Inorganic Chemistry Communications 186 (2026) 116214

Contents lists available at ScienceDirect

Inorganic Chemistry Communications

journal homepage: www.elsevier.com/locate/inoche

Phytochemicals-derived functional metal/metal oxide nanocomposites: Mechanistic insights and biological interactions

Mohammad Asim Saifi [a], Aayasha Negi [a,b,*], Amanpreet Kaur [a], Lakshya [c], Ramchander Merugu [d], Sadhna Negi [e], Mohamed Taha Yassin [f]

[a] Department of Chemistry, IFTM University, Moradabad, Uttar Pradesh 244102, India
[b] Department of Chemistry, HNB Garhwal University, Srinagar Garhwal 246174, India
[c] Department of Biotechnology, IFTM University, Moradabad, Uttar Pradesh 244102, India
[d] Department of Biochemistry, Mahatma Gandhi University, Nalgonda 508254, Telangana, India
[e] Department of Chemistry, School of Basic and Applied Science, S.G.R.R University, Dehradun, Uttarakhand 248001, India
[f] Department of Botany and Microbiology, College of Science, King Saud University, P.O. Box 22452, 11495, Riyadh, Saudi Arabia

ARTICLE INFO

Keywords:
Metal-based NCs
Green Synthesis
Mechanism
Phytoconstituents
Biological Potential

ABSTRACT

Phytochemically-derived metal and metal oxide nanocomposites (NCs) represent a pivotal advancement in sustainable nanomaterial synthesis. The core novelty of this review lies in proposing a predictive synthesis-structure-activity framework that systematically transitions green synthesis from an empirical methodology to a rational design paradigm. This analysis critically correlates phytochemical composition with precise control over NCs morphology, crystallinity, and surface properties, which in turn govern functional outcomes. The multifunctional bioactivity of these NCs, spanning antimicrobial, anticancer, antioxidant and regenerative applications, is examined with emphasis on their underlying synergistic mechanisms. These include phytochemical-metal interplay that modulates cellular internalisation, reactive oxygen species (ROS) generation and intracellular signalling pathways. Current limitations, such as reproducibility, toxicity and regulatory challenges, are addressed alongside prospects for biomedical and environmental applications. This review establishes a pioneering synthesis structure and activity framework that meticulously unpacks the green synthesis and multifunctional behaviour of plant-derived metal and metal oxide nanocomposites.

1. Introduction

Nanotechnology is a field focused on the design of structures, devices and systems through the manipulation of atoms and molecules at the nanoscale [1]. Critically, in medicine, nanotechnology is poised to revolutionise disease management through advanced modalities such as nanosurgery, targeted drug delivery and tissue engineering [2,3]. It has already been utilised by industrial sectors, including information and communications and is also applied in food, energy technology and certain medical products and medicines [4]. A key class of materials enabling these advances are nanocomposites (NCs), defined as solid-phase materials integrating at least one component at the nanoscale (1–100 nm) [5]. Due to their unique properties, including in electronics, drug delivery, energy storage and biomedical applications [6]. In nanobiotechnology, NCs function not only as therapeutic carriers but also as active components in diagnostics, prosthetics, and implantable devices. Nanotechnology offers substantial benefits and has the potential to significantly influence society. NCs can be used as stabilising, reducing and capping agents in the synthesis of NPs [7]. These methods are considered green because they use natural materials instead of synthetic chemicals. It reacts with metal ions and reduces them, similarly preventing NPs from clumping together and stabilising their colloidal solutions. The deposition of metal and metal oxide NCs on the desired position with a nanoscale has a promising potential to realise nanodevices for various applications in chemistry, optics, electronics and biomedicine [8]. These materials enable encapsulation and targeted delivery of these therapeutic agents through carriers such as liposomes, which have been extensively used in various drugs, including chemotherapeutics and antibiotics, for bone regeneration and implantations [9]. Their functionality stems from the interplay between the individual components, typically a combination of nanostructured metal oxides and an organic or inorganic matrix, resulting in tunable reactivity,

* Corresponding author at: Department of Chemistry, IFTM University, Moradabad, Uttar Pradesh 244102, India.
E-mail address: aisha.negi04@gmail.com (A. Negi).

https://doi.org/10.1016/j.inoche.2026.116214
Received 6 November 2025; Received in revised form 11 January 2026; Accepted 20 January 2026
Available online 25 January 2026
1387-7003/© 2026 Published by Elsevier B.V.

enhanced surface activity and controlled drug release. The synthesis of such NCs is generally classified into three main category such as solution-based, vapour-phase and gas-phase methods, each offering distinct advantages [10]. Notably, in systems where two different metals or metal oxides are integrated, shows different structural characteristics: if two constituents are chemically bonded at the atomic level, forming a single-phase or core–shell configuration, then the material is accurately described as a bimetallic nanostructure. However, when the two metal or metal oxide retain their distinct crystalline identities and coexist within a shared nanoscale framework, it is scientifically appropriate to classify the material as a NCs [11].

Metal and metal oxide nanocrystals (NCs) are versatile tools in nanomedicine, primarily serving as efficient carriers for therapeutic agents. They are often encapsulated within liposomes to enable targeted delivery to specific physiological sites, thereby minimising off-target effects and enhancing treatment efficacy [12]. Beyond drug delivery, these materials are crucial in implantable medical devices, where they improve mechanical durability, functionality, and integration with biological tissues. Researchers have widely explored the field of nanocomposites in recent years, Fig.1. (a). shows the commendable work of metal-based nanocomposites using various plant materials

Their role is particularly significant in bone tissue engineering. Here, metal and metal oxide NCs are engineered into nano-structured scaffolds designed to mimic the natural bone matrix. These scaffolds are frequently modified to optimise their biocompatibility, structural stability, and osteogenic potential, actively promoting bone regeneration [13]. Modifications are made to these scaffolds to increase their biocompatibility, stability and regeneration of bone tissue. Nanotechnology has the potential for cancer detection and therapy [14]. The synthesis of metal and metal oxide nanocrystals is prevalent due to their unique optical, electrical, magnetic and biological properties [15]. The methods of synthesis are usually classified into three classes: first, one is solution-based synthesis; second, one is vapour phase synthesis, and the third one is gas phase synthesis [16]. This synthetic method relies on the characteristics of NC materials; however, physical techniques offer the advantage of generating a substantial quantity of NCs. Metal and metal oxide nanocrystals can be synthesised using multiple techniques, which are depicted in Fig. 1. (b) Critically, the novelty and efficacy of plant-derived NCs stem from the direct and multifaceted role of phytochemicals as structural and functional determinants. The specific

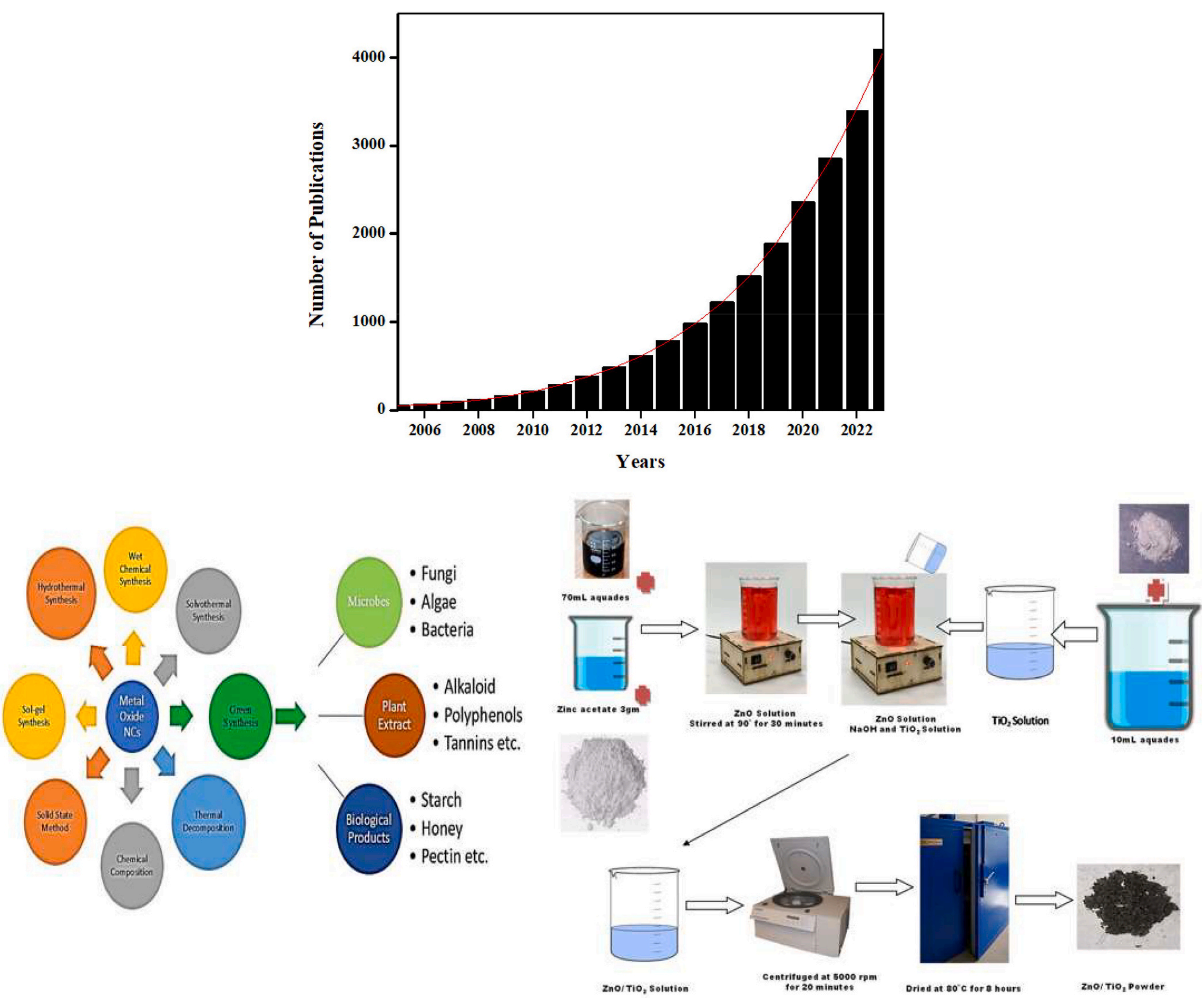

Fig. 1. (a) Number of publications in recent years in the field of nanocomposites using various plant materials. **(b).** Illustrates different methods of synthesizing Metal and metal Oxide NCs and the diverse sources from which they can be obtained, particularly highlighting biological and plant-based, via solution-based, vapour-phase and gas-phase routes with green alternatives using plant extracts. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

phytochemical profile comprising flavonoids, terpenoids, phenolics, and proteins does not merely act as a benign reducing agent but functions as an active architectural template. These biomolecules dictate the nucleation kinetics, crystal growth and final nanoscale architecture (size, morphology, crystallinity) while simultaneously functionalizing the NC surface. This phytochemical capping layer directly confers enhanced biocompatibility, colloidal stability and target-specific bioactivity, such as antioxidant, antimicrobial or anticancer properties [17]. Therefore, establishing a clear phytochemical-synthesis-structure-activity relationship is paramount; it shifts the paradigm from viewing plant extracts as simple green reagents to recognising them as rational design tools for engineering NCs with predictable and superior functional outcomes in biomedicine and catalysis.

This work systematically bridges this gap by providing researchers with design principles for creating application-ready nanomaterials. This review introduces three groundbreaking advances: (1) phytochemical-architectural blueprint, (2) **inherent phytocomposite bioactivity,** and (3) biological synthesis routes. Collectively, these contributions transform green synthesis from empirical observation into a predictive design discipline. In addition, it critically compares green synthesis methods in terms of cost, scalability and ecological impact. The novelty lies in linking the synthesis mechanisms with practical applications, providing a clear path to the development of sustainable nanomaterials for use in the health and environmental sectors as well as in the real-world.

