



OPEN One-pot synthesis of quercetin-functionalized silver and copper nanoparticles for enhanced optical, antimicrobial, and computational properties

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The emergence of multidrug-resistant bacterial strains has intensified the need for novel antimicrobial agents. Herein, we report a facile one-pot green synthesis of quercetin-stabilized silver (Qn@AgNPs) and copper (Qn@CuNPs) nanoparticles using quercetin as both reductant and capping ligand. The resulting nanocomposites were fully characterized by UV–Vis spectroscopy (surface plasmon resonance peaks at 420 nm for Ag and 580 nm for Cu), FTIR (confirming quercetin–metal coordination), SEM/EDX (spherical particles), and XRD (face-centered cubic Ag and Cu phases). Density functional theory (B3LYP/3-21G) calculations yielded frontier molecular orbital gaps of 0.164 eV for Qn@AgNPs and 0.245 eV for Qn@CuNPs, with corresponding high softness values (12.20 and 8.16 eV^{−1}), indicating enhanced electron-transfer propensity. Molecular electrostatic potential maps revealed increased charge polarization around the metal centers. Antibacterial assays against *Escherichia coli* and *Staphylococcus aureus* demonstrated minimum inhibitory concentrations of 2.11 ± 1.22 µg/mL and 4.69 ± 2.68 µg/mL for Qn@AgNPs, and 7.50 ± 0.00 µg/mL and 6.25 ± 0.17 µg/mL for Qn@CuNPs, significantly outperforming free quercetin (188 and 375 µg/mL). In silico docking against the *S. epidermidis* TcaR regulator (PDB: 1KZN) and *E. coli* DNA gyrase B (PDB: 1HSK) revealed strong binding affinities (−7.54 to −10.15 kcal·mol^{−1}), consistent with the observed antimicrobial potency. This integrated experimental–computational study elucidates the mechanistic underpinnings of quercetin-mediated nanoparticle bioactivity and provides a rational framework for designing next-generation flavonoid-functionalized metal nanotherapeutics.

Keywords Nanocomposite, Simulation, Antibacterial, Green synthesis, Docking, DFT

Antibacterial resistance has become a critical global health challenge, as multidrug-resistant strains of *Escherichia coli*, *Staphylococcus aureus* and other pathogens continue to emerge despite extensive antibiotic use^{1–4}. In response, metal nanoparticles particularly silver (AgNPs) and copper nanoparticles (CuNPs) have been intensively explored for their broad-spectrum bactericidal activity, which arises from mechanisms including membrane disruption, generation of reactive oxygen species (ROS), and direct interference with DNA and protein function^{5–7}. Moreover, these nanomaterials can inhibit biofilm formation, interfere with quorum-sensing pathways, and overcome efflux-pump-mediated resistance^{8–10}. Conventional chemical and physical synthesis of AgNPs and CuNPs typically relies on toxic reductants (e.g., NaBH₄) or energy-intensive conditions, posing environmental hazards and limiting biocompatibility¹¹. Green synthesis methods address these drawbacks by employing biological extracts or pure phytochemicals as both reductants and capping agents under ambient conditions^{12,13}. Notably, plant species from mineral-rich geothermal areas exhibit enhanced secondary-metabolite profiles, which can further boost nanoparticle yield and stability¹⁴. Among phytochemicals, quercetin stands out as a versatile bioreductant and capping ligand. Its multiple hydroxyl groups and carbonyl moieties confer

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strong metal-chelating ability and electron-donating capacity, yielding monodisperse Qn@AgNPs and Qn@CuNPs with enhanced colloidal stability and controlled ROS modulation^{15–18}. Recent studies have highlighted the continued potential of quercetin-functionalized metal nanoparticles in biomedical applications. Quercetin-modified AgNPs synthesized using plant extracts showed excellent biocompatibility and antibacterial activity¹⁹, while quercetin–metal complexes demonstrated strong antimicrobial effects against resistant strains through membrane disruption and DNA binding²⁰. Similar approaches using Ag or Au nanoparticles functionalized with quercetin have also shown improved anticancer selectivity and reduced toxicity in normal cells^{21,22}. Quercetin binding to AgNPs has also been shown to improve the aqueous solubility of the flavonoid and enhance the antibacterial potency of the nanoparticles²³. Recent work by Li et al. first demonstrated that quercetin-coated AgNPs exhibit significantly greater antibacterial efficacy against *E. coli* and *S. aureus* than bare AgNPs, attributing this to synergistic metal–flavonoid interactions that enhance membrane affinity and ion release control²⁴. Kemala et al. subsequently optimized the green fabrication of AgNPs using *Lantana camara* leaf extract rich in quercetin analogues achieving precise control over nanoparticle size and morphology via response-surface methodology²⁵. Fungal-mediated approaches have likewise produced both Ag and Cu nanomaterials with high yields and intrinsic biomolecular capping, underscoring the versatility of biogenic routes^{26,27}. Despite extensive experimental investigations of quercetin-functionalized metal nanoparticles, comprehensive computational studies remain scarce. Density Functional Theory (DFT) can yield global reactivity descriptors frontier orbital energies, chemical hardness/softness, and molecular electrostatic potentials that correlate with nanoparticle redox behavior and interaction propensity^{28,29} [1–10]. Molecular docking against clinically relevant bacterial targets (e.g., the *S. epidermidis* TcaR regulator, PDB ID 1KZN³⁰ and the *E. coli* DNA gyrase B subunit, PDB ID 1HSK³¹), can reveal key ligand-residue interactions hydrogen bonding, π – π stacking, and metal coordination that underpin enzymatic inhibition^{32,33}. To date, however, no study has systematically combined quercetin-mediated green synthesis of both AgNPs and CuNPs with DFT reactivity profiling and protein-docking analyses to fully elucidate the mechanistic basis of their antibacterial action. The aim of the present study, is building on these gaps, we report a one-pot, quercetin-mediated green synthesis of Qn@AgNPs and Qn@CuNPs, optimized with respect to pH and quercetin-to-metal ratio following methodologies of Kemala et al.²⁵. We undertake comprehensive physicochemical characterization (UV–Vis SPR, FTIR, SEM/EDX, and XRD), evaluate antimicrobial efficacy against *E. coli* and *S. aureus* via minimum inhibitory concentration assays and integrate DFT-derived global reactivity descriptors with in silico molecular docking against bacterial proteins, so this combined experimental–computational framework aims to provide mechanistic insight and guide the rational design of next-generation flavonoid-functionalized metal nanotherapeutics.

Materials and methods

Materials

Silver nitrate (AgNO_3), copper(II) nitrate trihydrate ($\text{Cu}(\text{NO}_3)_2 \cdot 3 \text{H}_2\text{O}$), glacial acetic acid (CH_3COOH), sodium carbonate (Na_2CO_3), ethanol, and quercetin were obtained from Sigma-Aldrich (St. Louis, MO, USA) and used as received without further purification. Potassium bromide (KBr, FTIR grade) was used for infrared spectroscopy analysis. Mueller Hinton Agar (MHA) and Sabouraud Dextrose Agar (SDA) media were purchased from HiMedia Laboratories (Mumbai, India) for antibacterial assessments. Distilled water served as the solvent for synthesis and preparation.

Green synthesis of silver nanoparticles (AgNPs) using Quercetin

The biosynthesis of silver nanoparticles was carried out using quercetin as a natural reducing and stabilizing agent²⁵. Initially, a 0.01 M silver nitrate (AgNO_3) solution was prepared by dissolving 0.1699 g of AgNO_3 (Merck, analytical grade) in 100 mL of distilled water. The solution was stored in a dark container covered with aluminum foil to prevent photodegradation. Separately, a 0.01 M solution of quercetin was prepared by dissolving 0.3022 g of quercetin (Sigma-Aldrich, $\geq 95\%$) in 100 mL of absolute ethanol under constant stirring until complete dissolution was achieved. For the nanoparticle synthesis, 10 mL of quercetin solution was added to each of four beakers, followed by the dropwise addition of 10 mL of AgNO_3 solution under magnetic stirring. The reaction mixtures were stirred continuously for 4 h at room temperature to facilitate the reduction of Ag^+ ions. To investigate the effect of pH on nanoparticle formation, the pH of the solutions was adjusted to pH 3, 7, 9, and 11 using 0.01 M sodium carbonate (Na_2CO_3) and 0.01 M acetic acid (CH_3COOH). Among the tested conditions, pH 9 was found to be optimal for the synthesis of stable and high-yield silver nanoparticles. Upon completion of the reaction, the colloidal AgNP solutions were centrifuged at 4000 rpm for 30 min to separate the nanoparticles. The resulting pellets were washed several times with distilled water to remove any unreacted precursors and residual quercetin. The purified nanoparticles were dried in an oven using a watch glass and stored at room temperature for subsequent characterization and antimicrobial testing.

Green synthesis of copper nanoparticles (CuNPs) using Quercetin

Copper nanoparticles were synthesized following a procedure analogous to that of AgNPs, using quercetin as a green reductant²⁵. A 0.01 M copper(II) nitrate trihydrate ($\text{Cu}(\text{NO}_3)_2 \cdot 3 \text{H}_2\text{O}$) solution was freshly prepared by dissolving 0.2416 g of the salt in 100 mL of distilled water. Concurrently, 0.3022 g of quercetin was dissolved in 100 mL of absolute ethanol to yield a 0.01 M quercetin solution. For the synthesis process, 10 mL of quercetin solution was placed in each of four separate beakers. Subsequently, 10 mL of 0.01 M $\text{Cu}(\text{NO}_3)_2 \cdot 3 \text{H}_2\text{O}$ solution was added dropwise under magnetic stirring. The reaction mixtures were stirred homogeneously for 4 h at ambient temperature to enable the bioreduction of Cu^{2+} ions. To assess the effect of pH, the pH of the reaction mixtures was adjusted to 3, 7, 9, and 11 using 0.01 M Na_2CO_3 and 0.01 M CH_3COOH . It was observed that nanoparticle formation was most favorable at pH 9, yielding more stable and well-dispersed CuNPs. Post-synthesis, the colloidal copper nanoparticle suspensions were centrifuged at 4000 rpm for 30 min. The

nanoparticle pellets were then washed thoroughly with distilled water to eliminate excess reactants and ethanol. The purified CuNPs were dried using a laboratory oven and stored in airtight containers at room temperature for subsequent characterization and bioactivity evaluation.

Characterization of synthesized quercetin, qn@agnps and qn@cunps

The synthesized silver and copper nanoparticles were subjected to comprehensive physicochemical characterization using multiple analytical techniques. The optical properties of the nanoparticles were analyzed using a high-performance UV–Vis spectrophotometer (Shimadzu, UV-1800, Japan), operating in the wavelength range of 300–700 nm with a 1 nm resolution. Absorption measurements were performed on freshly prepared colloidal dispersions using 1 cm path length quartz cuvettes. Distilled water and ethanol served as blanks for the AgNP and CuNP samples, respectively. Fourier-transform infrared (FTIR) spectroscopy was employed to identify the potential functional groups involved in the reduction and stabilization of the nanoparticles by quercetin. FTIR spectra were recorded using a One Spectrum FTIR Spectrometer (PerkinElmer, USA). For solid-state nanoparticles, KBr pellets were used in diffuse reflectance mode, while colloidal nanoparticles were analyzed using NaCl salt plates. The morphological features and surface topography of the nanoparticles were examined using Scanning Electron Microscopy (SEM) (Carl Zeiss EVO MA 10, Germany), operated at an accelerating voltage of 5–10 kV with a working distance of 5–13 mm and an emission current of 75–80 μ A. Elemental composition was confirmed using Energy-Dispersive X-ray Spectroscopy (EDX) coupled with SEM, operating at 127 keV and 20 μ A. The crystalline structure and phase purity of AgNPs, and CuNPs, were evaluated using X-ray Diffraction (XRD) analysis. XRD patterns were obtained using a drop-coated film method on a glass substrate, scanned over a 2θ range of 10° – 80° at room temperature. The average scanning duration was 2 h to ensure adequate peak resolution. UV–Vis and FTIR analyses were performed at Firat University (Elazığ, Turkey), while XRD, SEM, and EDX analyses were conducted at MUNZUR University Central Laboratory (Tunceli, Turkey).

Antimicrobial activity assay

The antimicrobial efficacy of the green synthesized Quercetin, Qn@AgNPs and Qn@CuNPs was evaluated against two bacterial strains, *Escherichia coli* (Gram-negative) and *Staphylococcus aureus* (Gram-positive), using the standard broth microdilution method. The assay was designed to determine the Minimum Inhibitory Concentration (MIC), which is defined as the lowest concentration of nanoparticles required to inhibit visible bacterial growth³⁴. Colloidal suspensions of nanoparticles (0.015 g) were serially diluted in nutrient broth to create a concentration gradient. Fresh overnight cultures of *E. coli* and *S. aureus* were inoculated into each dilution tube, and all samples were incubated at 37 °C for 24 h under aerobic conditions with shaking. Post-incubation, turbidity (indicative of bacterial growth) and clarity (indicative of growth inhibition) were visually assessed. The transition point between clear and turbid tubes was recorded as the MIC. At the MIC, a reduction of up to 6-log CFU/mL of both *E. coli* and *S. aureus* was observed, corresponding to a 99.9999% bacterial kill rate, indicating potent bactericidal activity. Additionally, growth inhibition was quantitatively confirmed by measuring the optical density at 600 nm (OD₆₀₀) using a UV-Visible spectrophotometer (Shimadzu UV-1800, Japan), comparing treated samples to untreated control cultures. All antimicrobial tests were performed in triplicate to ensure reproducibility and accuracy.

