peptide Potentiate the Cytotoxic Activity of an Anticancer Drug. Advanced Therapeutics. 2021;4(1):2000097. doi:https://doi.org/10.1002/adtp.202000097
52. Mussa Farkhani S, Asoudeh Fard A, Zakeri-Milani P, Shahbazi Mojarrad J, Valizadeh H. Enhancing antitumor activity of silver nanoparticles by modification with cell-penetrating peptides. Artificial Cells, Nanomedicine, and Biotechnology. 2017;45(5):1029-35. doi:https://doi.org/10.1080/21691401.2016.1200059
53. Pędziwiatr-Werbicka E, Gorzkiewicz M, Horodecka K, Abashkin V, Klajnert-Maculewicz B, Peña-González CE, et al. Silver Nanoparticles Surface-Modified with Carbosilane Dendrons as Carriers of Anticancer siRNA. International Journal of Molecular Sciences. 2020;21(13):4647. doi:https://doi.org/10.3390/ijms21134647

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