2. Plant-mediated synthesis of metal and metal oxide NCs

Sustainable synthesis of metal and metal oxide NCs utilising plants and microbes as primary sources of raw materials. The use of plant extracts for this purpose is advantageous compared to microbes due to ease of use and reduced biohazard risks. Additionally, it reduces the expenses associated with microorganism isolation and culture media, improving cost efficiency compared to traditional chemical and physical methods, while providing a more sustainable and eco-friendly alternative [18]. The synthesis of NCs using natural resources takes advantage of bioactive compounds found in these organisms [19]. In our recent study, the potential of a plant-mediated Z-scheme ZnO/TiO_2 photo- catalyst, for enhanced antibacterial activity and dye degradation has been explored, and the method of synthesis is illustrated in Fig.2 [20]. Fungal species have been widely used in the green synthesis of NCs due to their efficient metal accumulation capabilities and their ability to synthesise stable and uniform Nanoparticles (NPs). *Rhizopus stolonifer* is a fungus that has been used to synthesise silver-based NCs, where silver NPs integrate into the fungal matrix, exhibiting antimicrobial activity [21]. Similarly, *Fusarium oxysporum* and *Pleurotus ostreatus,* also fungi have been used to synthesise selenium-containing NCs, which show antioxidant and anticancer properties [22]. The presence of fungal enzymes and proteins provides a highly controlled and stable synthesis process with tailored properties [23]. Additionally, Algae and rich content of bioactive molecules have also been explored for the synthesis of NCs due to their rapid growth. *Sargassum* and *Spirulina platensis* are the two most common algae used for the biosynthesis of NCs [24]. The algae *Sargassum* produced gold and silver NCs, showing excellent stability and antibacterial properties. *Spirulina platensis* is also an algae used in the synthesis of copper oxide NCs with photocatalytic properties. These photocatalytic properties facilitate environmental applications, including water purification and pollutant degradation. Algal-based NCs utilise naturally occurring compounds like polysaccharides, proteins and lipids, serving as reducing and stabilising agents in the synthesis process [25]. The novelty of this plant-mediated synthesis lies in utilising the specific phytochemical profile of extracts as dual-purpose reducing and capping agents. This enables a single-step, energy-efficient fabrication of hybrid metal/metal-oxide nanocrystals with controlled interfaces and crystallinity structures that enhance functional performance and are difficult to achieve via conventional methods [26]. Plant-based NCs feature

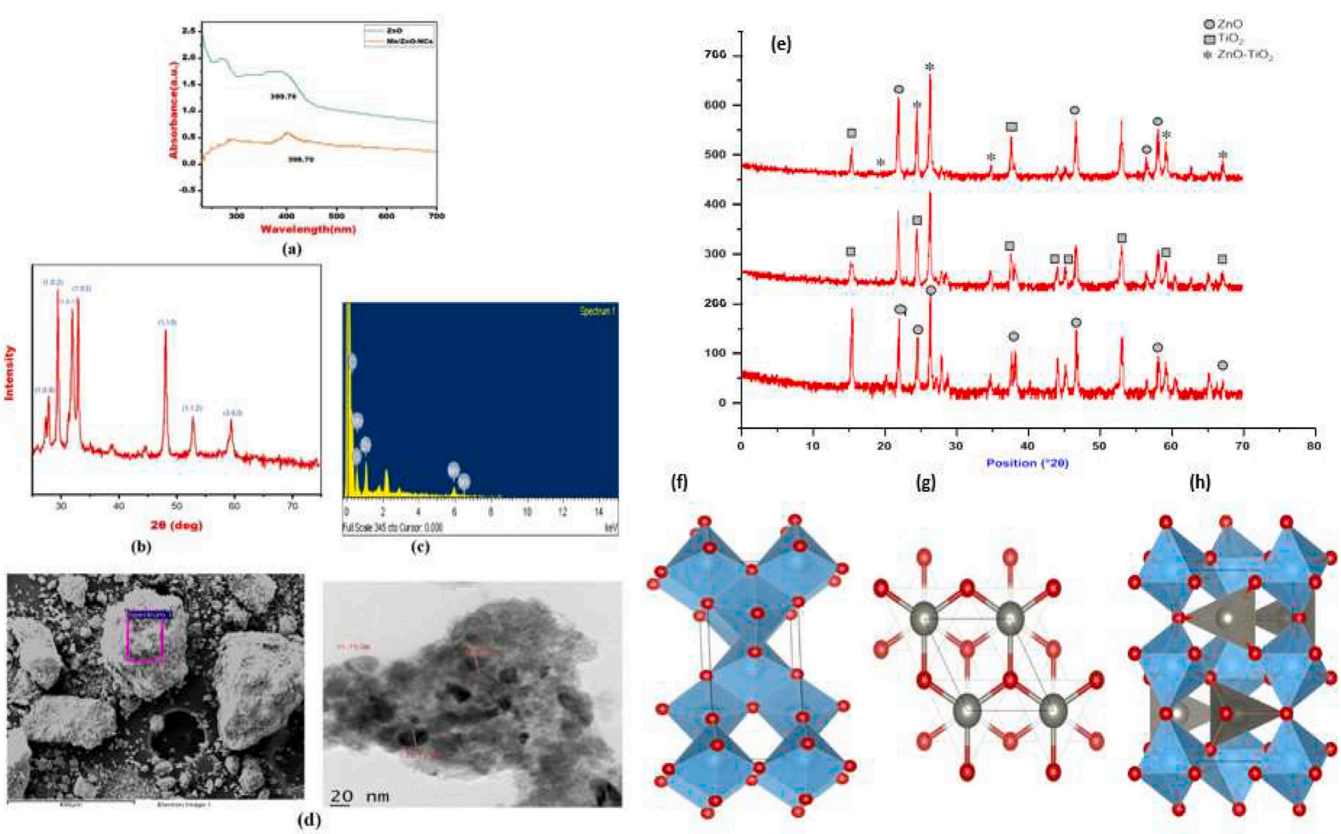

Fig. 2. Shows ZnO/TiO_2 NCs synthesis methodology via *Taraxacum officinale radix* plant.

bioactive structures with uniform geometry that facilitate interactions with the extracellular matrix in vivo, modulating cell-matrix and cell-cell interactions essential for the advancement of NCs in tissue engineering and regenerative medicine [27]. The various plant extracts like *Aloe vera*, *Azadirachta indica, chickpea leaves* and *Annona squamosa* have been used to synthesise various metal and metal oxide NPs as shown in Table 1. The primary advantage of plant-based synthesis lies in the versatility, scalability and availability of plant materials over fungal and algal routes [28]. Plants can be cultivated in a wide range of environments, and it provides sustainable, renewable resources for large scale NCs production. Unlike fungi and algae, plants can be easily harvested, processed and standardized for NCs synthesis. Furthermore, NCs derived from plants can be adapted for specific applications due to the diversity of these bioactive compounds present in plants [29]. The compounds facilitate precise control of nanoparticle size, shape and surface properties in the composite material, rendering them suitable for applications such as drug delivery, wound healing, environmental remediation and antimicrobial coatings [30].

3. Role of plant metabolites in the synthesis of NCs

The synthesis of metal and metal oxide nanocrystals using plant extract has gained significant attention as a sustainable and environmentally friendly alternative to chemical methods [31]. The extract can be obtained from different parts of plants, including leaves, stems, roots and flowers. It functions as a natural reducer, capper and stabiliser in nanoparticle formation. These extracts contain secondary metabolites that facilitate metal ion reduction, enhance stability and improve the biocompatibility of synthesised nanomaterials, as shown in Table 2. Among these metabolites, flavonoids are particularly prominent due to their potent antioxidant activity. These compounds are more effective than many other phytochemicals in reducing metal oxides and stabilising NCs, thereby lowering their toxicity. Beyond their role in synthesis, flavonoids possess therapeutic properties such as hepatoprotective, anticancer and antiviral effects, making flavonoid-assisted NCs especially promising for biomedical applications [32,33]. Flavonoids are abundant in plant parts such as seeds, fruits and leaves, and they contribute to plant colour, aroma and defence. In plants, they also regulate growth, attract pollinators and offer protection against environmental stresses. In the phenylpropanoid pathway, they can form a phenylpropanoid skeleton, while in polyketide pathway, they form a polymeric unit. The antioxidant properties of flavonoids result from the positioning of the hydroxyl group and the presence of the catechol moiety. The number of methoxy groups in phenolic acid molecules influences antioxidant activity. Phenolic acids possessing the same quantity of hydroxyl groups on an aromatic ring demonstrate uniform antioxidant properties. Since 4-hydroxy-3-methoxy benzoic acid has more antioxidant activity than 3-hydroxy-4-methoxy benzoic acid, the location of the hydroxyl group has a major impact on the flavonoid's antioxidant qualities. The antioxidant activity of phenolic acid molecules increases with the number of methoxy groups present. Metabolites prevalent in essential oils from plants and flowers are synthesised through glycolysis, yielding five-carbon intermediates like dimethylallyl diphosphate (DMAPP) and isopentenyl diphosphate (IPP). Terpenoids are a significant class of secondary metabolites originating from plants, consisting of multiple isoprene units. Terpenoids exhibit significant diversity, attracting considerable interest in anticancer and pharmacological applications. Certain terpenoids exhibit anticancer properties and are utilised to influence various stages of cancer progression [34]. Some other functional groups (isoprene and alcohols) present in the terpenoids enable them to act as effective reducing agents in green synthesis and also use in the conversion of metal ions like $HAuCl_2$ and $AgNO_3$ into stable NPs [35].Apart from flavonoids and terpenoids, phenolic compounds in general further enhance nanoparticle synthesis due to their strong antioxidant properties. These compounds scavenge free radicals, inhibit metal-induced oxidative stress and chelate metal ions, thus contributing both to the reduction process and to the stability of NCs [36]. They also serve as defence molecules in plants against UV radiation, pathogens and herbivores, while adding colour and flavour. Another critical component in plant extracts is proteins, which are released during the breakdown of plant cell walls. These proteins undergo enzymatic hydrolysis, forming small peptides that help stabilise NCs. Proteases function at optimal pH conditions to prevent protein denaturation while maintaining their activity [37]. These proteins also play an important role in the quality and texture of food, making them valuable in both biomedical and nutritional contexts. In addition to proteins, amino acids promote plant growth and contribute significantly to NCs synthesis, especially during plant growth stages such as tillering and flowering. They act as mobile nitrogen sources and are actively transported across plant membranes. Amino acids bind metal ions through their amino and carboxylate groups, forming stable complexes that guide the assembly of NPs. Specific amino acids such as cysteine, methionine, arginine and lysine facilitate the formation of silver metal NPs, by forming five-membered chelate rings with metal ions [38]. Furthermore, alkaloids are nitrogen-containing secondary metabolites that contribute to plant defense and possess well-known pharmacological effects, including anesthetic, anti-inflammatory and cardioprotective activities. Clinically important alkaloids include morphine, ephedrine, quinine and nicotine [39]. These derivatives exhibited strong inhibition of acetylcholinesterase enzymes, Aβ aggregation and NMDA receptors, along with a favourable safety profile in neuronal cell lines such as SH-SY5Y neuroblastoma cells. In green synthesis, alkaloids facilitate the reduction of metal ions, stabilise NCs and improve biocompatibility. They frequently collaborate with other phytochemicals, including terpenoids and phenolic compounds, to enhance the quality and functionality of nanomaterials. Natural compounds facilitate nanoparticle reduction and stabilisation, enhancing applicability in biomedical, environmental and agricultural fields. Plant-mediated nanotechnology represents a promising area for sustainable innovation [40].

4. Analytical characterisation techniques

The metal and metal oxide NCs are characterized using different based on their morphology, particle size, phase, composition, thermal stability, optical, magnetic, electrical and thermal properties and their various applications in medical and other fields. These NCs are characterized via various methods such as UV–visible spectroscopy, transmission electron microscopy (TEM) and X-ray diffraction (XRD) analysis affect the accuracy of measurements regarding size, shape and composition [41,42]. Spectroscopic methods such as UV–Vis, FTIR, X-ray photoelectron spectroscopy (XPS) and energy-dispersive X-ray spectroscopy (EDX) are commonly employed, as detailed in our latest publication [43]. UV–vis spectroscopy analysis of samples helps researchers understand electronic transitions and provided evidence to confirm the successful synthesis of NCs. In a recent report Ag/TiO_2 and $Ag/Co/TiO_2$-NCs are derived from *Ceratonia siliqua* extract and he found that the absorbance peak from *C. silique* extract reached 384 nm, but the corresponding low absorbance value of 0.217 revealed minimal interaction with UV light at this wavelength. The presence of visible-region peaks relative to the extract confirms the reduction of metal ions and successful NCs formation [44]. The NPs exhibit LSPR bands within the visible spectrum, associated with the excitation of MNPs conduction electrons resulting from their unique interaction with the electromagnetic field and light [45].In a recent report Mn/ZnO-NCs were derived from electronic waste, utilising *Borassus flabellifer* (toddy palm) and metals extracted from discarded batteries showing Mn and ZnO spectra depicted in Fig.3 (a). Shifts in these peaks indicate changes in particle size, aggregation or capping interactions.