Computational studies

Geometry optimization

In computational chemistry, quantum mechanical methods are fundamental for predicting molecular orbital configurations and electrostatic potential distributions. In this study, geometry optimization and structural refinement of all synthesized compounds were carried out using the Gaussian 09 software suite. The calculations employed Density Functional Theory (DFT) utilizing the 3-21G basis set in combination with Becke's exchange and Lee–Yang–Parr (LYP) correlation functionals (BLYP)³⁵. To simulate a more realistic chemical environment, water was selected as the solvent medium during the optimization phase. Following convergence, a range of global chemical reactivity descriptors were computed based on Koopmans' theorem and the conceptual DFT framework proposed by Parr and Pearson. These descriptors, along with their respective computational formulas, are detailed in the Supplementary Materials (Eqs. 1–6) and provide insight into the electronic behavior and reactivity of the studied nanocomposites.

Computational analysis of molecular Docking

To gain insight into the molecular basis of the antibacterial activity observed experimentally, we carried out in silico docking of quercetin (a) and its Ag- and Cu-based nanocomposites (b–e) against two bacterial target proteins, the *Staphylococcus aureus* transcriptional regulator TcaR (PDB ID: 1KZN) and the *Escherichia coli* DNA gyrase B subunit (PDB ID: 1HSK). All docking studies were performed using the Molecular Operating Environment software (MOE-Dock 2015.10)^{36,37}. At the ligand preparation, the 3D structures of compounds a–e were constructed within MOE using the “Build” module. Each ligand was protonated at physiological pH (7.4), and partial charges were assigned, also energy minimization was then carried out with the MMFF94x force field until the root-mean-square gradient fell below 0.01 kcal·mol^{−1}·Å^{−1}. In the protein preparation, crystal structures of 1KZN (resolution 2.00 Å) and 1HSK (resolution 1.95 Å) were retrieved from the RCSB Protein Data Bank, then water molecules and co-crystallized ions were removed, hydrogens were added, and protonation states were assigned using MOE's Protonate3D algorithm, then the structures were subjected to a restrained energy minimization using the AMBER99 force field to relieve any steric clashes while preserving the overall fold. For Active-site identification, the potential binding cavities were located with the MOE Alpha Site Finder. For 1KZN, the known tetracycline-binding pocket at the helix–turn–helix domain was selected; for 1HSK, the ATP-binding

cleft of the GHKL domain was chosen. Finally in the docking protocol, the ligands were docked into each active site using MOE-Dock's default settings, placement by Triangle Matcher, initial scoring with London dG, followed by rigid-receptor refinement of the top 30 poses, and rescoring with GBVI/WSA dG, also for each ligand–protein pair, the five lowest-energy poses were retained for analysis. In the validation, to verify the reliability of our protocol, the co-crystallized ligand from each PDB entry was re-docked into its native site, also the resulting RMSD between the heavy-atom coordinates of the re-docked and crystal conformations was 1.42 Å for 1KZN and 1.78 Å for 1HSK (both < 2 Å), confirming the accuracy of the docking procedure. In the analysis of docking results, the binding affinities (ΔG binding) and key ligand–residue interactions (hydrogen bonds, π – π stacking, and metal coordination) were examined for the top-scoring pose of each compound, finally the comparative analysis across quercetin and its nanocomposites allowed us to rationalize the enhanced antibacterial potency of structures b and c in terms of favorable chelation to active-site residues, augmented hydrophobic contacts, and, where applicable, metal–protein coordination.

Results and discussion

Optical properties and UV–Vis spectroscopy of the functionalized Quercetin AgNPs and CuNPs

In the present study, silver and copper nanoparticles (AgNPs and CuNPs) were successfully synthesized using a green, rapid one-pot method, employing quercetin as both a reducing and stabilizing agent. Quercetin, a plant-derived flavonoid known for its potent antioxidant and pharmacological activities, was selected due to the presence of biologically active functional groups such as hydroxyl, carbonyl, and aromatic rings³⁸. These functional moieties not only contribute to its redox potential but also facilitate the bioreduction of metal ions and the stabilization of the resulting nanoparticles. Among various synthetic routes available for nanoparticle production—including physical, chemical, biological, and green approaches—the green synthesis pathway offers significant advantages^{39,40}. It avoids the use of toxic chemicals, is environmentally benign, and is cost-effective, making it highly desirable for biomedical and pharmaceutical applications. The formation of quercetin-functionalized AgNPs and CuNPs (denoted as Qn@AgNPs and Qn@CuNPs, respectively) was visually confirmed by a distinct color change in the reaction mixtures. Specifically, a transition from yellow to dark brown indicated the formation of Qn@AgNPs (**Figure.S3**), while a shift from blue-green to deep yellow suggested the formation of Qn@CuNPs (**Figure.S4**)^{41,42}. These color changes are characteristic of localized surface plasmon resonance (LSPR) phenomena, which arise due to the collective oscillation of conduction electrons on the nanoparticle surface upon interaction with incident light⁴³. LSPR is highly sensitive to particle size, shape, composition, and dielectric environment, and thus serves as an effective indicator of nanoparticle formation⁴⁴. UV-Visible spectroscopy was employed as the primary technique to monitor the synthesis and assess the optical properties of the nanoparticles. As shown in Fig. 1, the absorption spectra of pure quercetin, Qn@AgNPs, and Qn@CuNPs revealed distinct surface plasmon resonance (SPR) peaks at 373.59 nm, 487.96 nm, and 472.82 nm, respectively, so these findings are consistent with previous literature reports (Pandian et al., 2018) and confirm the successful synthesis and colloidal stability of the nanoparticles in aqueous solution. The rapid bioreduction of Ag^+ and Cu^{2+} ions to their metallic forms (Ag^0 and Cu^0) were facilitated by the electron-donating capacity of quercetin's hydroxyl and carbonyl groups. These functional groups not only drive the reduction reaction but also play a crucial role in capping and stabilizing the nanoparticles, thus preventing aggregation and controlling size distribution. The uniformity and stability of the synthesized Qn@AgNPs and Qn@CuNPs were further confirmed by a series of characterization techniques, including FT-IR, SEM, EDX, and XRD, which collectively verified the formation of well-dispersed, functionalized nanocomposites.

FTIR study

FTIR spectroscopy was employed to confirm the functionalization of silver and copper nanoparticles with quercetin and to understand the nature of interactions between the metal ions and the phytochemical ligands. The FTIR spectrum of pure quercetin, shown in Fig. 2(a), displays prominent absorption bands at 3371 and 3298 cm^{-1} , attributed to O–H stretching vibrations of free hydroxyl and catechol–hydroxyl groups⁴⁵. These bands are particularly intense due to the presence of strong intramolecular hydrogen bonding within the quercetin molecule, as illustrated in Scheme 1. This hydrogen bonding network also contributes to the broad absorption profile observed between 3300 and 3450 cm^{-1} . Additional characteristic bands include C–H stretching and bending at ~ 2920 and ~ 1452 cm^{-1} , C=O stretching of the conjugated ketone group at ~ 1665 cm^{-1} , and C–O stretching of the ether group around ~ 1095 cm^{-1} ⁴⁶. After the formation of Ag-quercetin and Cu-quercetin nanocomposites, the FTIR spectra (shown in Fig. 2(b) and 2(c), respectively) reveal key changes that support the successful synthesis of the metal–quercetin composites. The broad O–H stretching band becomes less intense and shifts slightly to 3415 cm^{-1} (AgNPs) and 3462 cm^{-1} (CuNPs). This decrease in intensity and broadness is indicative of reduced hydrogen bonding, which results from the formation of new metal–oxygen (M–O) bonds as the hydroxyl groups of quercetin coordinate with silver and copper ions (Fig. 3), so this interaction effectively disrupts the original intramolecular hydrogen bonding present in pristine quercetin, confirming the role of hydroxyl groups in metal complexation and stabilization of the nanoparticles. Furthermore, the peaks corresponding to C=O stretching (~ 1642 cm^{-1} for AgNPs and ~ 1640 cm^{-1} for CuNPs) and C–H stretching (~ 2924 – 2930 cm^{-1}) remain largely unchanged, suggesting that the carbonyl and alkyl groups are not directly involved in the metal binding. Another notable observation is the disappearance of the split peaks near 814 cm^{-1} , which are characteristic of out-of-plane C–H bending vibrations in the ortho-dihydroxy-substituted benzene ring. Their absence in the nanocomposite spectra indicates that the catechol hydroxyl groups are involved in the coordination with metal ions, thus supporting the chelation mechanism, so these collective spectral modifications confirm the successful functionalization of Ag and Cu nanoparticles with quercetin, also the observed shift and reduction in the O–H band, along with the disappearance of dihydroxy-associated vibrations, provide strong

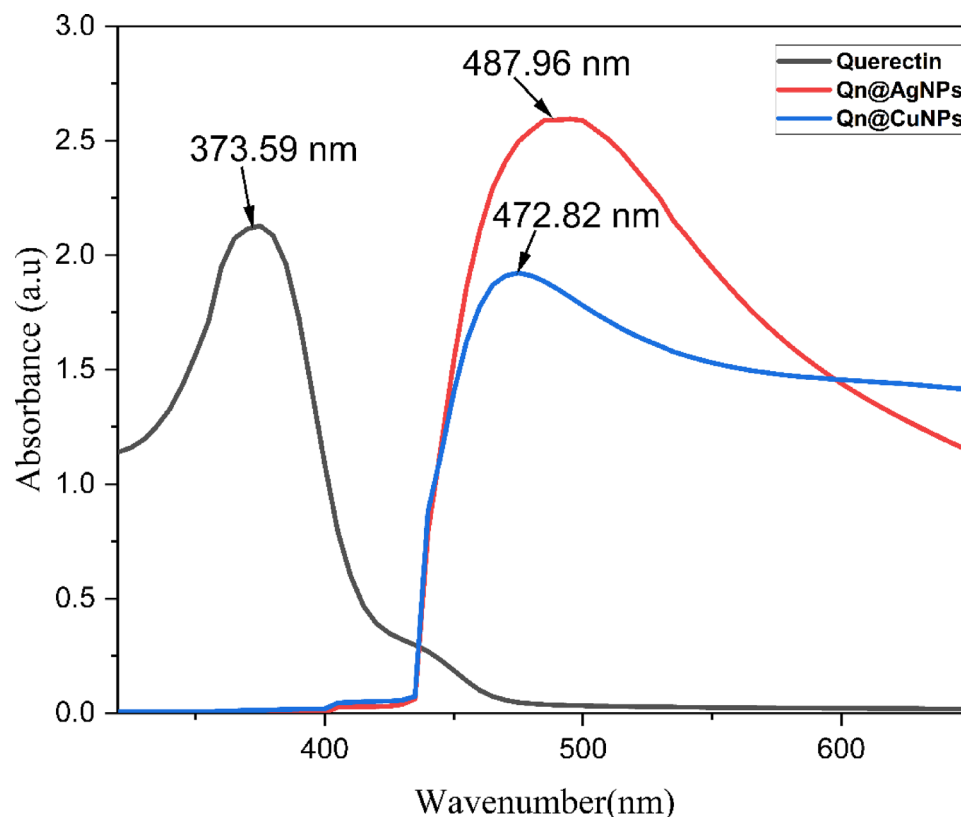


Fig. 1. UV-Vis spectra of quercetin, Qn@AgNPs and Qn@CuNPs, highlighting SPR peaks at 373.6, 487.9 and 472.8 nm.

evidence of metal–ligand interaction via the hydroxyl moieties of quercetin, leading to the formation of stable quercetin-metal nanocomposites.

Morphological and elemental characterization of qn@agnps and qn@cunps nanocomposites

The morphological features, particle size distribution, and elemental composition of the synthesized quercetin-functionalized silver and copper nanoparticles (Qn@AgNPs and Qn@CuNPs) were comprehensively analyzed using Scanning Electron Microscopy (SEM), Energy Dispersive X-ray Spectroscopy (EDX), and elemental mapping techniques.