Taraxacum officinale radix-based Z-scheme ZnO/ TiO_2-NCs were also studied for antibacterial potential and dye degradation. In XRD analysis of ZnO/ TiO_2-NCs, as per Fig.3 (b,e,f-h), a significant alignment between

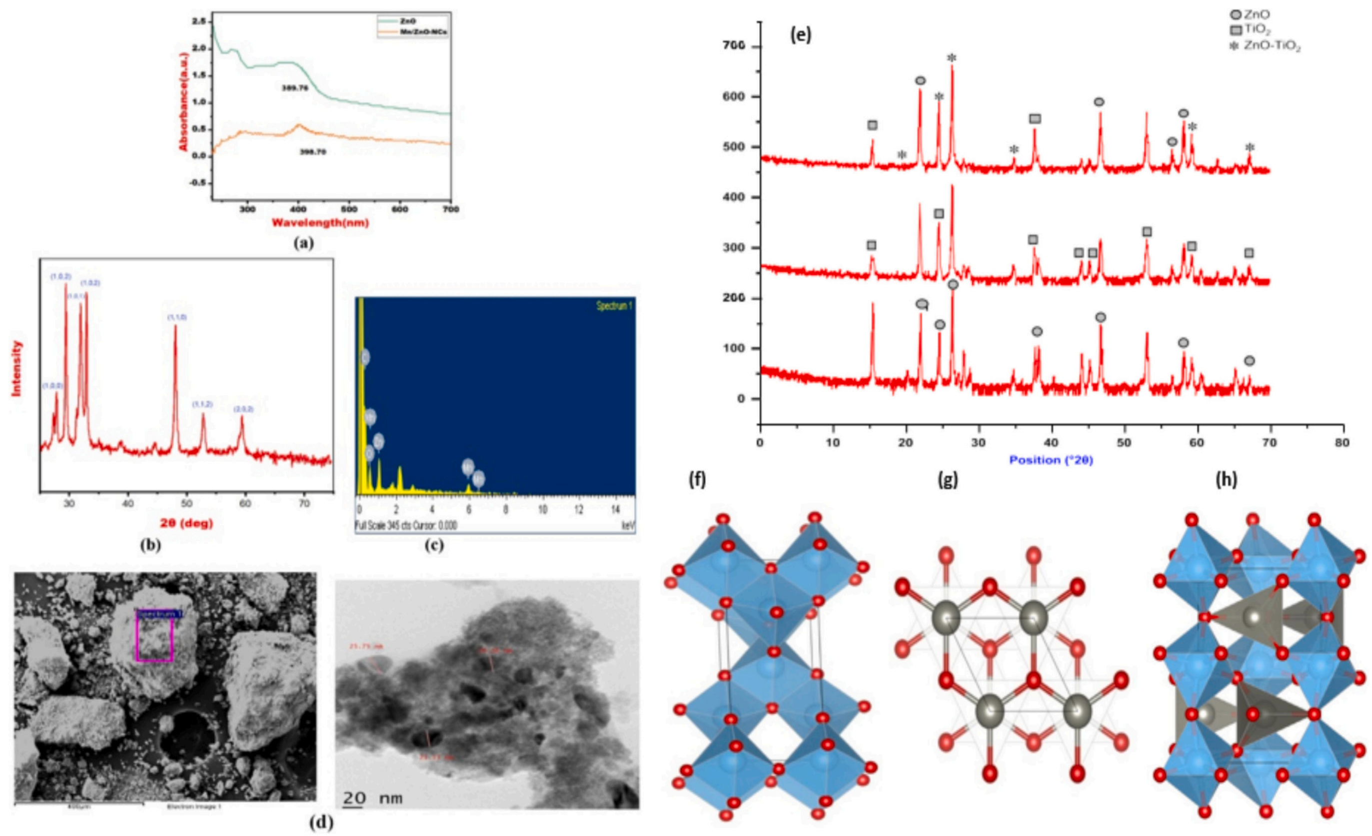

Fig. 3. ((a) UV–Vis spectra showing surface plasmon resonance, (b) XRD spectra showing crystalline structures (c) EDX elemental mapping. (d) SEM analysis revealing surface chemical states **(e)** XRD pattern for crystalline phases for ZnO, TiO_2 and ZnO/TiO_2-NCs (f) (g) (h) Tetragonal TiO_2, Hexagonal ZnO, and Orthorhombic ZnO/TiO_2 NCs respectively elucidated via XRD.

the (102) and (103) planes of ZnO and the (200) and (204) planes of TiO_2. This overlap points to a robust interaction between their lattice structures, conclusively confirming the formation of the ZnO/TiO_2 composite [46]. In another recent report, GO, rGO and the rGO/ZnO, rGO/CuO, rGO/TiO_2 and rGO/Ag_2O-NCs are prepared and characterised using XRD. The recorded XRD patterns were obtained from 5° to 60° (2θ) [47]. Notably, the absence of any impurity phase affirms the dual-phase composition of the synthesised heterojunction. These XRD results provide compelling evidence of the successful creation of the above NCs, showcasing distinct lattice interactions and the presence of two well-defined phases.

SEM provides surface topography and morphology, allowing visualisation of particle aggregation and surface texture [48]. FTIR spectroscopy delivers precise data on molecular bonds and functional groups exhibiting a permanent dipole moment. FTIR operates using longer wavelengths, which typically pose reduced risk to the samples. This feature allows for repeated analyses while maintaining sample integrity. Absorption bands are observed at O-H stretching approximately 3400 cm^{-1}, C=O stretching near 1700 cm^{-1} and N–H bending within 1500–1600 cm^{-1}, indicating the presence of hydroxyl, carboxyl and amine groups involved in the synthesis [49]. In another report, ZnO/CuO/AgO NCs were prepared by the hydrothermal method. The FTIR peaks occur at 546 cm^{-1}, 623 cm^{-1}, and 432 cm^{-1}, corresponding to Zn-O, CuO, and AgO stretching, respectively, further indicating the formation of a heterostructure [50]. The XPS technique provides a detailed surface chemical information, including oxidation states and bonding environments of the metal components. It confirms whether the NPs contain metallic or oxidised forms of elements like silver, zinc and iron [51]. EDX technique often coupled with SEM or TEM Fig.3(d), enables qualitative and semi-quantitative elemental analysis, verifying the presence of target metals and other residual plant-derived components, ensuring uniform distribution within the sample [52]. In a recent study, CuO-NiO-ZnO mixed metal oxide nanocomposite are synthesized and their EDX data showed that the distribution of Cu, Ni and Zn was not uniform across the selected area of the sample, which suggests that the oxides were not uniformly intermixed in the NCs. The average crystallite sizes for the three oxide phases in the NCs are found to be between 17 nm and 25 nm. The observed band gap of 1.68 eV lies between that of CuO, ZnO and NiO and shows that it is possible to tailor the band gap of the nanocomposite to suit certain applications [53]. For structural and morphological characterisation, techniques such as X-ray diffraction (XRD), transmission electron microscopy (TEM) and scanning electron microscopy (SEM) are extensively used. In another report, CuO-NiO-ZnO mixed metal oxide nanocomposite are synthesized and that observed TEM value to be in the range between 15 nm and 40 nm [53]. TEM provides more detailed internal structural information, including the size, shape distribution and lattice fringes of the particles [54]. High resolution TEM can detect crystal defects, nanoparticle interfaces and core-shell structures, which are important for understanding the properties of the NCs [55].

Dynamic light scattering (DLS) is a technique used to determine the hydrodynamic size and size distribution of NPs in suspension. Biologically synthesised NCs exhibit size variability; therefore, DLS provides complementary data to microscopy by indicating average particle behaviour in solution [56]. ZnO-based NCs were synthesized by heating Zn (II) acetylacetonate in oleic acid/oleylamine in the presence of 1,2-hexadecanediol at 220°C, and the DLS value 7nm [57]. Zeta potential analysis assesses surface charge and stability in colloidal dispersions [58]. A higher absolute value of zeta potential signifies enhanced electrostatic repulsion among particles, correlating with improved stability and reduced aggregation propensity. Additional techniques involve thermo-gravimetric analysis (TGA), utilised for assessing the thermal stability and organic content of the NCs. This is particularly effective for assessing the quantity of plant-based capping agents. Brunauer–Emmett–Teller (BET) analysis quantifies surface area and porosity, critical metrics in catalysis and adsorption applications [59]. Studies on NiO/BPAC, CuO/BPAC and ZnO/BPAC NCs showed specific surface areas of 88.2 m^2/g, 77.1 m^2/g and 72 m^2/g, respectively, indicating higher porosity and surface sites for adsorption, particularly for NiO/BPAC [60]. A higher surface area and appropriate pore structure enhance the material's interaction with gases, liquids or biological molecules.

Together, these techniques provide a comprehensive understanding of plant-based NCs, from their formation mechanism and structural features to their chemical composition and functional behaviour. Proper characterisation ensures that these green-synthesised materials meet the specific requirements for applications in biomedical, environmental and industrial fields.

5. Biological potential

Effective functionalization of green-synthesised materials with biological molecules significantly improves the therapeutic and diagnostic capabilities of metal and metal oxide NPs [61]. The following sections highlight their growing relevance in various areas of biomedical research.

5.1. Therapeutics

Biogenic metal and metal oxide nanostructures also show vast potential in therapeutic areas. These NPs have shown remarkable efficacy in fighting several diseases due to their anticancer, antidiabetic, anti-inflammatory and antioxidant properties [62]. The attractiveness of green-synthesised NPs lies in their enhanced bioavailability, eco-friendly synthesis and cost-effectiveness, which collectively establish them as a sustainable alternative to their chemically synthesised counterparts [63]. These properties have led to increased interest and research into their use in modern medical treatments.

5.1.1. Antibacterial properties

The antibacterial properties of a substance have an ability to kill bacteria and inhibit their growth. This can be achieved through a variety of mechanisms such as disrupting bacterial cell walls, interfering with bacterial enzymes or inhibiting bacterial replication. These properties are important in preventing and treating bacterial infections. Metal and metal oxide NCs exhibit significant antibacterial properties, making them promising candidates for fighting drug-resistant bacteria and various infectious diseases [64]. Their effectiveness arises from a combination of factors linked to nanoscale dimensions and the inherent properties of metal and metal oxide components. Multiple mechanisms contribute to the antibacterial activity of these NCs, as shown in Fig.4. Metal and metal oxide NCs catalyse the production of reactive oxygen species, including superoxide radicals (O^{2-}), hydrogen peroxide (H_2O_2) and hydroxyl radicals.

These highly reactive species can damage crucial bacterial components such as the cell wall, cell membranes, proteins, enzymes and DNA. Second, these NCs release the metal ions like silver (Ag) and copper (Cu), releasing metal ions (Ag^+ and Cu_2^+). These ions have strong antimicrobial effects and bind the cell wall of bacterial cells after interfering with the enzyme system, damaging the DNA [65]. In the third step, these NCs enter the cell and find the actual cause of internal damage and interfere with the electron transport chain, which reduces the production of ATP and leads to the death of the bacterial cell.

Currently, many scientists are investigating the antibacterial activity of these metal and metal oxide NCs on various bacterial infections using various synthetic techniques. These NCs are made synthetically and are being examined. Some metal and metal oxide NCs like NiO/ZnO and CuO/ZnO have been widely studied for their antibacterial and photocatalytic activities [66]. The results of the antibacterial activity show increased efficacy of NCs against Gram-negative bacteria, with the NCs at a molar ratio of 1:2:1 (Zn:Ni: Cu) exhibiting the largest zone of inhibition. Results indicate that NCs can efficiently purify contaminated water by degrading hazardous organic compounds and can be applied in antibacterial ointments. The antibacterial efficacy of Mn/ZnO-NCs was evaluated against four bacterial strains: *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus pneumoniae* and *Pseudomonas aeruginosa*. As shown in Fig. 5, the NCs exhibited a concentration-dependent bactericidal action, with increasing zones of inhibition at 50, 75 and 100 μg and no inhibition at 25 μg. The inhibition zones were 13 ± 0.11 mm for *S. aureus*, 15 ± 0.11 mm for *E. coli*, 15 ± 0.34 mm for *S. pneumoniae* and 14 ± 0.28 mm for *P. aeruginosa* at a dose of 100 μg. The analysis of Fe_3O_4 NPs and the synergistic effects of chitosan/Fe_3O_4-NCs revealed notable antibacterial efficacy, evidenced by an expanded inhibition zone [67,68]. CS/Fe_3O_4-NCs can serve as antimicrobial agents in food packaging and preservation applications. The antibacterial efficacy of Fe_2O_3 and Ag_2O-NCs is primarily linked to the liberation of silver ions (Ag^+) and iron oxide ions (Fe^{2+} and Fe^{3+}). These ions bind to the bacterial cell wall via electrostatic attraction, reacting with the thiol groups and

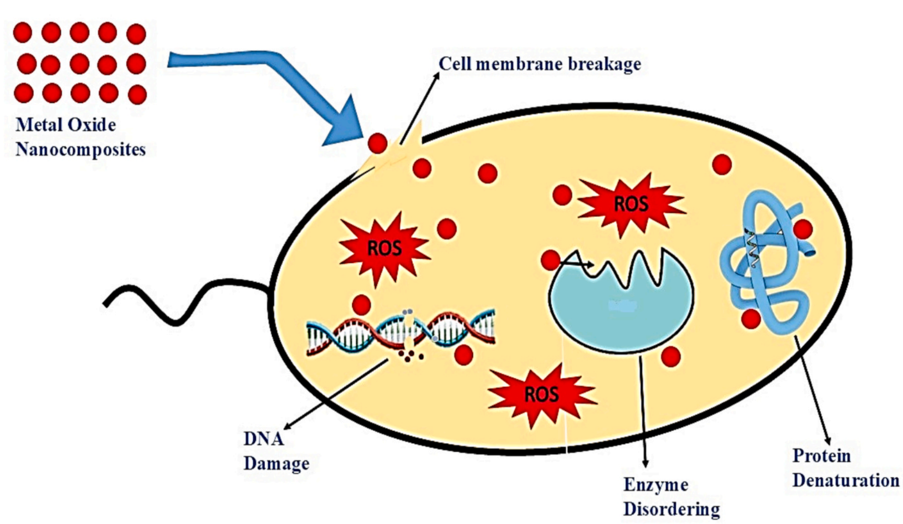

Fig. 4. Mechanisms of antibacterial action of biogenic metal and metal oxide NCs, including ROS generation, protein denaturation, DNA damage, and disruption of bacterial membranes.

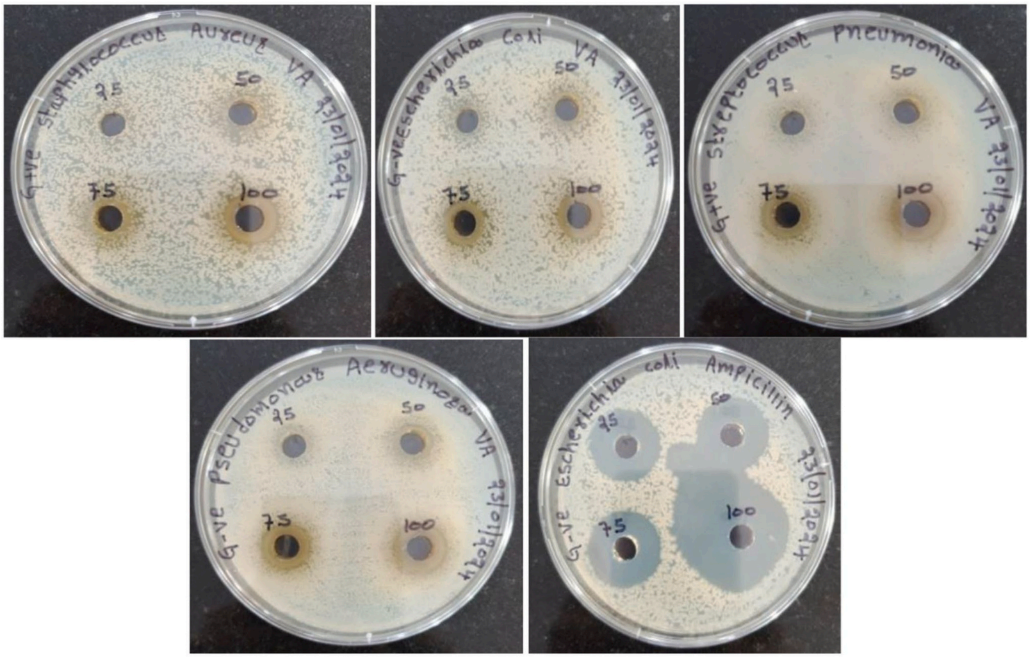

Fig. 5. Antibacterial zone of inhibition shown by Mn/ZnO-NCs against pathogens seen through disc images recently published in our own work @copyright springer 2025 [82].

obstructing nutrient transport, ultimately resulting in bacterial death [69]. In metal oxides, reactive oxygen species (ROS) significantly inhibit bacterial growth by inducing oxidative stress and reduction processes that impact bacterial or fungal cell components. CdO/CuO/ZnO NCs showed a good zone of inhibition against *Staphylococcus aureus* (28mm) and *Salmonella typhi* (22mm) [70]. Furthermore, Fe_2O_3/CuO/ZnO NCs give a good zone of inhibition against *E. coli, P. aeruginosa, S. typimurium, S. aureus* and *B. subtilis* with MICs 50, 50, 12.5, 50 and 25 μg/mL, respectively [71]. A key mechanistic pathway involves the disruption of the mitochondrial membrane potential (MMP). ROS attack compromises the integrity of the inner mitochondrial membrane, leading to depolarisation (a loss of MMP). This collapse disrupts the proton gradient essential for ATP synthesis, crippling cellular energy production. Consequently, the resulting bioenergetic crisis, coupled with amplified oxidative damage, initiates apoptosis or necrosis, leading to irreversible cell death [72]. This MMP-driven mechanism is a fundamental process underlying the potent bactericidal and fungicidal activity of these nanomaterials.

5.1.2. *Anticancer properties*

Metal and metal oxide NCs induce cytotoxic effects in cancer cells while sparing normal cells. Anticancer activity has been shown with NCs, both independently and in conjunction with various therapies, including photocatalytic therapy and certain anticancer medications [73]. Metal and metal oxide NCs are utilised in cancer therapy through passive or active mechanisms. A passive process utilises enhanced permeability and retention effects. During this process, the NCs are functionalised and directed towards cancerous cells, allowing biomolecules or ligands to bind as receptors to enhance delivery specifically to the targeted cancerous cells rather than normal cells. In anticancer therapy research, metal oxide NCs are utilised experimentally to eliminate tumour cells in vitro and in vivo, as illustrated in Fig. 6. These particles exhibit high biological activity while maintaining low cytotoxicity. Fe_2O_3 NPs exhibit biological activity in anticancer applications

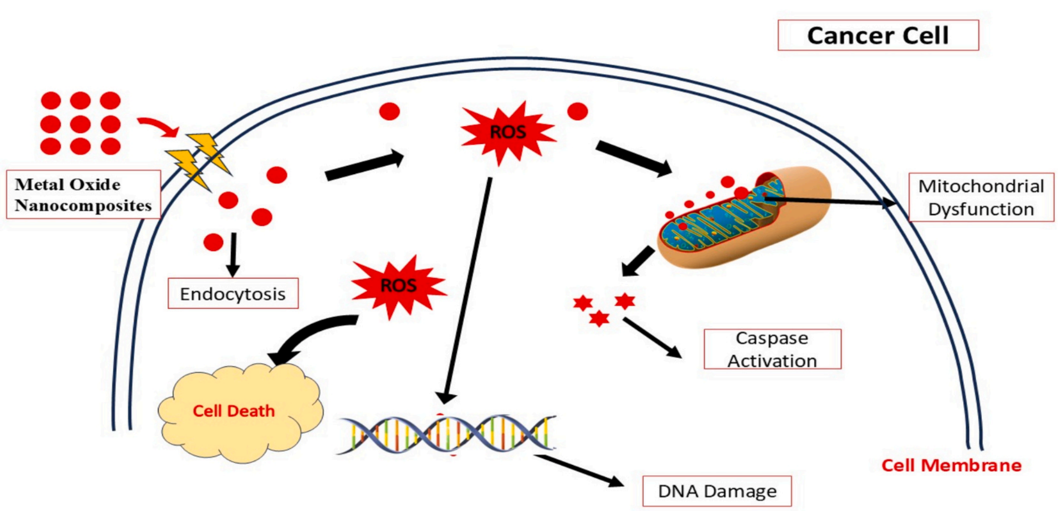

Fig. 6. Graphic representation of Anticancerous potential by nanocomposites.

due to their magnetic properties. Iron is a biological component of blood and certain enzymes [74]. These NCs primarily work by disrupting processes vital for cancer cell growth and division. They achieve this through several mechanisms, including DNA damage, cell cycle arrest and inhibition of angiogenesis, ultimately leading to cell death or reduced tumour growth [75]. In prior research, Mn/ZnO-NCs exhibited IC_{50} values of 195.5nM for BXPC3 cells, 178.10 nM for OVCAR3 cell lines, 128.1nM for MDA-MB231 cells and 65.08nM for SKOV3 cells. The synthesised NPs exhibited superior inhibition of SKOV3 cell lines compared to the other cell lines analysed, as illustrated in Fig. 7. Fe_2O_3/CuO/ZnO NCs give a good anticancer zone of inhibition with normal and cancerous cell lines. Results that the IC_{50} of Lnanocomp toward Wi-38 normal cell line was 196.4 μg/mL [71].

5.1.3. Tissue engineering and regenerative medicine

The goal of tissue engineering and regenerative medicine is to use biological materials and methods to replace, repair, or regenerate damaged tissues and organs [76]. Tissue engineering involves combining cells, biomaterials (scaffolds) and growth factors to create functional tissues, often in a lab setting [77]. Regenerative medicine builds upon tissue engineering by also incorporating the body's own healing capabilities, including stem cells and other therapies, to induce

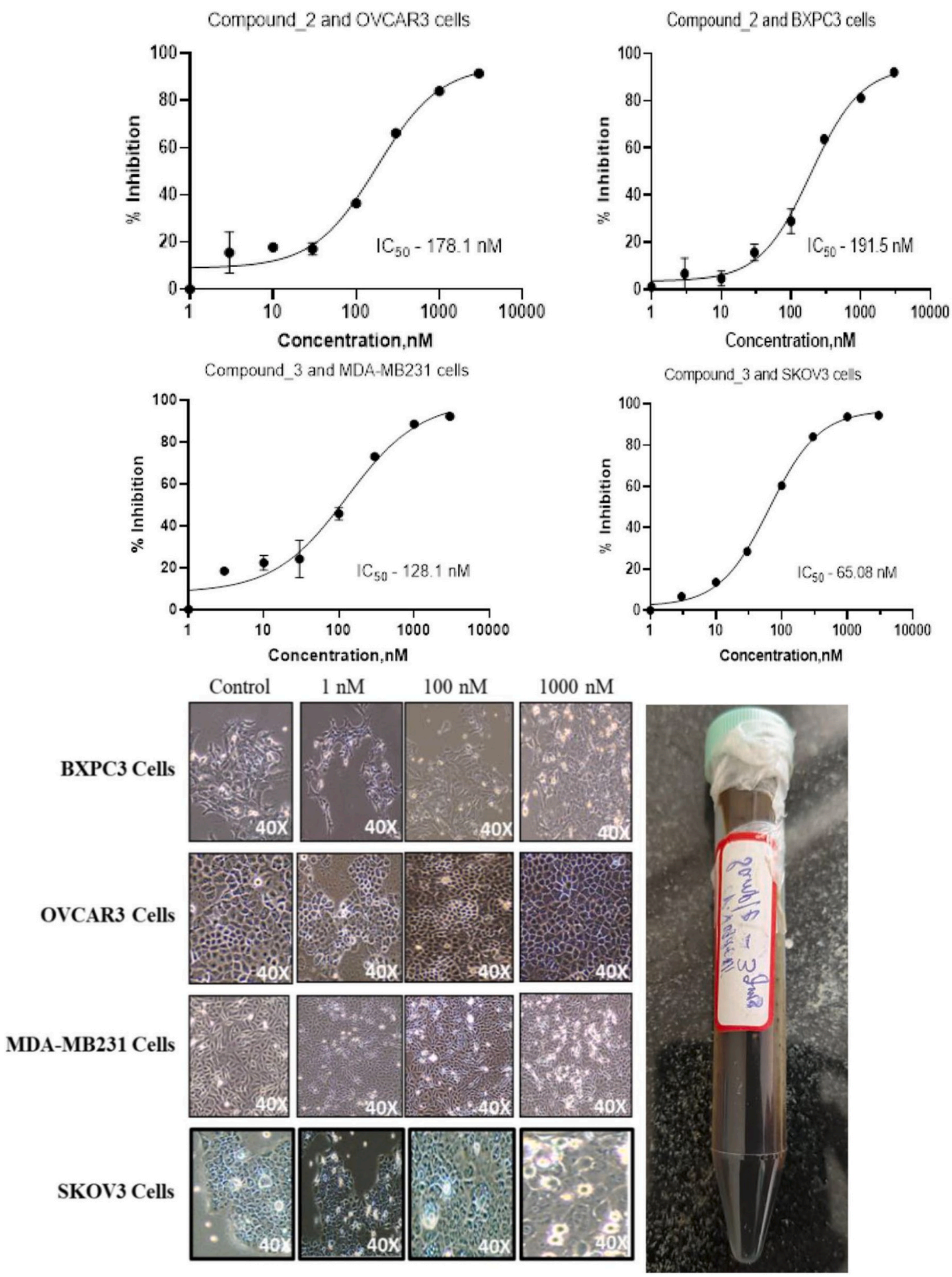

Fig. 7. Anticancer efficacy in BXPCE3 (human pancreatic cancer cell line) MDA-MB231 cells (triple-negative breast cancer cell line) SKOV3 cells (human ovarian cancer cell line) Cells and OVCAR3 (ovarian adenocarcinoma cell line) subjected to treatment with NCs. Image taken from our recently published work [82].