SEM analysis

The SEM micrographs of Qn@AgNPs, presented in Fig. 4(a) at magnifications of 500 μm , Fig. 4(b) 50 μm , and Fig. 4(c) 5 μm , respectively, revealed that at lower magnifications, the nanocomposites exhibit large, well-defined cubic plate-like structures with smooth and continuous surfaces. These morphological features suggest the formation of homogeneously distributed composites, indicative of efficient nucleation and stabilization by quercetin molecules during synthesis. At higher magnification (5 μm), the SEM images showed that the surface morphology transitions into uniformly dispersed spherical nanoparticles embedded within the larger matrix, consistent with a nanoscale architecture. This nanoscale formation is further supported by the particle size distribution analysis (Fig. 4(d)), which shows that the majority of particles ranged from 40 to 200 nm, with a calculated mean diameter of approximately 113.9 nm. This size range aligns closely with previously reported results for green-synthesized AgNPs using plant-based reductants, confirming the successful generation of nanoscale Ag structures. Similarly, the SEM analysis of Qn@CuNPs (Fig. 4(i)) displayed spherical nanoparticles with a significantly reduced mean particle size of 66.7 nm (Fig. 4(m)), demonstrating a finer and more compact distribution compared to the Qn@AgNPs. This observed reduction in particle size may be attributed to stronger complexation and capping interactions between copper ions and quercetin molecules, resulting in tighter growth regulation and enhanced dispersion.

EDX and elemental mapping

To elucidate the elemental composition of the synthesized nanocomposites, EDX spectroscopy was employed. For Qn@AgNPs, the EDX spectrum (Fig. 4(e)) confirmed the dominant presence of silver, accounting for 93.6 wt%, along with carbon and oxygen as minor constituents, which correspond to the quercetin capping and stabilizing layers. The high silver content and relatively lower organic signals suggest an effective reduction process and a thin organic coating. The elemental mapping analysis (Fig. 4(f–i)) further demonstrated the uniform distribution of Ag, C, and O elements throughout the nanocomposite, corroborating the successful surface functionalization

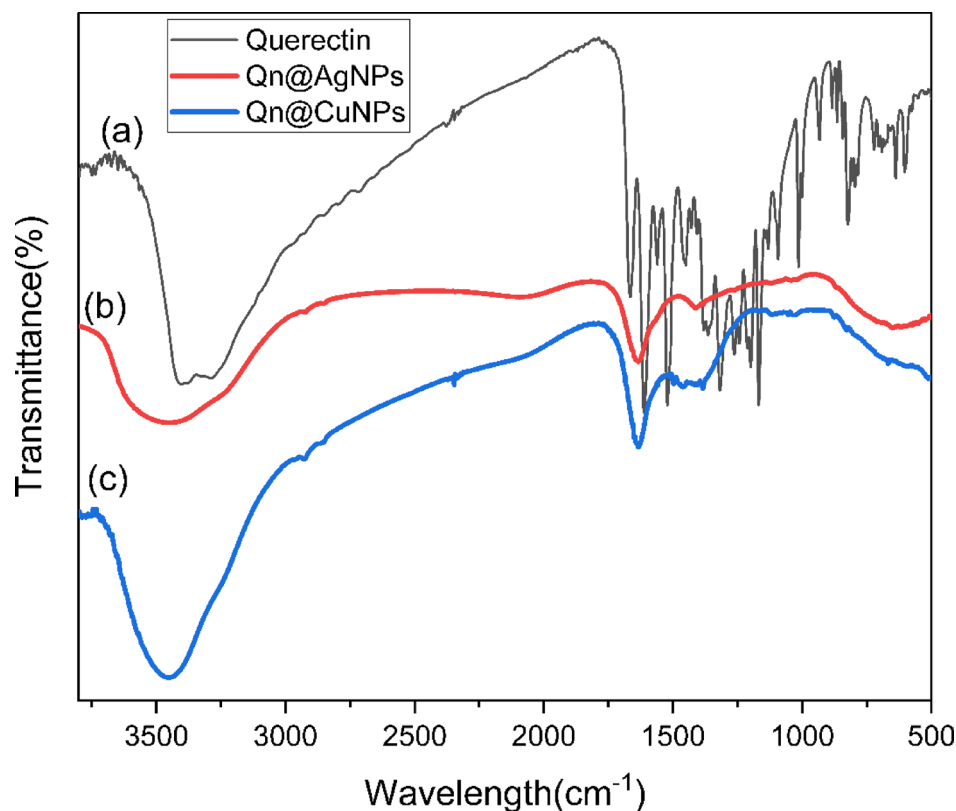


Fig. 2. FTIR spectra of quercetin, Qn@AgNPs and Qn@CuNPs.

and stabilization of AgNPs by quercetin. The even spatial dispersion of these elements provides strong evidence of compositional homogeneity and structural integrity at the nanoscale. In the case of Qn@CuNPs, EDX analysis (Fig. 4(n)) revealed a significantly different elemental distribution. Copper was detected at 18.8 wt%, while carbon and oxygen constituted 44.6 wt% and 34.1 wt%, respectively. Compared to Qn@AgNPs, the relatively lower copper content and higher organic composition suggest that a larger amount of quercetin was required to reduce and stabilize Cu^{2+} ions, likely due to the different redox potentials and coordination chemistry of copper. This observation aligns with the proposed molecular interaction model illustrated in Scheme 1, where quercetin's catechol moieties play a critical role in metal ion chelation and reduction. Furthermore, elemental mapping of Qn@CuNPs (Fig. 4(o–r)) confirmed the homogeneous distribution of Cu, C, and O elements across the composite matrix, supporting the formation of well-dispersed, functionalized nanostructures. Collectively, the SEM and EDX results provide compelling evidence for the successful green synthesis of quercetin-mediated Ag and Cu nanocomposites, with controlled morphology, nanoscale particle sizes, and uniform elemental distribution. The data also highlight the distinct differences in particle size and quercetin loading between Ag and Cu systems, which can be attributed to their unique redox behaviors and binding affinities with phytochemical ligands.

XRD analysis of qn@agnps and qn@cunps nanocomposites

X-ray diffraction (XRD) is a vital analytical technique used to investigate the crystallographic structure, phase purity, and average crystallite size of synthesized nanomaterials, so in the present study, XRD analysis was performed to confirm the crystalline nature and phase identification of the quercetin-functionalized silver and copper nanoparticles (Qn@AgNPs and Qn@CuNPs). The XRD pattern of Qn@AgNPs, shown in Fig. 5(a), exhibited a series of well-defined diffraction peaks at 2θ values of 34.02° , 38.06° , 44.24° , 64.44° , 77.38° , and 81.54° , corresponding to the crystallographic planes (122), (111), (200), (220), (311), and (222), respectively, so these diffraction peaks are in good agreement with the standard face-centered cubic (fcc) crystal structure of metallic silver, as indexed to the Joint Committee on Powder Diffraction Standards (JCPDS Card No. 04-0783)⁴⁷. The (111) reflection exhibited the highest intensity, which is characteristic of the preferred orientation of AgNPs and indicative of high crystallinity and well-ordered atomic arrangement at the nanoscale. The sharpness and intensity of the peaks further confirm the presence of highly crystalline silver nanoparticles, synthesized via the green reduction capability of quercetin. Notably, no additional peaks attributable to secondary phases or impurities were detected, suggesting the high phase purity of the synthesized nanocomposites. The consistency of the observed XRD pattern with earlier reports of green-synthesized AgNPs confirms the reliability of the employed eco-friendly synthetic approach^{48,49}. The XRD pattern of Qn@CuNPs, depicted in Fig. 5(b), displayed two primary diffraction peaks located at $2\theta = 27.44^\circ$ and 42.77° , which correspond to the crystallographic planes (112) and (111), respectively. These reflections are consistent with the body-centered cubic (bcc) structure of

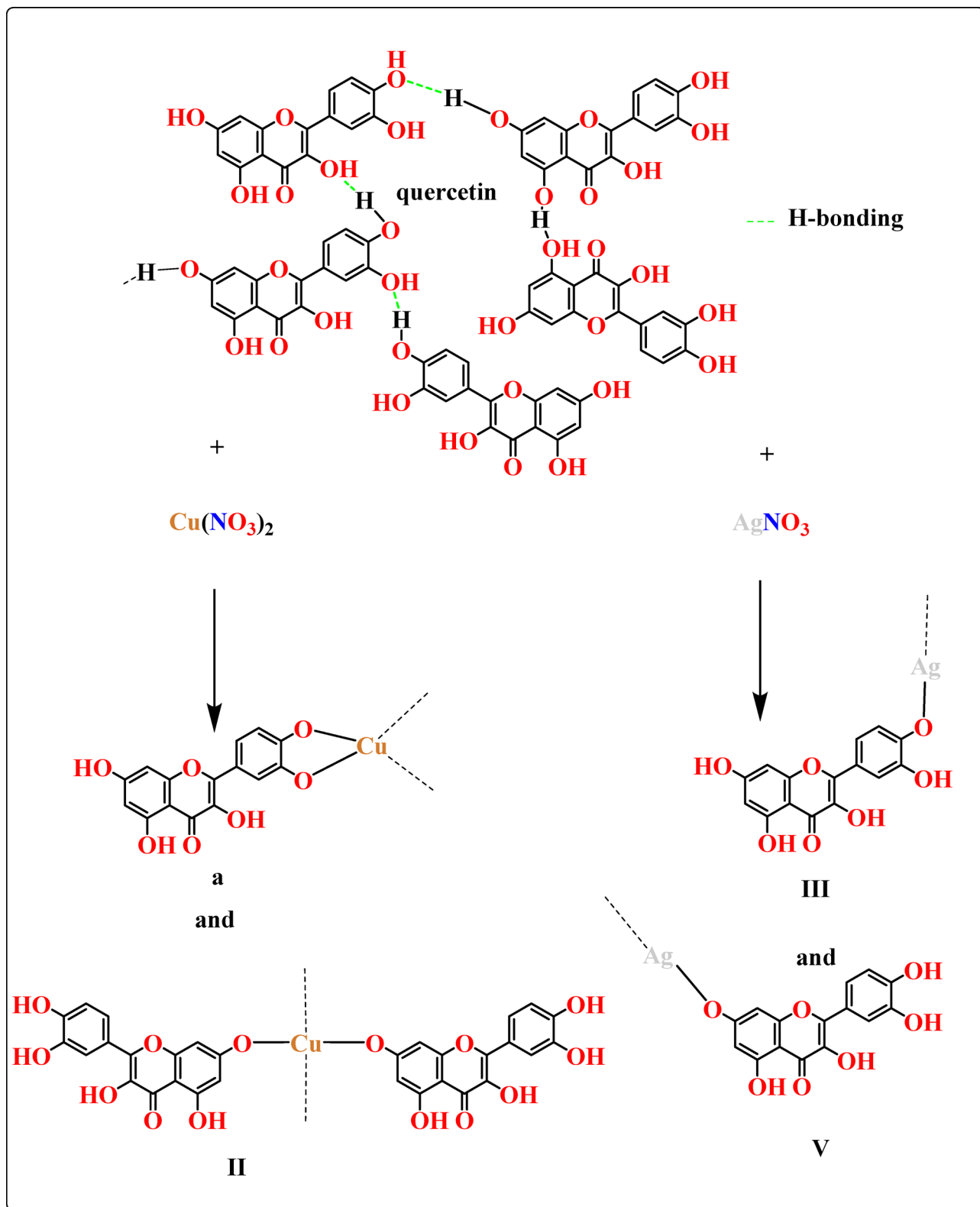


Fig. 3. Schematic diagram of synthesized nanocomposites.

copper nanoparticles and match the standard pattern described in JCPDS Card No. 89-2838⁵⁰. The peak at 27.44° appeared significantly broadened, indicating partial amorphous character likely induced by the presence of a large excess of quercetin molecules adsorbed onto the nanoparticle surface. This amorphous contribution may be attributed to the organic capping and stabilization effect provided by quercetin, which limits long-range crystal order in certain domains. Despite the lower peak intensities compared to Qn@AgNPs, the presence of