tissue regeneration in vivo. Metal and metal oxide NCs material is utilised in tissue engineering and regenerative medicine applications. Nanomaterials facilitate tissue repair and regeneration through the seeding of cells, bioactive agents and various growth factors. Tissue engineering is a rapidly advancing field focused on fabricating materials that mimic the body's tissues to replace or restore organ functionality [78]. This technique involves isolating cells, cultivating them in a biomaterial under specific conditions and subsequently transferring them to the target site. Common NCs, such as Chitosan, can effectively replicate the extracellular matrix of tissues. These NCs facilitate cell attachment and create an optimal microenvironment for tissue regeneration. The metal and metal oxide NCs are the most effective agents for faster wound healing among all the other wound healing materials [79]. These NCs have unique biological, optical and physicochemical properties. Some of them can be directly applied to the wounded area, or some of them can be incorporated into scaffolds to create a hydrogel matrix, which promotes wound healing through their antimicrobial, as well as anti-inflammatory and proangiogenic properties [80]. This review focuses on two prominent nanozymes, specifically Ce/FeO, which are extensively researched. Emphasis on applications including cardioprotection, therapeutic angiogenesis, bone tissue engineering and wound healing [81]. Gold polymer NCs for future therapeutic and tissue engineering applications enhance scaffold properties by integrating polymeric and inorganic nanomaterials. Because of their visual qualities, Au NPs have attracted a lot of interest in tissue engineering. NCs modify scaffold mechanical properties and improve cell adhesion. Cell adhesion and proliferation rely significantly on the elasticity and elastic moduli of scaffolds. Embedding 5 nm AuNPs in electrospun polylactic acid fibres improved Young's modulus, promoting skeletal muscle tissue development within the scaffold [82]. The incorporation can improve electrical conductivity and enable the transmission of electrical signals between cells, especially in cardiac tissue engineering. Different sizes and shapes of Au NPs are incorporated into natural or synthetic polymer matrices to enhance performance in tissue engineering applications [83].

5.1.4. *Antidiabetic activity*

Antidiabetic drugs, also known as antihyperglycemic agents, are medications used to manage and control high blood sugar levels in individuals with diabetes. These drugs aim to bring blood glucose levels in the normal range and help to prevent the long-term complications associated with diabetes. Metal and metal oxide NCs have antidiabetic properties, such as reducing diabetic enzyme levels, increasing insulin levels and lowering cholesterol [84]. Antidiabetic activity has been derived from various compounds, including alkaloids, phenols, steroids, saponins, terpenoids and tannins. Natural products effectively activate and translocate GLUT4, facilitating their use in diabetes treatment. Zn/ZnO-NCs exhibit several anti-diabetic effects: (a) they enhance insulin secretion and strengthen the antioxidant defence in pancreatic β-cells, (b) they lower blood glucose levels and improve glucose tolerance, (c) they boost insulin signalling and sensitivity, facilitating glucose uptake in the liver, skeletal muscle and adipose tissue, (d) they inhibit lipolysis in adipocytes and gluconeogenesis in hepatic cells [85]. Ag/CuO-NCs were synthesised using extracts from *Murraya koenigii* and *Zingiber officinale* through a chemical method. Phytochemical analysis verified the presence of active phytoconstituents in both extracts. Phyto-synthesised Ag/CuO-NCs exhibited enhanced antidiabetic activity against α-amylase, α-glucosidase and glucose-6-phosphatase enzymes. *Zingiber officinale* extract-mediated Ag/CuO-NCs exhibited enhanced antidiabetic activity relative to other synthesised nanomaterials, due to the elevated concentration of phytoconstituents present in the extract [86]. RGO/ZnO-NCs synthesised via the green route demonstrated DPPH scavenging activities that were found to be dose-dependent. RGO/ZnO demonstrated effective inhibition of α-amylase and α-glucosidase antidiabetic activities in vitro [87]. Synthesised Ag/ZnO/MEL/GA-NCs exhibited improved antidiabetic efficacy against α-amylase and α-glucosidase. Digestive enzymes like α-amylase and α-glucosidase play a vital role in carbohydrate digestion. This study employed the specified digestive enzymes to assess the antidiabetic effectiveness of the synthesised MEL/Ag NPs, MEL/ZnO-NPs and Ag–ZnO/MEL/GA-NCs. In another report, CuO/TiO_2 and ZnO/TiO_2 NCs were synthesised using *Parkia timoriana bark* extract and cheked it antioxidant and antidiabetic activities [88]. The antioxidant property in ZnO/TiO_2 (84.07%) was higher than in CuO/TiO_2 NCs (72.76%). The IC_{50} value of CuO/TiO_2 and ZnO/TiO_2 in α-amylase inhibition assay was 72.12 μg/mL and 75.95 μg/mL, respectively, and the IC_{50} value of CuO/TiO_2 and ZnO/TiO_2 in α-glucosidase inhibition assay was 30.80 μg/ml and 25.69 μg/ml [89].

5.1.5. *Anti-inflammatory estimation*

Inflammation serves as a vital defence mechanism of the body against harmful stimuli, including pathogens, allergens, irritants and damaged cells. Long-term inflammation, while crucial for the body's defence mechanisms, can lead to various diseases such as cardiovascular issues, arthritis and gastrointestinal disorders. Developing effective treatments for inflammation is a significant challenge in medical science. A promising approach utilises metal-based NC materials that combine NPs with a matrix such as polymers, ceramics or metals. These NCs have shown enhanced therapeutic effects, including improved stability, bioactivity and targeted delivery, making them an effective solution for inflammatory diseases [90]. The ability of metal-based NCs to penetrate inflamed cells and tissues allows for more selective and efficient treatment, making it possible to reduce adverse effects associated with conventional treatments. Many metal based NCs have been explored in the literature for their anti-inflammatory properties. One of the best studied materials is silver based NCs. Silver NPs are widely known for their antimicrobial and anti-inflammatory activities. Silver has been incorporated into polymers such as chitosan and polyethylene glycol creating blends with improved biocompatibility and anti-inflammatory properties. These compound work by modulating the immune response, inhibiting the production of pro-inflammatory cytokines and reducing oxidative stress [91,92]. Several studies have shown that these silver-based NCs effectively reduce inflammation by blocking the activation of nuclear factor kappa B (NF-κB) and cyclooxygenase-2 (COX-2), two key regulators of the inflammatory process. Copper oxide NCs can modulate inflammatory cytokines such as TNF-α and IL-1β, which are central to the inflammatory response. Copper NPs are believed to reduce the production of reactive oxygen species (ROS) and inhibit the activation of inflammatory pathways, making them effective in conditions where oxidative stress plays a key role. Zinc oxide has long been used in dermatological applications for its soothing and healing effects and its incorporation into NCs has been found to enhance its efficacy [93]. Zinc oxide-polymer NCs, particularly those made from biogenic sources, have been found to be capable of reducing inflammation by modulating the activity of COX-2 and preventing the denaturation of albumin. These composites have been studied for their potential in treating chronic wounds, inflammatory skin diseases and arthritis. Zinc oxide-silver NCs also show superior anti-inflammatory and antimicrobial properties, suggesting their potential for use in wound care and other inflammatory conditions. Another promising metal-based NCs is cerium oxide (CeO_2) which is known for its antioxidant properties. Studies have shown that cerium oxide NCs can inhibit the activation of NF-κB and MAPK pathways, which are central to the inflammatory process. Additionally, cerium oxide NCs have shown promising results in treating neuroinflammatory diseases such as Alzheimer's and Parkinson's, by reducing inflammation in the brain and preventing neurodegeneration. Titanium dioxide based composites are used in biomedical applications due to their ability to induce oxidative stress in macrophages, which in turn suppresses inflammatory responses [94]. TiO_2-NCs have been found to be able to reduce platelet aggregation, a common feature of inflammatory vascular diseases by modifying the thrombin-anti-thrombin (TAT) complex. This property makes TiO_2-NCs suitable for the treatment of conditions where inflammation contributes to disease progression. In the current study, Cu-doped ZnO NCs were synthesised. The Anti-inflammatory inhibition was observed at using low concentration (100 μg/mL) with enhancing 23.85% while at high concentrations 500 and1000 μg/mL. The anti-inflammatory activity was approximately similar with enhancing 3.91% and 1.99%, respectively [95].

In addition to these individual metal-based NCs, hybrid NCs, which combine multiple metals and metal oxides, have shown improved anti-inflammatory effects. For example, silver-titanium oxide hybrid NCs have both anti-inflammatory and antimicrobial properties [96]. These composites leverage the synergistic effects of silver's antimicrobial activity and titanium oxide able to modulate inflammatory pathways. Studies have shown that these hybrid NCs effectively reduce pro-inflammatory cytokine levels, providing dual benefits in treating inflammatory diseases, especially where infection and inflammation coexist. Aluminium oxide (Al_2O_3) NCs have been investigated for their potential applications in treating inflammatory conditions. Aluminium oxide-polymer NCs exhibit notable anti-inflammatory properties in animal models of arthritis and inflammatory bowel disease. These compounds decrease pro-inflammatory cytokine production and block the activation of inflammatory signalling pathways. Aluminium oxide-based NCs are effective in drug delivery systems, enabling targeted delivery of therapeutic agents to inflamed tissues, thus enhancing treatment efficacy [97].

5.1.6. *Drug delivery*

Drug delivery refers to the process of delivery therapeutic compounds to specific areas of the body with high precision, ensuring that drugs reach their target sites in the required dose, timing and concentration. However, conventional drug delivery systems often face significant challenges, such as poor bioavailability, rapid degradation of drugs, difficulty in targeting specific tissues and unwanted systemic side effects [98]. These limitations highlight the critical need for advanced drug delivery technologies that can improve the efficacy and safety of treatments. The effective drug delivery is essential for treating a wide range of diseases, particularly cancer, infections, cardiovascular diseases and chronic conditions. Inadequate distribution often results in inadequate concentrations of drugs at their intended site of action, resulting in diminished therapeutic outcomes or undesirable side effects. As a result, there has been a rise in research focusing on controlled, targeted and sustained release systems, with NCs emerging as a promising solution. The blends integrate the unique properties of NPs with the matrix's functional characteristics, leading to improved drug delivery. Metal and metal oxide-based NCs demonstrate significant potential for enhancing drug delivery systems owing to their distinct properties. These NCs provide multiple benefits, including enhanced surface area for drug encapsulation, improved stability and controlled release profiles [99]. The surface of these NCs can also be functionalized, enabling the attachment of targeting ligands, antibodies, or peptides that can specifically recognize and bind to receptors on the target tissues or cells, ensuring precise delivery and reducing systemic side effects. In addition, NCs can provide sustained or controlled release of the drug over time, which is importanr for maintaining therapeutic drug concentrations and preventing toxicity. The release of drugs from NCs can be triggered by various factors, such as pH changes, temperature fluctuations, light or even external magnetic fields, depending on the type of NCs and the drug being delivered [100].

NCs exhibit drug release mechanisms that can be classified into three primary processes: diffusion-based release, degradation-based release and external stimuli-based release as can be seen in Fig.8. Diffusion-based release involves the gradual diffusion of the drug through the NCs, resulting in an extended release profile, beneficial for chronic disease management. In degradation-based release, the nanocarrier material disintegrates gradually, resulting in drug release upon matrix breakdown. This is applicable for controlled drug delivery, where the material's degradation rate governs the drug release rate [100].

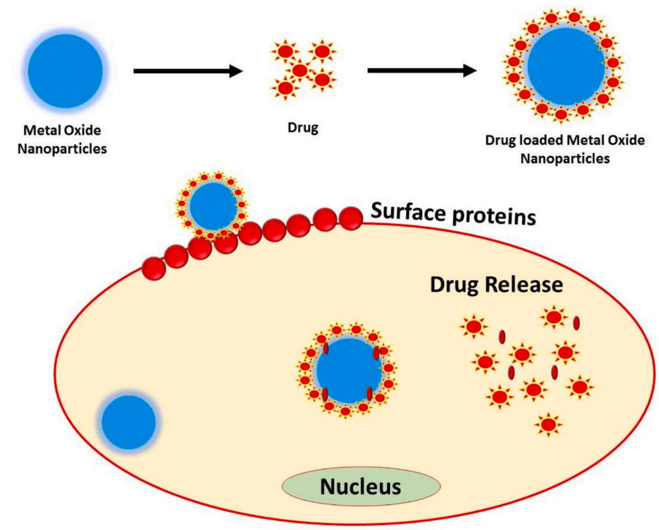

Fig. 8. Schematic of drug delivery mechanisms in NCs: diffusion-based, degradation-triggered, and stimuli-responsive systems (pH, temperature, UV light) for precise and sustained therapeutic release.

Conversely, release driven by external stimuli entails drug release triggered by variations in external conditions, including pH, temperature or light exposure. Titanium oxide (TiO_2)-based NCs enable drug release upon UV light exposure, facilitating precise and time-sensitive delivery. Metal and metal oxide-based NCs exhibit significant potential in drug delivery systems owing to their unique properties. Gold NPs (Au-NPs) are commonly utilised in NCs due to their superior biocompatibility and straightforward functionalisation process. NCs can be designed to release drugs upon light exposure, allowing for precise drug delivery control. They can also be modified to target specific cancer cells, improving therapeutic efficacy and reducing side effects. Silver NPs (Ag-NPs) exhibit antimicrobial properties and are integrated into nanocarriers for precise antibiotic delivery, especially in wound healing scenarios [101]. These NCs enable continuous antibiotic release, minimising infection risk and enhancing tissue regeneration. Iron oxide NPs (Fe-NPs) exhibit magnetic properties that allow for manipulation via external magnetic fields, facilitating targeted drug delivery. Iron oxide-based nanocarriers facilitate the targeted delivery of anticancer drugs to tumours, minimising the systemic toxicity linked to conventional chemotherapy. Zinc oxide (ZnO) nanocrystals are recognised for their biocompatibility and have been investigated for the delivery of anticancer drugs and antibiotics, enabling controlled release over time. TiO_2-NCs utilise photocatalytic properties to release drugs under UV light, optimising local drug delivery applications. Numerous studies demonstrate the effectiveness of metal and metal oxide NCs in drug delivery applications. Gold nanoclusters have been utilised for the targeted delivery of the chemotherapeutic agent doxorubicin to cancer cells. Gold NPs are modified with targeting ligands that bind to cancer cell receptors, facilitating direct drug delivery to the tumour site and reducing harm to healthy cells. Ag based NCs effectively control the release of antibiotics in wound healing applications, ensuring prolonged therapeutic effects and minimising infection risk. Iron oxide NPs enhance anticancer drug targeting to tumour sites by utilising an external magnetic field to concentrate the drug precisely at the tumour location, improving therapeutic outcomes and minimising side effects [102].

5.2. *Diagnostic*

Accurate and reliable diagnostic tools are crucial for uncovering cellular and molecular mechanisms, allowing scientists to visualise and analyse the behaviour and alterations of cellular components. Biologically synthesised metal and metal oxide NPs show great promise in this realm due to their unique surface plasmon resonance (SPR) properties [103]. These NPs are highly sensitive to their surrounding environment, allowing for the accurate detection of analytes and their metabolic byproducts. Their excellent sensing capabilities make them excellent candidates for applications in biosensing and molecular imaging.

5.2.1. Biosensing

Biosensor is an analytical device used to detect the presence or concentration of a specific substance (analyte) in a sample through a biological component (e.g., enzyme or antibody). This detection transforms biological interactions into quantifiable signals, including electrical, optical, or thermal signals. Metal and metal oxide nanocrystals serve as nanosensors due to their extensive surface area, elevated sensitivity and capability to identify diverse substances [104]. These properties can be tailored by changing the size, shape and composition of the metal oxide NCs. In nanosensing, metal and metal oxide NCs is electrical resistance changes when they react with specific gases. These NCs are used in many applications, including environmental monitoring, health tracking and gas leak detection. Many metals and their oxides exhibit biosensor activity, especially in electrochemical sensing applications. Prominent examples include ZnO (zinc oxide), TiO_2 (titanium dioxide), Fe_2O_3 (iron oxide), NiO (nickel oxide) and CuO (copper oxide) [105]. Some other applications of nanosensors are shown in Fig. 9.

Produces metal oxide semiconductors for biosensor applications. A biosensor structure can be decomposed into a biotransducer. The biotransducer features a biocompatible layer containing biological recognition entities, including enzymes, proteins and probe molecules, which are affixed to the transducer surface. Most biosensors are utilised for glucose, H_2O_2 and uric acid [106]. Employed CuO/Graphene NCs in biosensor applications to address the constraints of enzymatic sensors. TEM images show uniform dispersion of size-selected CuO NPs on the graphene surface. Amperometric detection of glucose demonstrates a detection limit of 1 μmol L−1 and a linear range extending from 1 μmol L−1 to 8 mmol L−1 with CuO/graphene modified glassy carbon (GC).

5.3. Cell imaging

Cell imaging is the visualisation of cells, their components and processes using microscopy techniques. It is a crucial tool in biological research, allowing scientists to study the structure and function of cells in detail. This includes observing organelles, macromolecules and dynamic processes within living cells, as well as their interactions with each other and their environment as depicted in Fig.10. Metal and metal oxide NCs are used in cell imaging because of their unique properties, including their size, shape and surface functionality. They can be used in a variety of imaging techniques, including optical imaging, magnetic resonance imaging (MRI) and computed tomography (CT). Cell imaging is the process of using microscopes and other techniques to see cell structures and processes. It's a key tool in biological research, disease treatment and clinical diagnosis. In this, the metal and metal oxide NCs are used to detect and capture the image of the cancer cell [107]. Fabricate iron oxide NPs for biomedical use. Iron oxide-based biomagnetic NCs, known for their notable properties, have been employed in MRI and cancer treatment for decades. The presence of adverse effects constrains the expansion of clinical applications. Limitations stem from suboptimal material design and reduced magnetic relaxivity, leading to agglomeration and insufficient functionality. Various synthesis methods and modification strategies have been employed to optimise the size, shape and properties of iron oxide nanoparticle-based NCs in response to these challenges. The resulting NCs demonstrate considerable potential in cell imaging, therapeutic applications, diagnostics and theranostics, encompassing MRI, anticancer and antimicrobial activities [108].

6. Challenges in plant-mediated synthesis of metal and metal oxide NCs

Metal and metal oxide NCs synthesised via plant mediated methods provide an environmentally friendly alternative to normal chemical synthesis. However, despite its green appeal, there are several challenges associated with this approach, including the following:

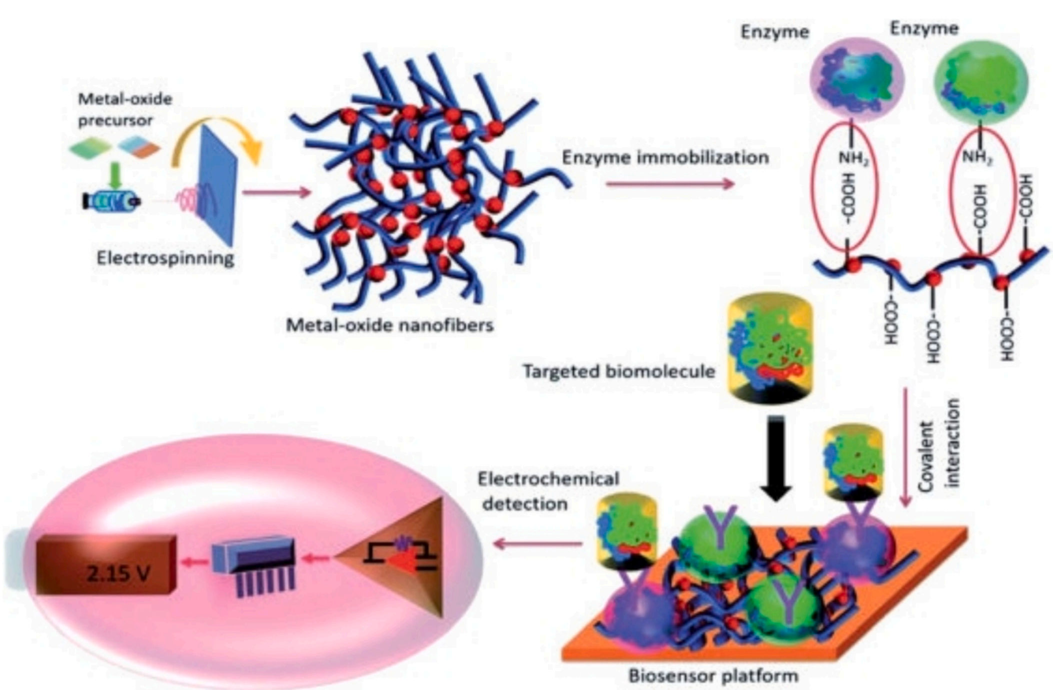

Fig. 9. Applications of NCs in biosensing, highlighting their SPR-based detection capabilities, transduction principles, and electrochemical sensing for glucose and disease markers @copyrights RSC advances 2016[115].

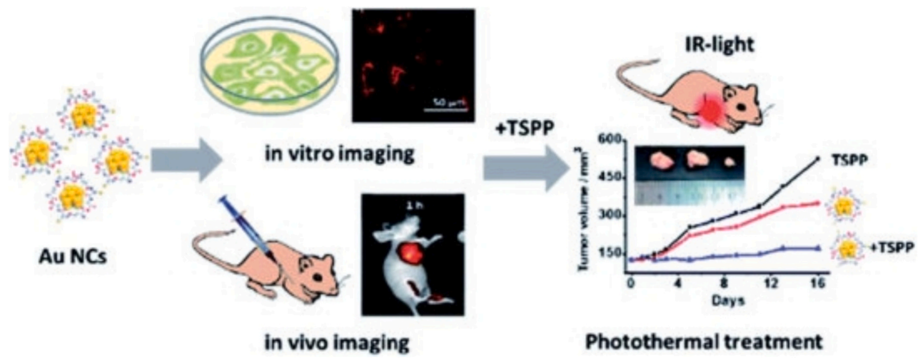

Fig. 10. Role of NCs in cell imaging and theranostics, demonstrating their integration in MRI, CT imaging and real-time cellular tracking (@copyright RSC Advances [118]).

6.1. Lack of standardisation in plant extracts

One of the most persistent issues is the lack of standardisation in the preparation of plant extracts. The phytochemical profile of extracts comprising flavonoids, phenolics, terpenoids, alkaloids and proteins varies with plant species, geographic origin, season, age and even the part of the plant used. This natural variability directly affects nanoparticle morphology, size, crystallinity and yield. Inconsistencies in preparation and composition make it difficult to reproduce results and maintain batch-to-batch consistency [109]. Additionally, controlling critical reaction parameters such as pH, temperature and concentration in plant-based systems is complex and less precise than chemical synthesis. This often results in a wide distribution of nanoparticle sizes and shapes, limiting control over physical and chemical properties. Furthermore, the underlying biochemical mechanisms of nanoparticle formation via plant extracts are not yet fully understood, hindering the optimisation of reaction conditions for better performance. While these methods are practical at the laboratory level, scalability remains a concern, especially when attempting to maintain the bioactivity of extracts and the consistency of nanoparticle characteristics on an industrial scale [110].

6.2. Biological and biomedical application challenges

Although green-synthesised NCs are often labelled as biocompatible, their biological interactions can still be unpredictable and potentially harmful under certain conditions. A major concern is cytotoxicity, particularly when these materials are used in concentrations or for long periods of time. Metal based NCs can inspire oxidative stress by generating reactive oxygen species (ROS), which damage vital cellular components such as proteins, DNA and lipids [111]. This oxidative damage can lead to apoptosis or necrosis and disrupt essential cellular processes such as mitochondrial respiration and cell signalling. Additionally, NCs can alter autophagic activity, either by excessively inducing it or blocking autophagic flux, which interferes with cellular waste disposal and homeostasis. In immune cells, NCs may provoke inflammatory responses by stimulating the release of cytokines like IL-1, IL-6 and TNF-α and activating immune pathways such as T-cell proliferation and dendritic cell maturation. Although these responses are part of the body's natural defence mechanisms, disturbances in their regulation can result in long-term chronic inflammation or immune suppression [112]. In biomedical applications such as drug delivery, NCs synthesised via plant extracts often lack specificity for targeted tissues, increasing the risk of off-target effects and reducing therapeutic efficacy. Furthermore, the formation of a protein corona around NPs in biological fluids can alter their surface properties, affecting biodistribution, immune recognition and cellular uptake in unexpected ways. These biological complexities highlight the need for more comprehensive in vitro and in vivo studies to understand and predict the full scope of NC behaviour in living systems.