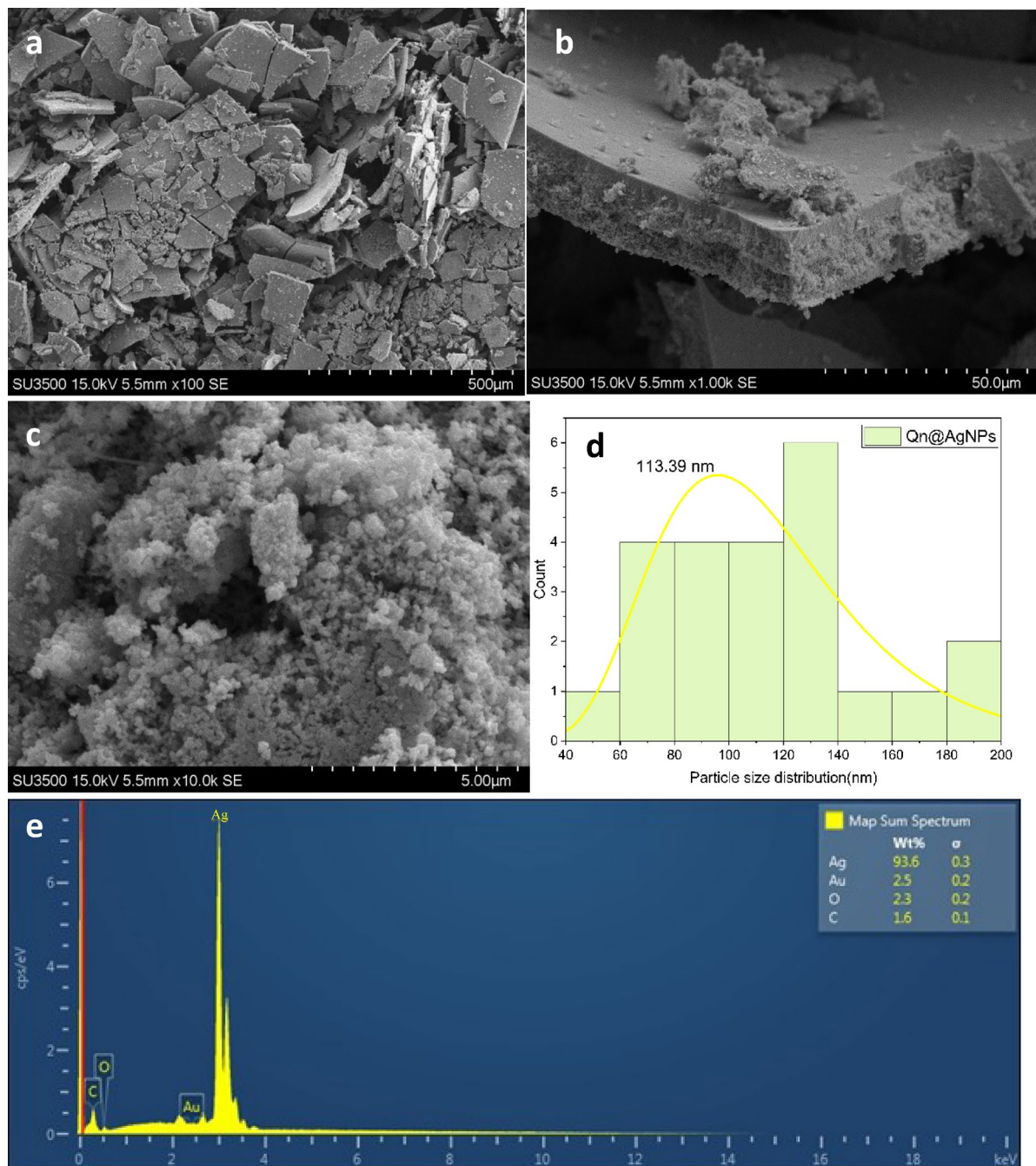


Fig. 4. SEM images of Qn@AgNPs (a–c), particle size distribution (d), EDX spectrum (e), and elemental mapping (f–i); SEM of Qn@CuNPs (j–l), particle size (m), EDX (n), and elemental mapping (o–r).

characteristic copper diffraction planes confirms successful reduction of Cu^{2+} ions and formation of crystalline CuNPs. The findings are in line with previous studies reporting the green synthesis of CuNPs with partial crystallinity due to strong organic surface functionalization^{51,52}. Collectively, the XRD analysis validates the successful formation of crystalline silver and copper nanoparticles functionalized with quercetin. The distinct differences in peak broadening and intensity between the two systems reflect their unique crystallization behavior, metal-ligand interactions, and the influence of quercetin on particle nucleation and growth.

Antimicrobial activity of qn@agnps and qn@cupns

The antimicrobial efficacy of the biosynthesized nanocomposites Qn@AgNPs and Qn@CuNPs was evaluated against two clinically significant bacterial strains, *Escherichia coli* (Gram-negative) and *Staphylococcus aureus* (Gram-positive) (Figure S1, Table 1). The minimum inhibitory concentration (MIC), defined as the lowest concentration of material required to achieve a 6-log reduction (99.9999% kill rate) in bacterial load, was determined using the standard broth microdilution technique, based on turbidity assessment following 24-hour

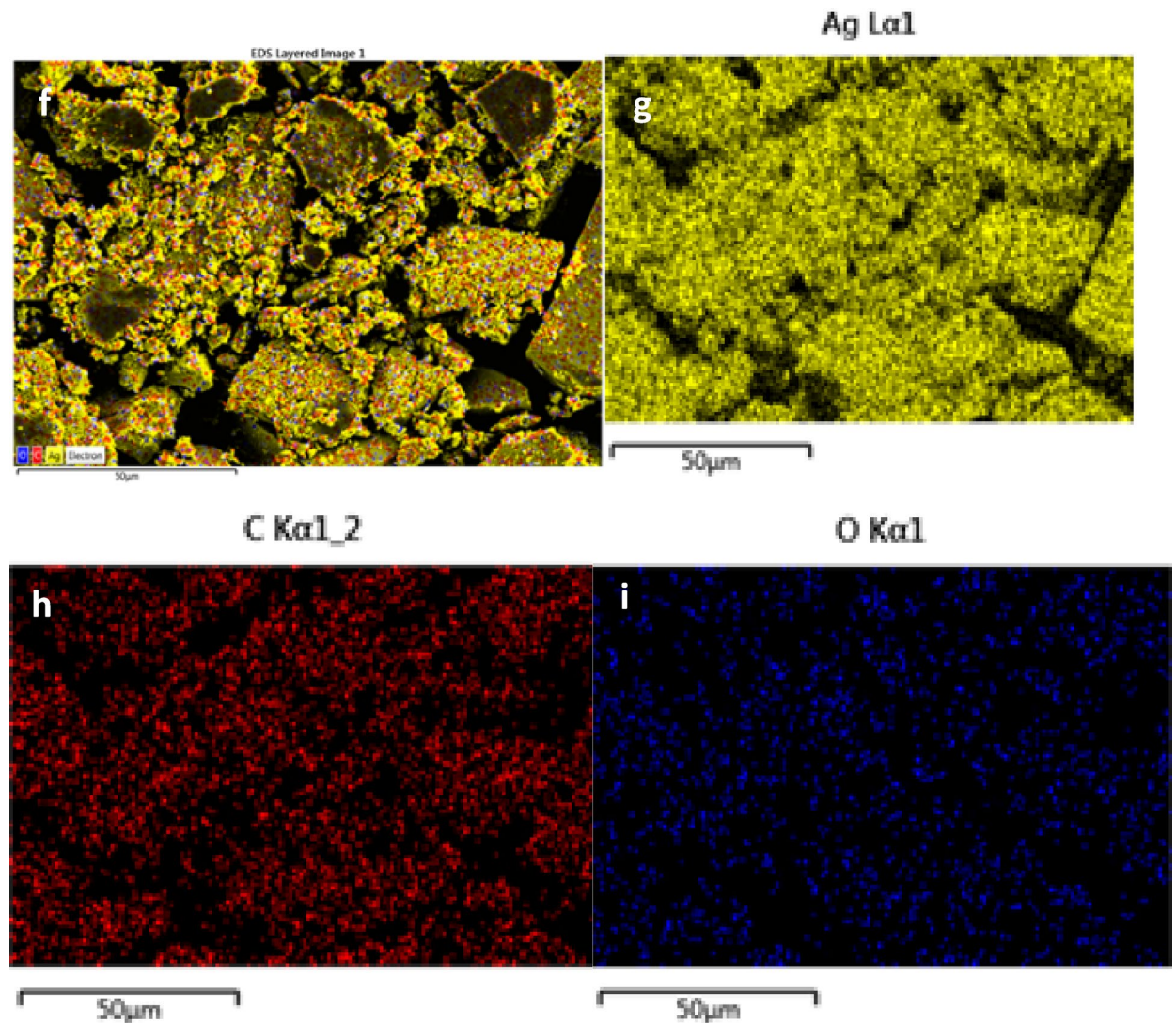


Fig. 4. (continued)

incubation at 37 °C. The Qn@AgNPs nanocomposite exhibited potent antibacterial activity with MIC values of 2.11 ± 0.22 $\mu\text{g/mL}$ for *E. coli* and 4.69 ± 2.68 $\mu\text{g/mL}$ for *S. aureus*, indicating a significantly lower effective dose compared to its individual components. In contrast, pure quercetin required substantially higher concentrations 188 ± 0.81 $\mu\text{g/mL}$ for *E. coli* and 375 ± 1.62 $\mu\text{g/mL}$ for *S. aureus* to achieve comparable antibacterial effects. Similarly, silver ions (Ag^+) alone showed MIC values of 26 ± 9 $\mu\text{g/mL}$ and 21 ± 0.9 $\mu\text{g/mL}$ for *E. coli* and *S. aureus*, respectively. For Qn@CuNPs, the MIC values were 7.50 ± 0.00 $\mu\text{g/mL}$ for *E. coli* and 6.25 ± 0.17 $\mu\text{g/mL}$ for *S. aureus*. Again, these values were markedly lower than those required for the corresponding uncoordinated species: quercetin (188 ± 0.81 $\mu\text{g/L}$ and 375 ± 1.62 $\mu\text{g/mL}$) and copper ions (Cu^{2+} : 2832 ± 1.98 $\mu\text{g/mL}$ and 1416 ± 0.91 $\mu\text{g/mL}$) against *E. coli* and *S. aureus*, respectively. A comparative analysis revealed that Qn@AgNPs required the lowest MIC values among all tested agents, highlighting superior antibacterial potency, especially against Gram-negative *E. coli*. This enhanced activity can be attributed to the synergistic effect between the antimicrobial properties of silver and the biofunctional capping offered by quercetin. The phenolic and hydroxyl groups in quercetin may facilitate better nanoparticle stabilization and promote membrane interaction, improving the bioavailability and cellular penetration of silver and copper species. The functionalization of nanoparticles with quercetin not only improved the antimicrobial efficacy but also suggests a promising route for drug delivery applications. The organic shell formed by quercetin provides a biocompatible and versatile platform for loading additional antibacterial agents or therapeutic molecules. Therefore, these nanocomposites can potentially serve as dual-function systems, combining intrinsic antibacterial activity with drug-loading capabilities for targeted therapeutic interventions.

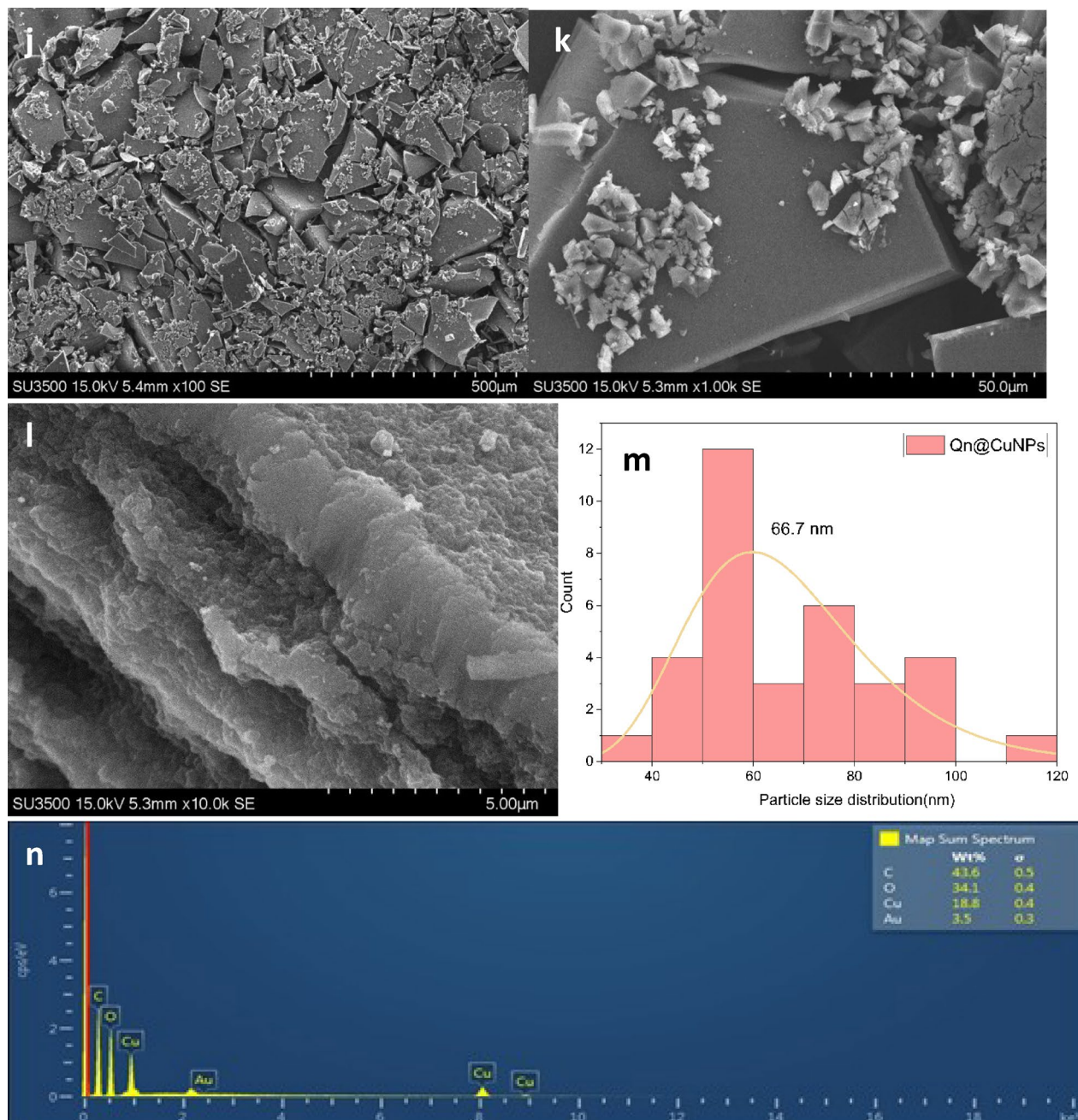


Fig. 4. (continued)

Computational studies

Frontier molecular orbital analysis

To model the electronic behavior of the synthesized nanocomposites, we constructed simplified molecular structures (b–e) representing quercetin coordinated with either Ag^+ or Cu^{2+} ions at different sites, so these models reflect the coordination modes suggested by FTIR and EDX data specifically, the interaction of catechol hydroxyl groups and carbonyl moieties with the metal centers. Structures b and c simulate 1:1 complexes of quercetin with Ag and Cu, respectively, corresponding to the experimentally optimized formulations. Structures d and e include extended coordination or bimetallic configurations to explore how additional binding or aggregation influences electronic properties, so these theoretical constructs are not exact replicas of entire nanoparticles but serve as representative molecular fragments to approximate local bonding environments at the metal–ligand interface. Frontier molecular orbitals (FMOs) provide critical insight into the electronic stability and reactivity of our quercetin–Ag/Cu nanocomposites (**Structures(a–e)**, see Fig. 6, Fig. S2). Table 2 summarizes the computed HOMO and LUMO energies, the energy gap (ΔE), chemical hardness (η), softness (S), chemical potential (μ), electronegativity (χ) and electrophilicity index (ω) for each derivative.

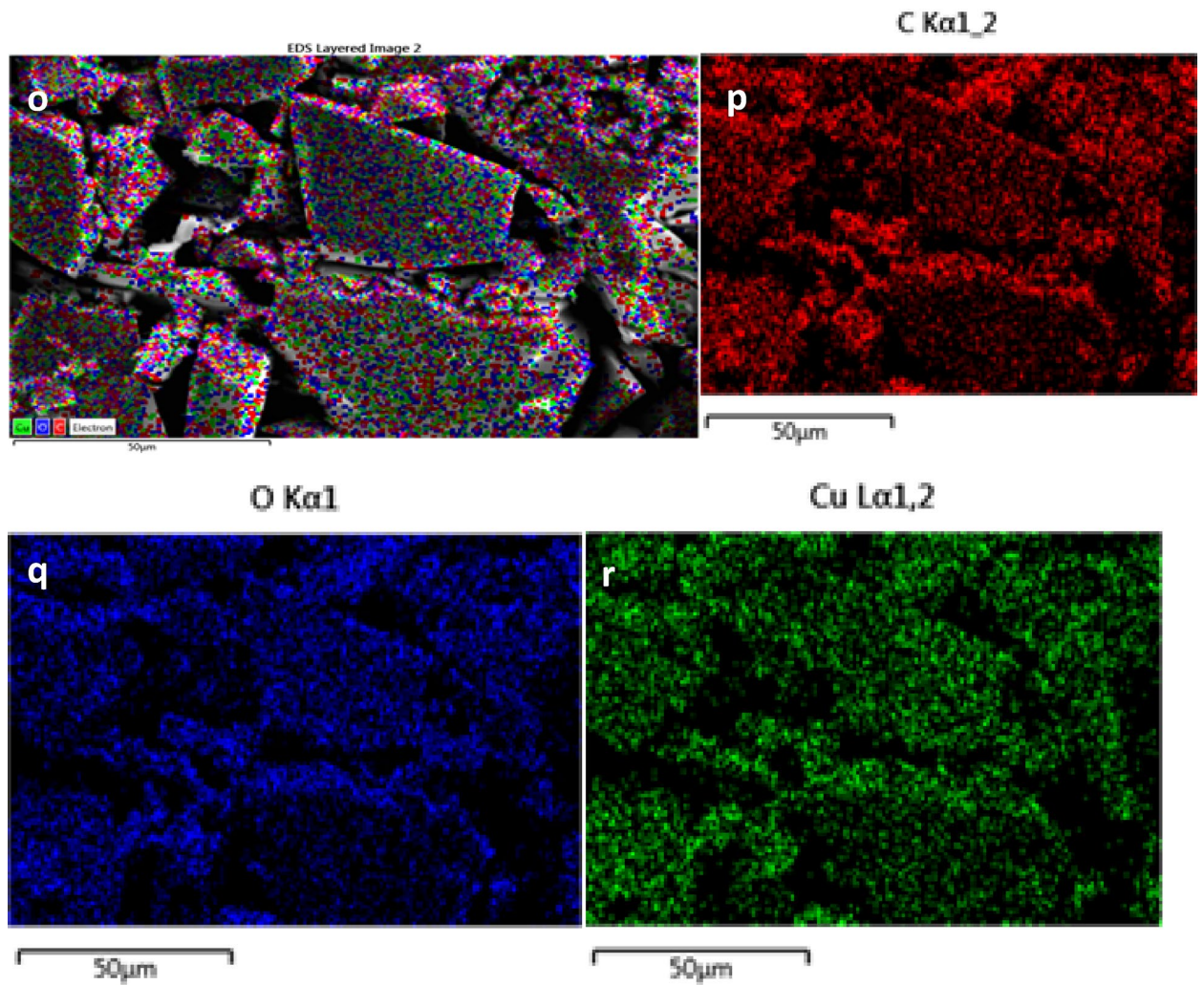


Fig. 4. (continued)

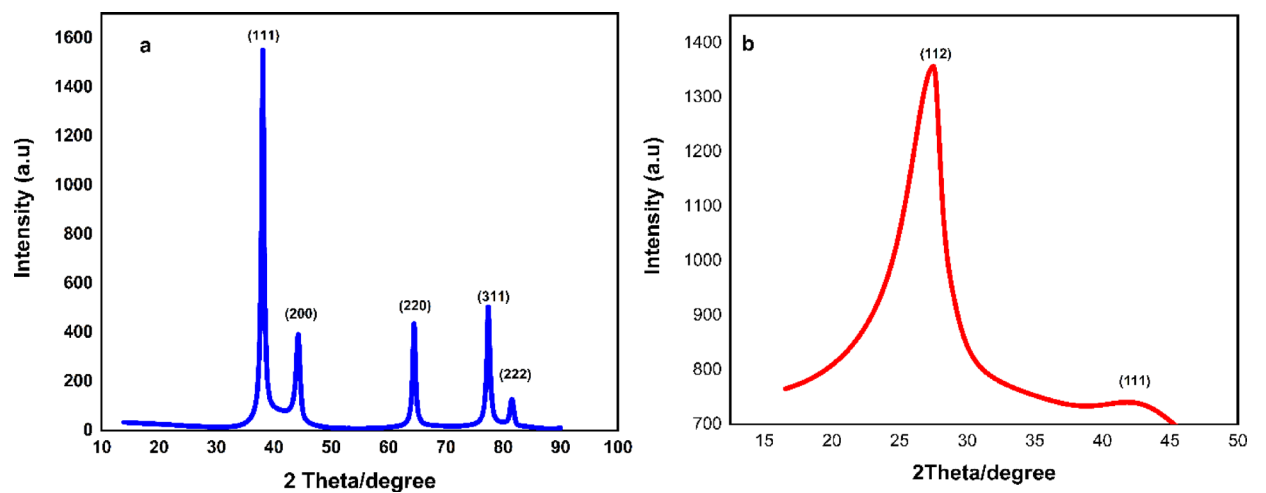


Fig. 5. XRD patterns of Qn@AgNPs (a) and Qn@CuNPs (b) showing crystalline structure and phase composition.

No	Materials	MIC ug/mL	
		<i>Escherichia coli</i>	<i>Staphylococcus aureus</i>
1	Qn@AgNPs	2.11 ± 1.22	4.69 ± 2.68
2	Quercetin	188 ± 0.81	375 ± 1.62
3	Ag ⁺	26 ± 9	21 ± 0.9
4	Qn@CuNPs	7.50 ± 0.00	6.25 ± 0.17
5	Cu ⁺⁺	2832 ± 0.98	1416 ± 0.49

Table 1. Minimum inhibitory concentrations (MICs) of quercetin, metal ions, and qn@ag/cunps against *E. coli* and *S. aureus*. All values are expressed in µg/mL.

A larger ΔE correlates with enhanced kinetic stability and diminished chemical reactivity, as greater energy is required to promote an electron from the HOMO to the LUMO. Among the series, structure a exhibits the largest gap (2.698 eV), coupled with the highest hardness ($\eta = 1.349$ eV) and the lowest softness ($S = 0.741$ eV⁻¹), indicating it is the most electronically stable species with the least propensity for electron transfer. In contrast, structure b shows the smallest ΔE (0.164 eV), lowest hardness ($\eta = 0.082$ eV) and highest softness ($S = 12.195$ eV⁻¹), identifying it as the most chemically “soft” and therefore the most reactive derivative. Structure c follows closely, with $\Delta E = 0.245$ eV and $S = 8.163$ eV⁻¹, suggesting significant facility for redox activity. Chemical potential (μ) and electronegativity (χ) further mirror these trends: more negative μ values (structure a: $\mu = -6.788$ eV; structure b: $\mu = -5.224$ eV) denote stronger tendencies to attract electrons. The electrophilicity index (ω) orders the compounds in terms of their ability to accept electron density, with structure a again being the strongest electrophile ($\omega = 23.038$ eV), followed by e (17.591 eV), c (14.148 eV), b (13.645 eV) and d (12.261 eV). Taken together, these FMO results indicate that metal incorporation markedly tunes the electronic landscape of quercetin: the pristine ligand (a) is the most stable and least reactive, whereas Ag/Cu coordination (particularly in b and c) produces markedly softer, low-gap species that should exhibit enhanced interaction with substrates or charge carriers. Moreover, the outstanding electronic features of our Ag- and Cu-based nanocomposites are borne out by their remarkable antibacterial efficacy (Table 1). Whereas pristine quercetin showed only moderate activity (MICs of 188 ± 0.81 µg/mL against *E. coli* and 375 ± 1.62 µg/mL against *S. aureus*), and simple Ag⁺ and Cu²⁺ ions exhibited MICs in the tens and thousands of micrograms per milliliter respectively, the quercetin–metal nanocomposites achieved dramatically lower MICs. In particular, Qn@AgNPs–our structure b analogue–recorded MICs of just 2.11 ± 1.22 µg/mL for *E. coli* and 4.69 ± 2.68 µg/mL for *S. aureus*. Qn@CuNPs (structure c) likewise displayed potent inhibition (7.50 ± 0.00 µg/mL and 6.25 ± 0.17 µg/mL, respectively). This strong antibacterial performance aligns directly with the FMO-derived descriptors: Qn@AgNPs (structure b) exhibited the smallest HOMO–LUMO gap ($\Delta E = 0.164$ eV), highest softness ($S = 12.195$ eV⁻¹) and substantial electrophilicity ($\omega \approx 13.6$ eV), signifying facile electron donation/acceptance processes at the microbial interface. Such electronic malleability likely enhances generation of reactive oxygen species and promotes disruptive interactions with bacterial membranes. Similarly, Qn@CuNPs (structure c) combined low ΔE (0.245 eV) with elevated softness ($S = 8.163$ eV⁻¹), rationalizing its superior activity relative to free Cu²⁺ (which, by contrast, has a wide gap and low softness). Taken together, the concordance between our computational predictions and empirical MIC data robustly substantiates that metal coordination markedly lowers the frontier orbital gap and increases molecular softness of quercetin, directly translating into enhanced antibacterial potency.

Molecular electrostatic potential (MESP) analysis

Molecular electrostatic potential (MESP) mapping provides a three-dimensional visualization of the charge distribution over a molecule’s van-der-Waals surface, thereby pinpointing regions susceptible to electrophilic or nucleophilic attack. For each quercetin derivative (Structures a–e), we performed MESP calculations at the B3LYP/3-21G level following full geometry optimization. The resulting potential values (in atomic units, a.u.) spanned the ranges listed in Table 3 and are graphically depicted in Fig. 7.

In the MESP color scheme (Fig. 7), red regions denote high electron density (most negative potential, favorable to electrophiles), blue regions indicate electron-deficient zones (most positive potential, favorable to nucleophiles), and green regions correspond to neutral potential, so pristine quercetin (a) exhibits its most negative potentials (-0.09043 a.u.) localized around the catechol and 3-hydroxyl oxygen atoms, reflecting strong hydrogen-bond donating sites, following metal coordination, both Ag- (b) and Cu- (c) composites show slightly broader and more intense red patches (up to -0.09110 a.u. in c), signaling enhanced electron delocalization around the metal–ligand interface. Derivative e displays the widest MESP span (-0.09658 to $+0.09658$ a.u.), with pronounced negativity around both metal centers and adjacent oxygen atoms, implying the strongest polarization and, consequently, the greatest propensity for selective electrophilic engagement, conversely, structure d has the narrowest MESP range, suggesting the least perturbation of quercetin’s native potential upon complexation. Overall, the progressive increase in maximum negative potential from a→e correlates with the degree of metal-induced polarization, so these MESP insights corroborate our frontier orbital findings: enhanced charge separation in the nanocomposites fosters more reactive hotspots, thereby rationalizing their superior interaction with bacterial targets and other electrophilic species.