6.3. Other technical and environmental challenges

Beyond synthesis and biological performance, additional concerns limit the widespread adoption of plant mediated NCs. One such issue is the colloidal stability and shelf life of these metal and metal oxide NCs. Without proper surface functionalization, green synthesised NCs often tend to aggregate, leading to decreased stability and reduced effectiveness. Storage conditions such as temperature, light and humidity can also accelerate degradation. From an environmental perspective, although the synthesis process is eco-friendly, the long-term fate and ecological impact of these NPs are still not fully understood. Once released into the environment intentionally through agricultural applications or unintentionally via waste, they may interact with soil, water and living organisms in ways that are not yet fully predictable. Another challenge lies in the complexity of plant extracts. Although the presence of multiple active compounds enhances their reducing and stabilising capabilities, it also complicates efforts to isolate and identify the specific molecules responsible for nanoparticle synthesis. This makes mechanistic studies difficult and hinders the development of targeted, reproducible formulations [113]. Reproducibility is further affected by seasonal and geographical variability in plant composition, which remains a major hurdle for industrial applications. Lastly, regulatory and safety assessment frameworks tailored to plant-based NCs are still lacking. Most current nano-toxicological protocols are based on chemically synthesised NPs and may not accurately capture the behaviour or risks associated with biologically derived nanomaterials. Without clearly defined safety standards, risk assessment models and regulatory pathways, the clinical and commercial translation of these promising materials remains limited.

7. Future directions

Metal and metal oxide NCs have significant potential and applications, drawing considerable interest from researchers across various fields, including medicine, agriculture, optics, wastewater treatment, biomedicine, pharmaceuticals, information technology, electronics, catalysis, environmental science, energy and energy storage. New nanomaterials are under development, demonstrating potential for energy production from light, temperature variations, movement and other sources with high conversion efficiency. New hybrid NCs are emerging as a superior alternative to conventional nano carriers for enhancing antibiotic delivery at infection sites, effectively eradicating bacterial infections and addressing antimicrobial resistance. They can precisely regulate antibiotic release at the infection site, thereby improving and extending their antimicrobial effectiveness. The design of engineering hybrid NCs involves a complex hierarchical assembly using various complementary materials to create functional systems. Recent developments in nanotechnology, synthetic methods and supramolecular chemistry have resulted in the creation of advanced hybrid nanostructures for drug delivery applications. Engineered hybrid nanosystems have significant potential to optimise antibacterial drug delivery and improve the treatment of bacterial infections.

8. Conclusion

This review highlights the potential of plant-mediated metal and metal oxide NCs synthesis as a sustainable and eco-friendly alternative to conventional nanomaterials. This green approach transcends mere environmental sustainability by capitalising on the inherent phytochemical complexity of plant extracts to dictate nucleation, growth and stabilization, thereby synthesizing NCs with enhanced biocompatibility, targeted therapeutic efficacy and optimized catalytic interfaces. This paradigm transitions green synthesis from an empirical method to a predictive design strategy for engineering NCs with superior antimicrobial, anticancer, anti-inflammatory, and photocatalytic functionalities. The demonstrated efficacy across biomedical and environmental applications validates these NCs as high-performance, application-specific materials. However, their clinical and industrial translation requires systematically overcoming key barriers: standardizing plant extracts to ensure batch-to-batch reproducibility, elucidating long-term biocompatibility and fate, and developing scalable, cost-effective production protocols. Future research must leverage this phytochemical blueprint to design next-generation, stimuli-responsive hybrid systems. By addressing these interdisciplinary challenges, plant-derived NCs can evolve from a promising sustainable alternative into a cornerstone of advanced nanomedicine and environmental remediation technologies.

CRediT authorship contribution statement

Mohammad Asim Saifi: Formal analysis, Data curation. **Aayasha Negi:** Supervision, Investigation, Conceptualization. **Amanpreet Kaur:** Software. **Lakshya:** Investigation. **Ramchander Merugu:** Investigation. **Sadhna Negi:** Validation. **Mohamed Taha Yassin:** Conceptualization.

Consent to participate

All authors of this paper consent to participate.

Consent to publish

All authors give their consent to publish the manuscript in present form.

Ethical Approval

Not Applicable.

Funding

This work was not funded.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.inoche.2026.116214.

Data availability

The figures in the paper contain data that supports the reported results.

References

[1] C. Demetzos, C. Demetzos, Introduction to Nanotechnology, Fundamentals and Practical Applications, Pharmaceutical Nanotechnology, 2016, pp. 3–15.
[2] V.V.E. Mitin, V.A. Kochelap, M.A. Stroscio, Introduction to Nanoelectronics: Science, Nanotechnology, Engineering, and Applications, Cambridge University Press, 2008.
[3] L. Theodore, Nanotechnology: Basic Calculations for Engineers and Scientists, John Wiley & Sons, 2006.
[4] A. Haleem, et al., Applications of nanotechnology in medical field: a brief review, Global Health Journal 7 (2) (2023) 70–77.
[5] M. Sen, *Nanocomposite materials.* Nanotechnology and the, Environment 27 (2020) 1–2.
[6] A. Sharma, Nanocomposite Materials for Biomedical and Energy Storage Applications, BoD–Books on Demand, 2022.
[7] S. Pedroso-Santana, N. Fleitas-Salazar, The use of capping agents in the stabilization and functionalization of metallic nanoparticles for biomedical applications, Part. Part. Syst. Charact. 40 (2) (2023) 2200146.
[8] Y.F. Mustafa, Modern developments in the application and function of metal/metal oxide nanocomposite–based antibacterial agents, BioNanoScience 13 (2) (2023) 840–852.
[9] W. Cui, J. Li, G. Decher, Self-assembled smart nanocarriers for targeted drug delivery, Adv. Mater. 28 (6) (2016) 1302–1311.
[10] D. Wang, T. Xie, Y. Li, Nanocrystals: solution-based synthesis and applications as nanocatalysts, Nano Res. 2 (2009) 30–46.
[11] Y. Mao, T.-J. Park, S.S. Wong, Synthesis of classes of ternary metal oxide nanostructures, Chem. Commun. 46 (2005) 5721–5735.
[12] O. Długosz, et al., Methods for reducing the toxicity of metal and metal oxide NPs as biomedicine, Materials 13 (2) (2020) 279.
[13] M. Awais, et al., A review on the recent advancements on therapeutic effects of ions in the physiological environments, Prosthesis 4 (2) (2022) 263–316.
[14] A.G. Cuenca, et al., Emerging implications of nanotechnology on cancer diagnostics and therapeutics, Cancer 107 (3) (2006) 459–466.
[15] T. Puttaraju, et al., Biogenic approach for synthesis of ZnO/NiO nanocomposites as a highly efficient photocatalyst and evaluation of their biological properties, Braz. J. Chem. Eng. 42 (1) (2025) 95–108.
[16] X. Wang, Y. Li, Solution-based synthetic strategies for 1-D nanostructures, Inorg. Chem. 45 (19) (2006) 7522–7534.
[17] K. Gurushankar, et al., Investigation of the newly characterized baimantuoluoamide a and baimantuoluoamide b alkaloids as potential cyclin-dependent kinase 4 (CDK4) inhibitors using molecular docking and molecular dynamics simulations, J. Mol. Struct. 1230 (2021) 129925.
[18] R.S. Hamida, et al., Lichens—a potential source for nanoparticles fabrication: a review on nanoparticles biosynthesis and their prospective applications, Journal of Fungi 7 (4) (2021) 291.
[19] K. Sayadi, et al., Methods of green synthesis of au NCs with emphasis on their morphology: a mini-review, Heliyon 7 (6) (2021).
[20] Z. Aba, A. Goktas, A. Kilic, Characterization of Zn1-xLaxS thin films; compositional, surface, optical, and photoluminescence properties for possible optoelectronic and photocatalytic applications, J. Sol-Gel Sci. Technol. 109 (1) (2024) 260–271.
[21] A. Boroumand Moghaddam, et al., Nanoparticles biosynthesized by fungi and yeast: a review of their preparation, properties, and medical applications, Molecules 20 (9) (2015) 16540–16565.
[22] S. Gorska, A. Maksymiuk, J. Turło, Selenium-containing polysaccharides—structural diversity, biosynthesis, chemical modifications and biological activity, Appl. Sci. 11 (8) (2021) 3717.
[23] G.S. Dhillon, et al., Green approach for nanoparticle biosynthesis by fungi: current trends and applications, Crit. Rev. Biotechnol. 32 (1) (2012) 49–73.
[24] F. Menaa, et al., Marine algae-derived bioactive compounds: a new wave of nanodrugs? Mar. Drugs 19 (9) (2021) 484.
[25] T. Muneeswaran, et al., Nano-biomaterials for therapeutic and diagnostic applications, in: Applications of Multifunctional Nanomaterials, Elsevier, 2023, pp. 617–649.
[26] P. Pujar, et al., Trends in low-temperature combustion derived thin films for solution-processed electronics, Advanced Electronic Materials 6 (10) (2020) 2000464.
[27] A. Mondal, et al., Natural polymeric nanobiocomposites for anti-cancer drug delivery therapeutics: a recent update, Pharmaceutics 15 (8) (2023) 2064.
[28] R. Seth, And a, *An eco-friendly and green synthesis approach.* Clean Technologies and Environmental Policy, Meena, *Enzymes-based nanomaterial synthesis*, 2024, pp. 1–24.
[29] S.M. Petrovic, M.-E. Barbinta-Patrascu, Organic and biogenic nanocarriers as bio-friendly systems for bioactive compounds' delivery: state-of-the art and challenges, Materials 16 (24) (2023) 7550.
[30] M.M. Mihai, et al., Nanomaterials for wound healing and infection control, Materials 12 (13) (2019) 2176.
[31] A. Ullah, S.I. Lim, Plant extract-based synthesis of metallic nanomaterials, their applications, and safety concerns, Biotechnol. Bioeng. 119 (9) (2022) 2273–2304.
[32] Gajender, et al., A comprehensive review of the pharmacological importance of dietary flavonoids as hepatoprotective agents, Evid. Based Complement. Alternat. Med. 2023 (1) (2023) 4139117.