Studies involving molecular Docking

To rationalize the exceptional antibacterial properties of our quercetin synthesized nanocomposites (a–e), we conducted molecular docking against the *Staphylococcus epidermidis* transcriptional regulator TcaR (PDB ID:

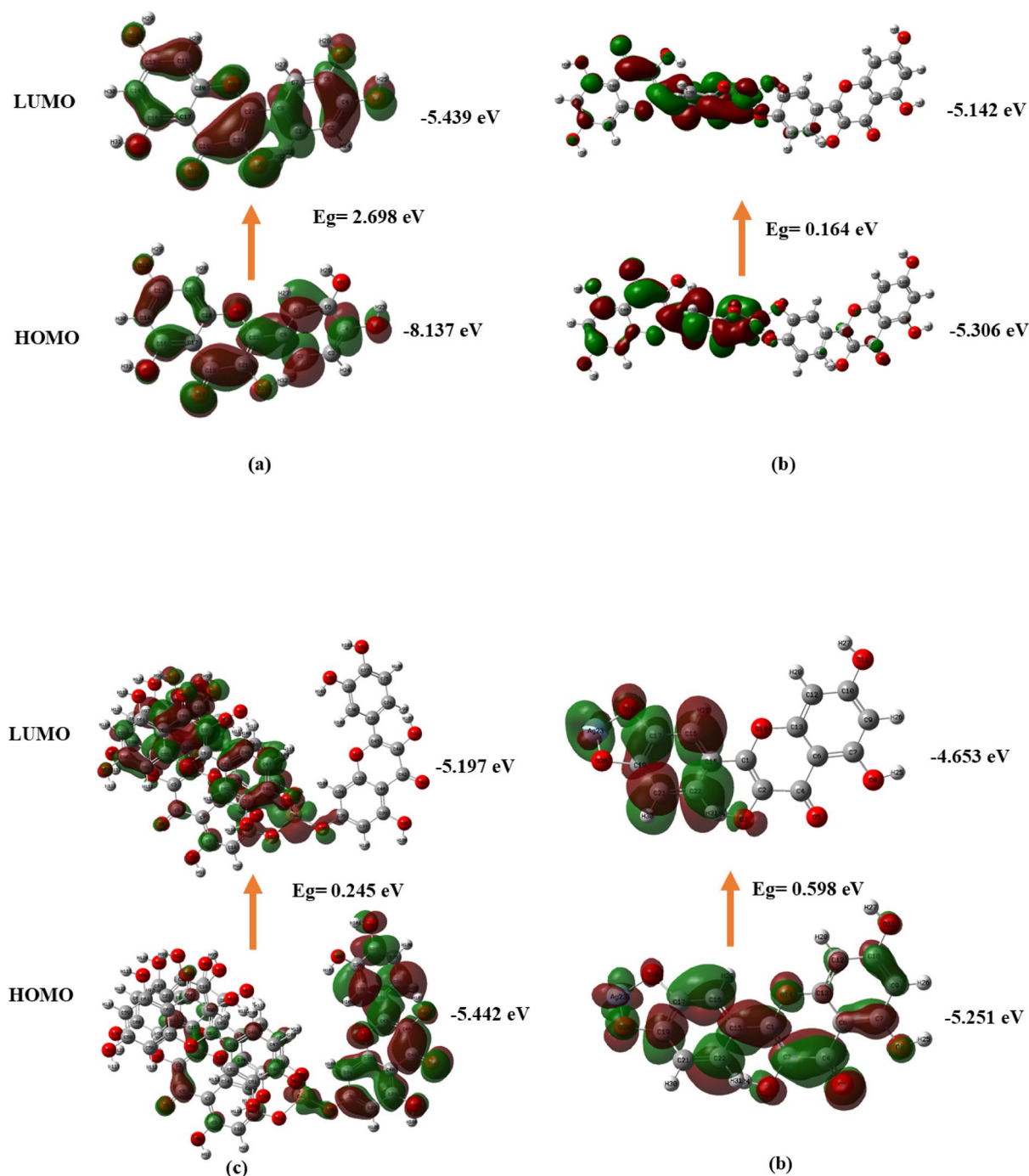


Fig. 6. FMO orbitals and the energy gap between the HOMO and LUMO states in quercetin **a** and proposed nanocomposite structures **b-e**.

1KZN) and the *Escherichia coli* DNA gyrase B subunit (PDB ID: 1HSK). The top-scoring poses are illustrated in Figs. 8 and 9 (left: 2D interaction maps; right: 3D surface views), and the detailed binding energies, interacting ligand atoms, receptor residues, interaction types and distances are summarized in Table 4. Regarding docking to 1KZN, all five structures fit snugly within TcaR's helix–turn–helix binding pocket, with binding energies spanning -6.291 to -9.562 kcal·mol $^{-1}$. Structure **c** displayed the strongest affinity (-9.562 kcal·mol $^{-1}$), stabilized by three hydrogen bonds—O9...GLY117 (3.352 Å), O19...GLU150 (2.895 Å), O65...HIS95 (3.061 Å) and an additional H-acceptor contact O41...VAL120 (2.951 Å). Structure **e** followed (-8.343 kcal·mol $^{-1}$) via an O28...ARG76 hydrogen bond (2.940 Å). Structure **b** exhibited moderate binding (-7.540 kcal·mol $^{-1}$), forming three hydrogen bonds (O11...ASP49 at 3.101 Å; O43...ASN46 at 2.981 Å; O5...GLY117 at 3.302 Å) plus a π -H interaction between its aromatic ring and ILE90 (4.364 Å). By contrast, structure **a** (-6.501 kcal·mol $^{-1}$) engaged only O5...ASP73 (2.731 Å), and structure **d** (-6.291 kcal·mol $^{-1}$) coordinated its Ag atom with VAL71 (2.704 Å),

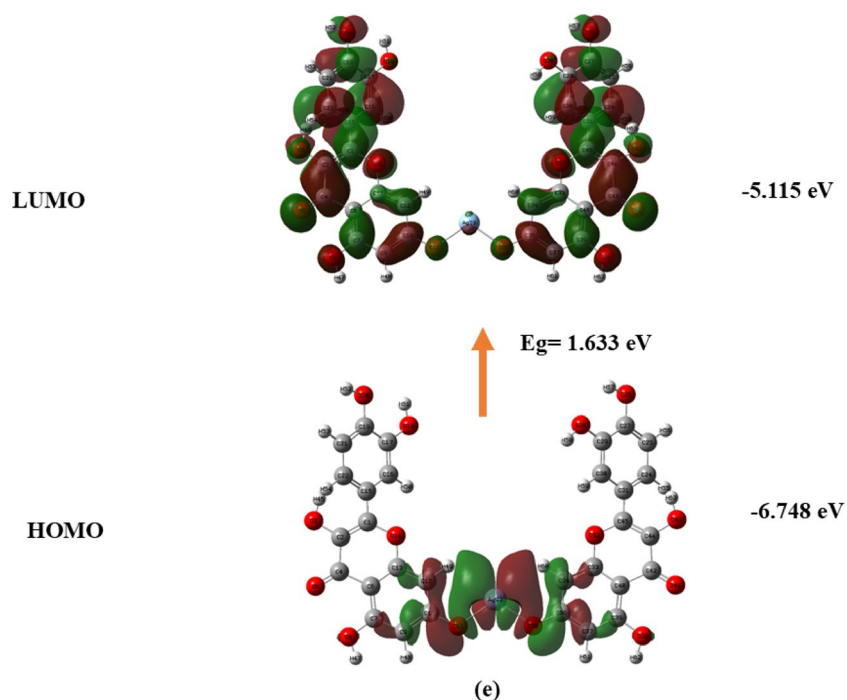


Fig. 6. (continued)

Structures	LUMO	HOMO	ΔE	η	S	μ	χ	ω
a	-5.439	-8.137	2.698	1.349	0.741	-6.788	6.788	23.038
b	-5.142	-5.306	0.164	0.082	12.195	-5.224	5.224	13.645
c	-5.197	-5.442	0.245	0.122	8.163	-5.319	5.319	14.148
d	-4.653	-5.251	0.598	0.299	3.344	-4.952	4.952	12.261
e	-5.115	-6.748	1.633	0.816	1.224	-5.931	5.931	17.591

Table 2. HOMO–LUMO energy levels and calculated global reactivity descriptors for Quercetin and nanocomposite models (b–e), computed using B3LYP/3-21G in aqueous phase.

Structure	MESP range (a.u.)
a	-0.09043 to +0.09043
b	-0.09073 to +0.09073
c	-0.09110 to +0.09110
d	-0.08961 to +0.08961
e	-0.09658 to +0.09658

Table 3. Computed MESP extrema for Quercetin (a) and ag/cu nanocomposites (b–e).

accounting for their weaker affinities. On the other hand, docking to 1HSK, in the ATP-binding cleft of DNA gyrase B, binding energies ranged from -6.682 to -10.151 kcal·mol $^{-1}$, so structure **e** again achieved the highest affinity (-10.151 kcal·mol $^{-1}$), anchored by three H-acceptor bonds (O5...SER238 at 2.634 Å; O41...GLY79 at 3.205 Å; O41...GLY81 at 2.991 Å) and a π - π interaction of its aromatic ring with TYR149 (3.593 Å), also structure **c** scored -9.751 kcal·mol $^{-1}$ through dual hydrogen bonds to GLU184 (O26...GLU184 at 2.873 Å; O28...GLU184 at 2.762 Å). Structure **b** (-9.294 kcal·mol $^{-1}$) was stabilized by one π -cation interaction (ring...ARG188 at 3.662 Å) and two π - π contacts with TYR149. Weaker binders **a** (-6.812 kcal·mol $^{-1}$) and **d** (-6.682 kcal·mol $^{-1}$) formed single hydrogen bonds with LEU197 and GLY81, respectively, so these docking results align closely with our MIC determinations, our proposed structures **c** and **e** which exhibit the lowest binding energies and most extensive hydrogen-bonding networks also showed the most potent antibacterial activity, so the combination of strong electrostatic and π -stacking interactions rationalizes the enhanced membrane disruption and enzyme inhibition observed for these quercetin–metal nanocomposites.

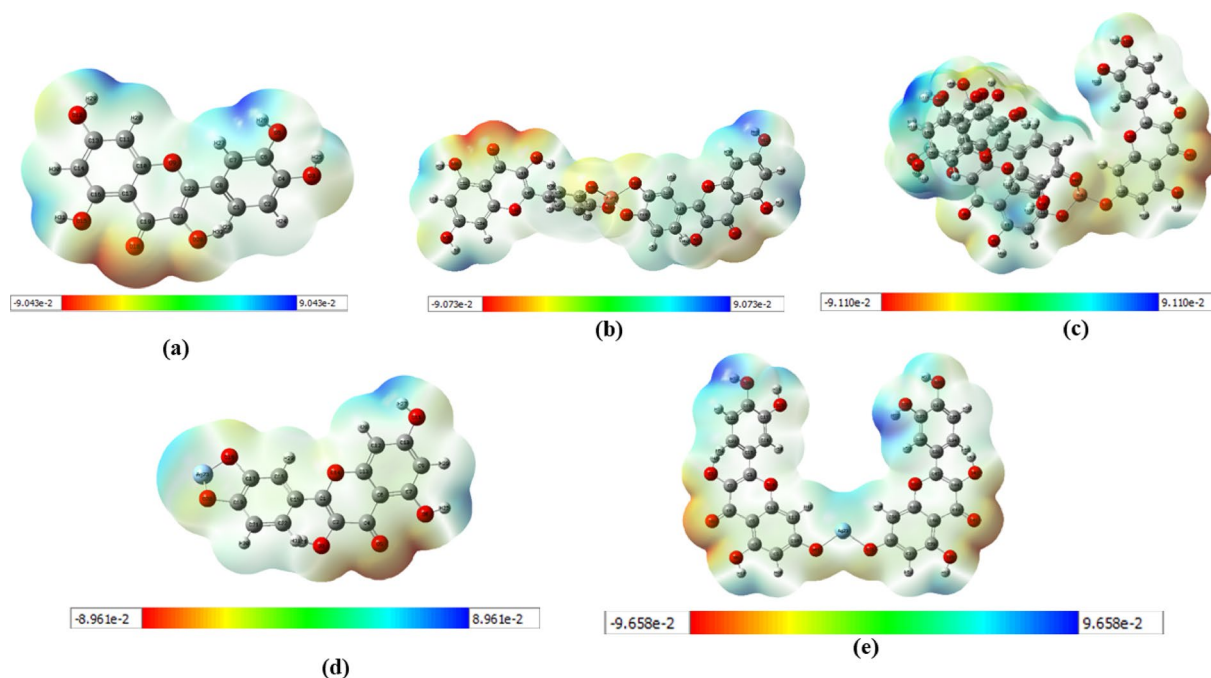
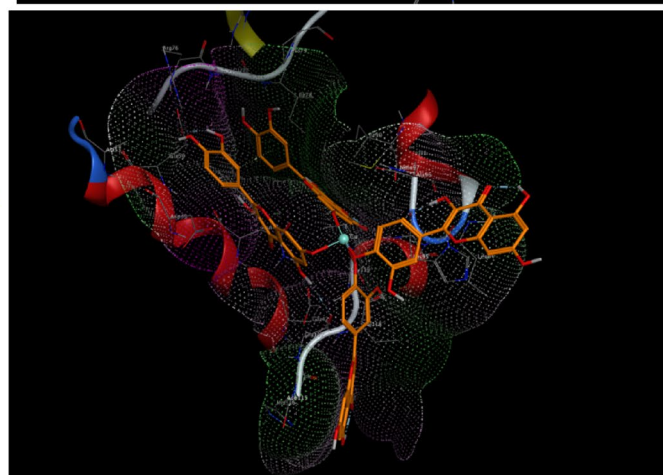


Fig. 7. The molecular electrostatic potential surface of proposed structures.

Conclusion

We have successfully demonstrated that quercetin can serve as an effective green reductant and stabilizer for the synthesis of uniformly sized silver and copper nanoparticles under mild, one-pot conditions. Comprehensive characterization confirmed formation of stable Qn@AgNPs and Qn@CuNPs with preserved quercetin functionality. DFT analyses highlighted that metal coordination substantially narrows the HOMO–LUMO gap and increases molecular softness, promoting electron-transfer interactions critical for antimicrobial action. Molecular docking further identified strong, specific interactions between the nanocomposites and key bacterial proteins, rationalizing the low MIC values measured *in vitro*. Compared to free quercetin and metal ions, the quercetin-capped nanocomposites exhibited dramatically enhanced bactericidal efficacy at sub-10 $\mu\text{g}/\text{mL}$ concentrations. By integrating green nanofabrication with computational modeling, this work addresses a significant gap in the literature and establishes a versatile platform for the rational design of flavonoid-based metal nanotherapeutics with tunable electronic properties and potent antimicrobial activity.



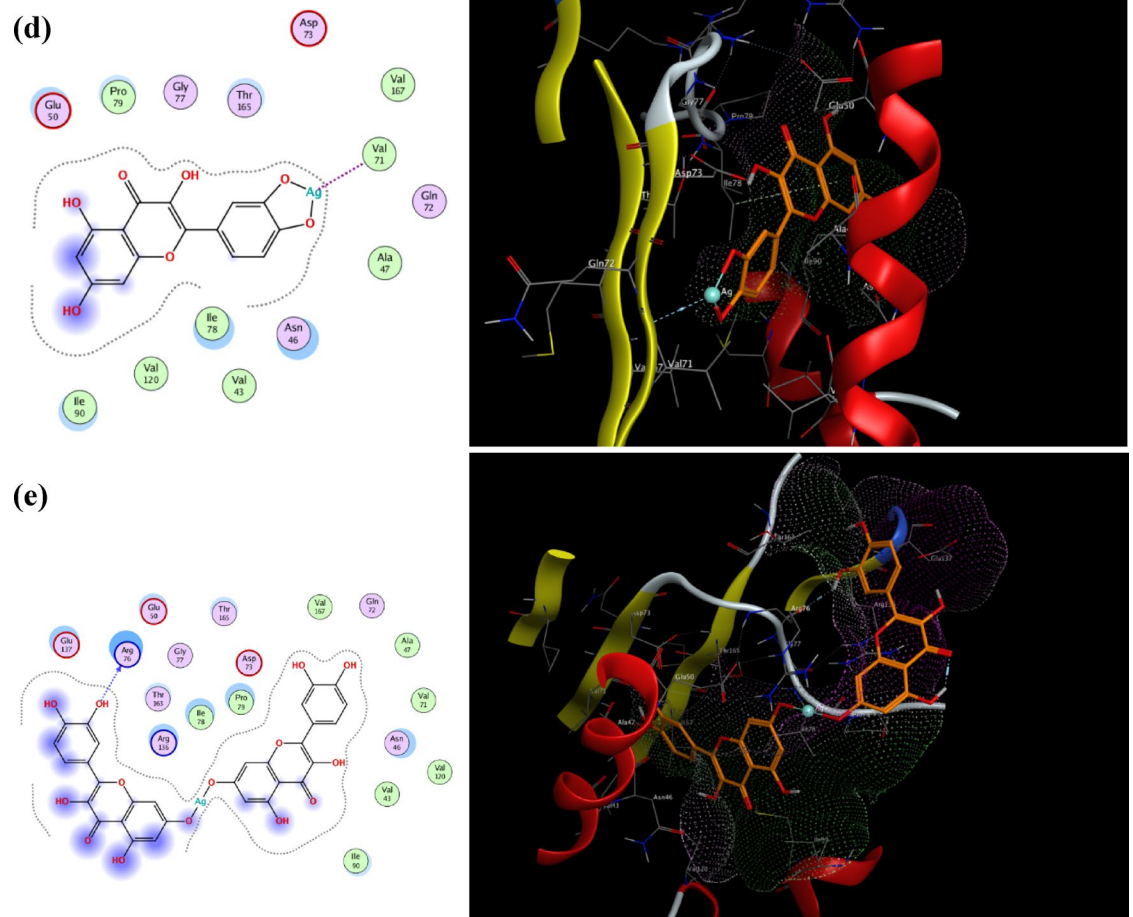


Fig. 8. (continued)

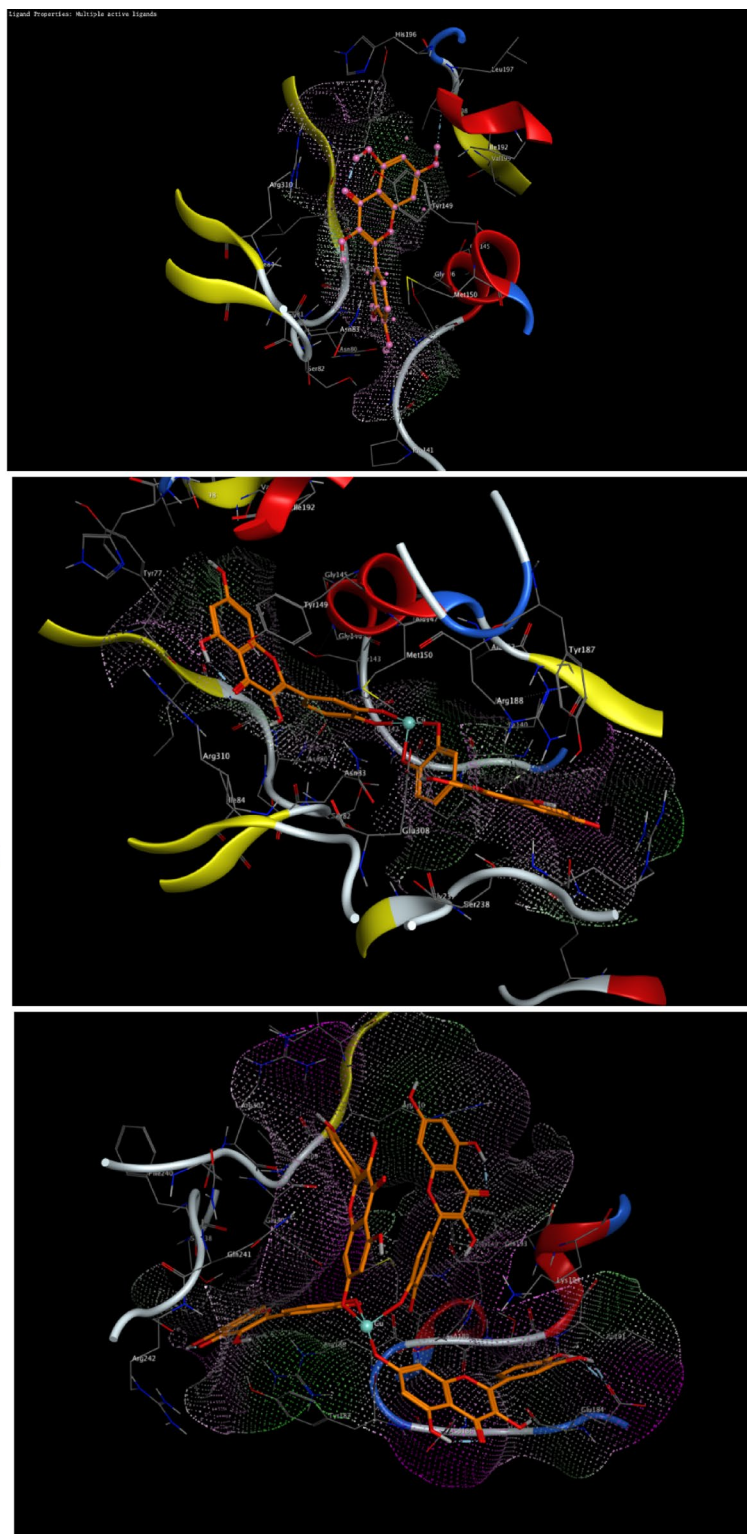
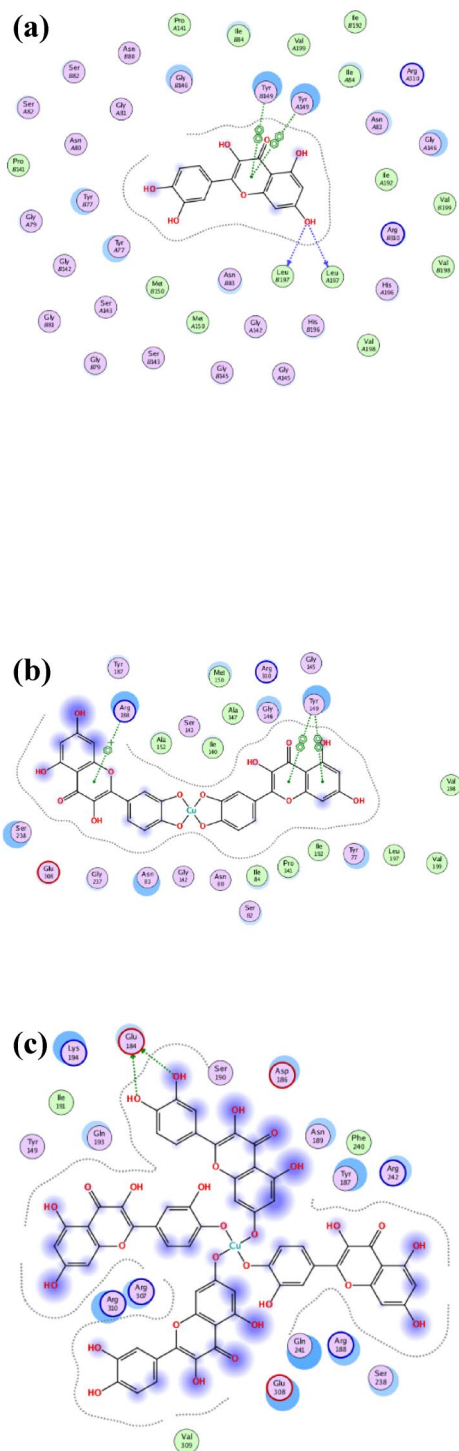
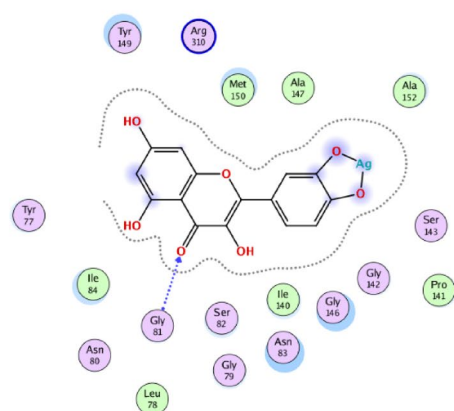


Fig. 9. The quercetin synthesized nanocomposites (a–e) vs. the *Escherichia coli* DNA gyrase B subunit (PDB ID: 1HSK). left 2D and right 3D.

(d)



(e)

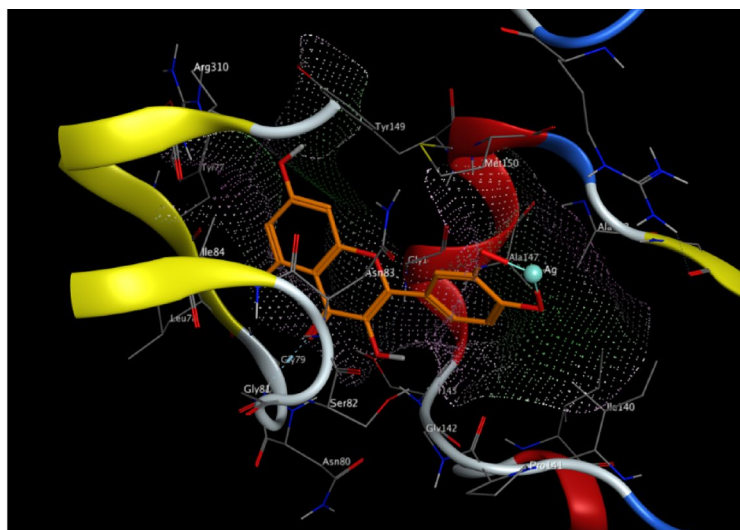
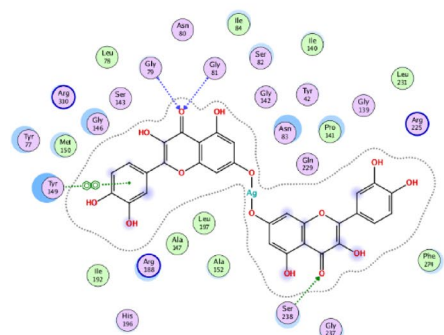


Fig. 9. (continued)

Protein (PDB)	Structure	ΔG (kcal·mol ⁻¹)	Ligand atom(s)	Residue(s)	Interaction Type	Distance (Å)
1KZN	a	-6.501	O5	ASP73	H-donor	2.731
	b	-7.540	O11, O43, O5, 6-ring	ASP49, ASN46, GLY117, ILE90	H-donor, H-acceptor, π -H	3.101, 2.981, 3.302, 4.364
	c	-9.562	O9, O19, O65, O41	GLY117, GLU150, HIS95, VAL120	H-donor, H-acceptor	3.352, 2.895, 3.061, 2.951
	d	-6.291	Ag23	VAL71	Metal-coord.	2.704
	e	-8.343	O28	ARG76	H-donor	2.940
1HSK	a	-6.812	O12, 6-ring	LEU197, TYR149	H-donor, π - π	3.351, 3.950
	b	-9.294	6-ring ($\times 3$)	ARG188, TYR149	π -cation, π - π	3.662, 3.940, 3.844
	c	-9.751	O26, O28	GLU184	H-donor	2.873, 2.762
	d	-6.682	O5	GLY81	H-acceptor	3.14
	e	-10.151	O5, O41 ($\times 2$), 6-ring	SER238, GLY79, GLY81, TYR149	H-acceptor, π - π	2.634, 3.205, 2.991, 3.593

Table 4. Docking results of structures, a–e with 1KZN and 1HSK.

Data availability

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

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References

- Agyare, C. et al. Antibiotic use in poultry production and its effects on bacterial resistance, in *Antimicrobial resistance-A global threat*. IntechOpen. (2018).
- Odonkor, S. T. & Addo, K. K. Prevalence of multidrug-resistant *Escherichia coli* isolated from drinking water sources. *Int. J. Microbiol.* **2018** (1), 7204013 (2018).
- Ogawara, H. Comparison of antibiotic resistance mechanisms in antibiotic-producing and pathogenic bacteria. *Molecules* **24** (19), 3430 (2019).
- Ferreira, R. L. et al. High prevalence of multidrug-resistant *Klebsiella pneumoniae* harboring several virulence and β -lactamase encoding genes in a Brazilian intensive care unit. *Front. Microbiol.* **9**, 3198 (2019).
- Sardar, S. et al. Silver nanoparticle modulates the aggregation of beta-lactoglobulin and induces to form rod-like aggregates. *Int. J. Biol. Macromol.* **125**, 596–604 (2019).
- Sánchez-López, E. et al. Metal-based nanoparticles as antimicrobial agents: an overview. *Nanomaterials* **10** (2), 292 (2020).
- Gahlawat, G. & Choudhury, A. R. A review on the biosynthesis of metal and metal salt nanoparticles by microbes. *RSC Adv.* **9** (23), 12944–12967 (2019).
- Naskar, A. & Kim, K. Nanomaterials as delivery vehicles and components of new strategies to combat bacterial infections: advantages and limitations. *Microorganisms* **7** (9), 356 (2019).
- Vestby, L. K. et al. Bacterial biofilm and its role in the pathogenesis of disease. *Antibiotics* **9** (2), 59 (2020).
- Karygianni, L. et al. Biofilm matrixome: extracellular components in structured microbial communities. *Trends Microbiol.* **28** (8), 668–681 (2020).
- Slepíčka, P. et al. Methods of gold and silver nanoparticles Preparation. *Materials* **13** (1), 1 (2019).
- Gour, A. & Jain, N. K. Advances in green synthesis of nanoparticles. *Artif. Cells Nanomed. Biotechnol.* **47** (1), 844–851 (2019).
- Salem, S. S. & Fouda, A. Green synthesis of metallic nanoparticles and their prospective biotechnological applications: an overview. *Biol. Trace Elem. Res.* **199** (1), 344–370 (2021).
- Abubakar, A. et al. Chemometric classification of geothermal and non-geothermal ethanol leaf extract of *seurapoh* (*Chromolaena odorata* Linn) using infrared spectroscopy. in *IOP Conference Series: Earth and Environmental Science*. IOP Publishing. (2021).
- Kopustinskiene, D. M. et al. Flavonoids as anticancer agents. *Nutrients* **12** (2), 457 (2020).
- Niedzwiecki, A. et al. Anticancer efficacy of polyphenols and their combinations. *Nutrients* **8** (9), 552 (2016).
- Sathishkumar, P. et al. Flavonoids mediated 'green'nanomaterials: A novel nanomedicine system to treat various diseases–Current trends and future perspective. *Mater. Lett.* **210**, 26–30 (2018).
- Talib, W. H. et al. Flavonoid-based nanomedicines to target tumor microenvironment. *OpenNano* **8**, 100081 (2022).
- Aiswarriya, G. et al. Green synthesis, characterization and biocompatibility study of quercetin-functionalized biogenic silver nanoparticles. *Nano* **18** (07), 2350055 (2023).
- Gandhi M, Chavda V, Ranga S. Quinoline schiff bases (QSBs) and their derivatives: emerging trends in antimicrobial agents. *Journal of Coordination Chemistry*. 2025 Jun 18;78(12):1303–36.
- Zong JY, Yue LJ, Gong FL, Yang XY, Zhang YH. Ag₂O decoration on WO₃ nanosheets for ultra-sensitive H₂S detection with robust humidity resistance at low temperatures. *Materials Letters*. 2025 Jun 2:138840.
- Lee, J., Sangubotla, R. & Kim, J. Synthesis and characterization of Quercetin-Functionalized gold nanoparticles for screening anticancer potentials: A flow cytometry approach. *Korean J. Chem. Eng.* **41** (11), 3095–3103 (2024).
- Hosseinpour-Moghadam, R. et al. Prevention of abdominal adhesion by a polycaprolactone/phospholipid hybrid film containing Quercetin and silver nanoparticles. *Nanomedicine* **16** (27), 2449–2464 (2021).
- Li, X. et al. The antibacterial activity and formation mechanism of quercetin-coated silver nanoparticles and protein complex. *J. Mol. Struct.* **1334**, 141878 (2025).
- Kemala, P. et al. Eco-friendly synthesis of silver nanoparticles: enhancing optimization reaction, characterization, and antimicrobial properties with *Lantana camara* from geothermal area. *S. Afr. J. Chem. Eng.* **51** (1), 57–67 (2025).
- Sidhu, A. K. et al. Fungal-mediated synthesis of multimetallic nanoparticles: mechanisms, unique properties, and potential applications. *Front. Nanotechnol.* **7**, 1549713 (2025).
- Anjum, S., Vyas, A. & Sofi, T. Fungi-mediated synthesis of nanoparticles: characterization process and agricultural applications. *J. Sci. Food. Agric.* **103** (10), 4727–4741 (2023).
- Kaya, S. & Putz, M. V. Atoms-in-molecules' faces of chemical hardness by conceptual density functional theory. *Molecules* **27** (24), 8825 (2022).
- Anderson, R. M. et al. A theoretical and experimental approach for correlating nanoparticle structure and electrocatalytic activity. *Acc. Chem. Res.* **48** (5), 1351–1357 (2015).
- Aziz, D. M. et al. A synergistic investigation of azo-thiazole derivatives incorporating thiazole moieties: a comprehensive exploration of their synthesis, characterization, computational insights, solvatochromism, and multimodal biological activity assessment. *RSC Adv.* **13** (49), 34534–34555 (2023).
- Hassan, S. A. et al. Synthesis and characterization of Azo-Azomethine derivatives bearing thiazole moiety: in vitro antimicrobial, in vitro and in vivo anti-inflammatory, and cytotoxicity assessment, accompanied by computational molecular docking, RDG, ELF, DFT, and MEP analysis. *J. Mol. Struct.* **1318**, 139294 (2024).
- Nashre-ul-Islam, S. M. et al. Antiproliferative evaluation and supramolecular association involving electrostatically enhanced π - π interaction in isostructural coordination solids of Mn (II), Co (II) and Zn (II) chlorobenzoates: experimental and theoretical studies. *Inorg. Chim. Acta.* **498**, 119161 (2019).
- Kumar, S. & Choudhary, M. Structural and theoretical investigations, Hirshfeld surface analysis and anti-SARS CoV-2 of nickel (II) coordination complex. *J. Biomol. Struct. Dynamics.* **41** (2), 402–422 (2023).
- Parvekar, P. et al. The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of silver nanoparticles against *Staphylococcus aureus*. *Biomaterial Investigations Dentistry.* **7** (1), 105–109 (2020).
- Tüzün, B. & Kaya, C. Investigation of DNA–RNA molecules for the efficiency and activity of corrosion Inhibition by DFT and molecular Docking. *J. Bio-and Tribo-Corrosion.* **4** (4), 69 (2018).
- Hassan, S. A. et al. Design and synthesis of Oxazepine derivatives from sulfonamide schiff bases as antimicrobial and antioxidant agents with low cytotoxicity and hemolytic prospective. *J. Mol. Struct.* **1292**, 136121 (2023).
- Hamad, H. Q., Taher, S. G. & Aziz, D. M. Synthesis and molecular Docking studies of new series of bis-Schiff bases thiadiazoles derived from disulfides and thioethers with potent antibacterial properties. *Sci. J. Univ. Zakho.* **10** (3), 130–139 (2022).
- Baková, Z. & Kolesář, A. Bioflavonoid quercetin-food sources, bioavailability, absorption and effect on animal cells. *J. Microbiol. Biotechnol. Food Sci.* **2** (2), 426–433 (2012).
- Arsenov, D. et al. Nanomaterials as endorsed environmental remediation tools for the next generation: Eco-safety and sustainability. *J. Geochem. Explor.* **253**, 107283 (2023).
- Sudagar, A. J. *Synthesis, characterization, and testing of catalytic nanomaterials–greener route to synthetic methods*. (2022).
- Karthik NS, Biju TS, Veeraraghavan VP, Gayathri R. Synthesis, Characterisation, and Antibacterial Studies of Quercetin Silver Nanoparticles Loaded Alginate Chitosan Film for Potential Water Treatment and Remediation Applications. In *Case Studies on Holistic Medical Interventions 2024* (pp. 756–761). CRC Press.
- Anh, N. T. et al. Cost-Effective tween 80-Capped copper nanoparticles for ultrasensitive colorimetric detection of thiram pesticide in environmental water samples. *J. Nanomaterials.* **2021** (1), 5513401 (2021).

43. Yousefbeyk, F. et al. Phytochemical analysis and antioxidant activity of eight cultivars of tea (*Camellia sinensis*) and rapid discrimination with FTIR spectroscopy and pattern recognition techniques. *Pharm. Sci.* **29** (1), 100–110 (2022).
44. Ghasemi, S. et al. Process optimization for green synthesis of silver nanoparticles using *Rubus discolor* leaves extract and its biological activities against multi-drug resistant bacteria and cancer cells. *Sci. Rep.* **14** (1), 4130 (2024).
45. Liu, D. et al. Novel colorimetric films based on Polyvinyl alcohol/sodium carboxymethyl cellulose doped with anthocyanins and betacyanins to monitor pork freshness. *Food Chem.* **404**, 134426 (2023).
46. Qu, H. et al. Biomimetic nanomodulator regulates oxidative and inflammatory stresses to treat Sepsis-Associated encephalopathy. *ACS Nano*. **18** (41), 28228–28245 (2024).
47. Kavishri S, Geetha A, Ilangoar IG, Vasugi S, Sivaperumal P, Balachandran S. Facile synthesis of silver nanoparticles from sustainable *Sargassum* sp. seaweed material and its anti-inflammatory application. *Cureus*. 2024 Apr 7;16(4).
48. Sharma, N. K. et al. Green route synthesis and characterization techniques of silver nanoparticles and their biological adeptness. *ACS Omega*. **7** (31), 27004–27020 (2022).
49. Asif, M. et al. Green synthesis of silver nanoparticles (AgNPs), structural characterization, and their antibacterial potential. *Dose-Response* **20** (2), 15593258221088709 (2022).
50. Khashan, K., Jabir, M. & Abdulameer, F. *Preparation and characterization of copper oxide nanoparticles decorated carbon nanoparticles using laser ablation in liquid*. in *Journal of Physics: Conference Series*. IOP Publishing. (2018).
51. Shahzeydi, A. et al. Facile and green synthesis of copper nanoparticles loaded on the amorphous carbon nitride for the oxidation of cyclohexane. *Chem. Eng. J.* **370**, 1310–1321 (2019).
52. Saran, M. et al. Green synthesis and characterisation of cupns: insights into their potential bioactivity. *IET Nanobiotechnol.* **12** (3), 357–364 (2018).

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Competing interests

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Conflict of interest

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