[33] C. Majee, et al., An insight into the hepatoprotective activity and structure-activity relationships of flavonoids, Mini Rev. Med. Chem. 23 (2) (2023) 131–149.
[34] F.D. Mabou, I.B.N. Yossa, TERPENES: structural classification and biological activities, IOSR J Pharm Biol Sci 16 (2021) 25–40.
[35] V. Sanchez-Mendieta, A.R. Vilchis-Nestor, Green synthesis of noble metal (au, ag, Pt) nanoparticles, assisted by plant-extracts, Noble metals 18 (2012) 392–408.
[36] S. Flora, M. Mittal, A. Mehta, Heavy metal induced oxidative stress & its possible reversal by chelation therapy, Indian J. Med. Res. 128 (4) (2008) 501–523.
[37] P.V. Iyer, L. Ananthanarayan, Enzyme stability and stabilization—aqueous and non-aqueous environment, Process Biochem. 43 (10) (2008) 1019–1032.
[38] H. Sigel, R.B. Martin, Coordinating properties of the amide bond. Stability and structure of metal ion complexes of peptides and related ligands, Chem. Rev. 82 (4) (1982) 385–426.
[39] A. Sharma, et al., Plant secondary metabolites: An introduction of their chemistry and biological significance with physicochemical aspect, in: Plant Secondary Metabolites: Physico-Chemical Properties and Therapeutic Applications, Springer, 2022, pp. 1–45.
[40] S. Griffin, et al., Natural nanoparticles: a particular matter inspired by nature, Antioxidants 7 (1) (2017) 3.
[41] W. Suksatan, et al., A controllable study on ultrasound assisted synthesis of a novel Ni/Zn based hybrid MOF nanostructures for dextranase immobilization, Inorg. Chem. Commun. 139 (2022) 109410.
[42] K. Kannan, et al., Investigation of the electrochemical behavior of CuO-NiO-Co3O4 nanocomposites for enhanced supercapacitor applications, Materials 17 (16) (2024) 3976.
[43] A. Negi, et al., Plant-mediated Z-scheme ZnO/TiO2-NCs for antibacterial potential and dye degradation: experimental and DFT study, Sci. Rep. 14 (1) (2024) 7955.
[44] K.M. Elattar, et al., Green synthesis of ag/TiO2 and ag/co/TiO2 nanocomposites from Ceratonia siliqua extract for antioxidant and antibacterial applications, ChemistrySelect 10 (38) (2025) e03394.
[45] L. Mahmudin, et al., Optical properties of silver nanoparticles for surface plasmon resonance (SPR)-based biosensor applications, J. Mod. Phys. 6 (8) (2015) 1071–1076.
[46] K. Chinnaiah, et al., Bioengineered ag/NiO nanocomposites as advanced battery-supercapacitor electrodes for highly efficient symmetric hybrid devices, Ionics 30 (3) (2024) 1691–1707.
[47] B. Avar, M. Panigrahi, Synthesis and characterization of binary reduced graphene oxide/metal oxide nanocomposites, Physics and Chemistry of Solid State 23 (1) (2022) 101–112.
[48] M.-N. Pons, et al., Particle morphology: from visualisation to measurement, Powder Technol. 103 (1) (1999) 44–57.
[49] Y.S. Ch'ng, et al., Vasorelaxation study and tri-step infrared spectroscopy analysis of Malaysian local herbs, J. Pharm. 19 (2) (2016) 145.
[50] V. Siva, et al., One-step hydrothermal synthesis of transition metal oxide electrode material for energy storage applications, J. Mater. Sci. Mater. Electron. 31 (22) (2020) 20472–20484.
[51] S. Farhadi, et al., Immobilization of Lepidium draba peroxidase on a novel Zn-MOF nanostructure, Int. J. Biol. Macromol. 173 (2021) 366–378.
[52] M. Descostes, et al., Use of XPS in the determination of chemical environment and oxidation state of iron and sulfur samples: constitution of a data basis in binding energies for Fe and S reference compounds and applications to the evidence of surface species of an oxidized pyrite in a carbonate medium, Appl. Surf. Sci. 165 (4) (2000) 288–302.
[53] A.O. Juma, et al., Synthesis and characterization of CuO-NiO-ZnO mixed metal oxide nanocomposite, J. Alloys Compd. 723 (2017) 866–872.
[54] K. Chinnaiah, et al., Enhancing supercapacitor and antimicrobial performance of bioengineered ag/Mn3O4 composite nanorods, J. Ind. Eng. Chem. 147 (2025) 329–340.
[55] K. Chinnaiah, et al., Exploring the potential of Withania somnifera-mediated ag/Mn3O4 nanocomposites as electrode material for high-performance supercapattery device, J. Taiwan Inst. Chem. Eng. 157 (2024) 105441.
[56] K. Chinnaiah, et al., Exploring ag/Mn3O4 composite nanorods as an attractive battery-type electrode material for supercapacitors, J. Phys. Chem. Solid 196 (2025) 112310.
[57] S. Suehiro, et al., Efficient solution route to transparent ZnO semiconductor films using colloidal nanocrystals, J. Asian Ceramic Soc. 4 (3) (2016) 319–323.
[58] J. Lim, et al., Characterization of magnetic nanoparticle by dynamic light scattering, Nanoscale Res. Lett. 8 (2013) 1–14.
[59] P. Sinha, et al., Surface area determination of porous materials using the Brunauer–Emmett–teller (BET) method: limitations and improvements, J. Phys. Chem. C 123 (33) (2019) 20195–20209.
[60] A. Rafat, S. Hashemian, M.R. Shishabor, Preparation and characterization of nano composites from metal oxides and activated carbon from banana peel (MO@ BPAC, MO= NiO, CuO and ZnO) for 2 nitrophenol removal from aqueous solutions, Heliyon 11 (1) (2025).
[61] K.K. Bharadwaj, et al., Green synthesis of gold nanoparticles using plant extracts as beneficial prospect for cancer theranostics, Molecules 26 (21) (2021) 6389.
[62] A. Velidandi, et al., Catalytic and eco-toxicity investigations of bio-fabricated monometallic nanoparticles along with their anti-bacterial, anti-inflammatory, anti-diabetic, anti-oxidative and anti-cancer potentials, Colloid Interface Sci. Commun. 38 (2020) 100302.
[63] F.U. Haider, et al., Harnessing plant extracts for eco-friendly synthesis of iron nanoparticle (Fe-NPs): characterization and their potential applications for ameliorating environmental pollutants, Ecotoxicol. Environ. Saf. 281 (2024) 116620.
[64] L.B. Rice, R.A. Bonomo, Mechanisms of resistance to antibacterial agents, Manual of clinical microbiology (2011) 1082–1114.
[65] J.A. Lemire, J.J. Harrison, R.J. Turner, Antimicrobial activity of metals: mechanisms, molecular targets and applications, Nat. Rev. Microbiol. 11 (6) (2013) 371–384.
[66] M.Z. Ishaque, et al., Fabrication of ternary metal oxide (ZnO: NiO: CuO) nanocomposite heterojunctions for enhanced photocatalytic and antibacterial applications, RSC Adv. 13 (44) (2023) 30838–30854.
[67] Demetzos, C., N. Pippa, and N. Naziris, *Functional Materials in Biomedical Applications*. 2023: Jenny Stanford Publishing.
[68] K. Chinnaiah, et al., Electrical and electrochemical characteristics of withania somnifera leaf extract incorporation sodium alginate polymer film for energy storage applications, J. Inorg. Organomet. Polym. Mater. 32 (2) (2022) 583–595.
[69] S. Kavitha, R. Ranjith, N. Jayamani, Facile construction of novel Ag2O combined TiO2 nanocomposites with enhanced dye degradation under visible-light photocatalytic activity, Mater. Technol. 37 (9) (2022) 1205–1219.
[70] K. Kannan, et al., Photocatalytic and antimicrobial properties of microwave synthesized mixed metal oxide nanocomposite, Inorganic Chemistry Communications 125 (2021) 108429.
[71] S. Selim, et al., Synthesis, characterization, anticancer, antibacterial and antifungal activities of nanocomposite based on tertiary metal oxide Fe2O3@ CuO@ ZnONPs, starch, ethylcellulose and collagen, Int. J. Biol. Macromol. 301 (2025) 140376.
[72] H. Zhang, et al., ATP Cellotoxicity, ATP-induced cell death and ATP depletion, International Journal of Public Health and Medical Research 1 (2) (2024) 35–38.
[73] M.P. Vinardell, M. Mitjans, Antitumor activities of metal oxide nanoparticles, Nanomaterials 5 (2) (2015) 1004–1021.
[74] S. Ukanwa, E. Ozgor, Synthesis of Iron oxide nanoparticle using Propolis from northern Cyprus and evaluation of its antibacterial, anticancer potential on MDA-MB 231 cells, J. Chem. Soc. Pak. 45 (4) (2023).
[75] J.G. Teodoro, S.K. Evans, M.R. Green, Inhibition of tumor angiogenesis by p53: a new role for the guardian of the genome, J. Mol. Med. 85 (2007) 1175–1186.
[76] F. Berthiaume, T.J. Maguire, M.L. Yarmush, Tissue engineering and regenerative medicine: history, progress, and challenges, Annu. Rev. Chem. Biomol. Eng. 2 (1) (2011) 403–430.
[77] H. Hemati, et al., Design and evaluation of liposomal sulforaphane-loaded polyvinyl alcohol/polyethylene glycol (PVA/PEG) hydrogels as a novel drug delivery system for wound healing, Gels 9 (9) (2023) 748.
[78] J.L. Olson, A. Atala, J.J. Yoo, Tissue engineering: current strategies and future directions, Chonnam Med. J. 47 (1) (2011) 1–13.
[79] V. Vijayakumar, et al., Recent advancements in biopolymer and metal nanoparticle-based materials in diabetic wound healing management, Int. J. Biol. Macromol. 122 (2019) 137–148.
[80] M.M. Jansman, L. Hosta-Rigau, Cerium-and iron-oxide-based nanozymes in tissue engineering and regenerative medicine, Catalysts 9 (8) (2019) 691.
[81] P.P.P. Kumar, D.-K. Lim, Gold-polymer nanocomposites for future therapeutic and tissue engineering applications, Pharmaceutics 14 (1) (2021) 70.
[82] A. Topsakal, et al., Study on the cytocompatibility, mechanical and antimicrobial properties of 3D printed composite scaffolds based on PVA/gold nanoparticles (AuNP)/ampicillin (AMP) for bone tissue engineering, Mater. Today Commun. 28 (2021) 102458.
[83] M. Borzenkov, et al., Gold nanoparticles for tissue engineering, Environmental Nanotechnology 1 (2018) 343–390.
[84] P. Chauhan, S. Mahajan, G. Prasad, Preparation and characterization of CS-ZnO-NC nanoparticles for imparting anti-diabetic activities in experimental diabetes, J. Drug Delivery Sci. Technol. 52 (2019) 738–747.
[85] D.S.A. Selvan, et al., Antidiabetic activity of phytosynthesized ag/CuO nanocomposites using Murraya koenigii and Zingiber officinale extracts, J. Drug Delivery Sci. Technol. 67 (2022) 102838.
[86] A.R. Malik, et al., Green synthesis of RGO-ZnO mediated Ocimum basilicum leaves extract nanocomposite for antioxidant, antibacterial, antidiabetic and photocatalytic activity, J. Saudi Chem. Soc. 26 (2) (2022) 101438.
[87] A. Bakur, et al., Comparative study of antidiabetic, bactericidal, and antitumor activities of MEL@ AgNPs, MEL@ ZnONPs, and ag–ZnO/MEL/GA nanocomposites prepared by using MEL and gum arabic, RSC Adv. 9 (17) (2019) 9745–9754.
[88] S. Gupta, et al., Biosynthesis of silver nanoparticles using Raphanus sativus Ethanolic leaf extract and their photocatalytic degradation of dyes from polluted water and biological activities, ES Food and Agroforestry 23 (2025) 1953.
[89] R. Papitha, et al., Green synthesis of CuO/TiO2 and ZnO/TiO2 nanocomposites using Parkia timoriana bark extract: enhanced antioxidant and antidiabetic activities for biomedical applications, Ceram. Int. 50 (20) (2024) 39109–39121.
[90] Q. Qiao, et al., Nanomedicine for acute respiratory distress syndrome: the latest application, targeting strategy, and rational design, Acta Pharm. Sin. B 11 (10) (2021) 3060–3091.
[91] N.K. Bhol, et al., The interplay between cytokines, inflammation, and antioxidants: mechanistic insights and therapeutic potentials of various antioxidants and anti-cytokine compounds, Biomed. Pharmacother. 178 (2024) 117177.
[92] M. Mrityunjaya, et al., Immune-boosting, antioxidant and anti-inflammatory food supplements targeting pathogenesis of COVID-19, Front. Immunol. 11 (2020) 570122.

[93] M. Raszewska-Famielec, J. Flieger, Nanoparticles for topical application in the treatment of skin dysfunctions—an overview of dermo-cosmetic and dermatological products, Int. J. Mol. Sci. 23 (24) (2022) 15980.
[94] N. Suresh Kumar, et al., A review on biological and biomimetic materials and their applications, Applied Physics A 126 (6) (2020) 445.
[95] A.M. Al-Rajhi, et al., In situ green synthesis of cu-doped ZnO based polymers nanocomposite with studying antimicrobial, antioxidant and anti-inflammatory activities, Appl. Biol. Chem. 65 (1) (2022) 35.
[96] G.R. Rudramurthy, et al., Nanoparticles: alternatives against drug-resistant pathogenic microbes, Molecules 21 (7) (2016) 836.
[97] Y.K. Mohanta, et al., Nanotechnology in combating biofilm: a smart and promising therapeutic strategy, Front. Microbiol. 13 (2023) 1028086.
[98] B. Homayun, X. Lin, H.-J. Choi, Challenges and recent progress in oral drug delivery systems for biopharmaceuticals, Pharmaceutics 11 (3) (2019) 129.
[99] M.A. Subhan, Advances with metal oxide-based nanoparticles as MDR metastatic breast cancer therapeutics and diagnostics, RSC Adv. 12 (51) (2022) 32956–32978.
[100] Z. Li, et al., Recent advances of using hybrid nanocarriers in remotely controlled therapeutic delivery, Small 12 (35) (2016) 4782–4806.
[101] Z.B. Nqakala, et al., Advances in nanotechnology towards development of silver nanoparticle-based wound-healing agents, Int. J. Mol. Sci. 22 (20) (2021) 11272.
[102] F.M. Kievit, M. Zhang, Surface engineering of iron oxide nanoparticles for targeted cancer therapy, Acc. Chem. Res. 44 (10) (2011) 853–862.
[103] J. Zhou, Y. Wang, G.-J. Zhang, State-of-the-art strategies of surface plasmon resonance biosensors in clinical analysis: a comprehensive review, Coord. Chem. Rev. 520 (2024) 216149.
[104] S. Thatai, et al., Nanoparticles and core–shell nanocomposite based new generation water remediation materials and analytical techniques: a review, Microchem. J. 116 (2014) 62–76.
[105] Delekar, S.D., *Advances in metal oxides and their composites for emerging applications*. 2022: Elsevier.
[106] Y.-W. Hsu, et al., Synthesis of CuO/graphene nanocomposites for nonenzymatic electrochemical glucose biosensor applications, Electrochim. Acta 82 (2012) 152–157.
[107] Y. Yang, et al., Iron oxide nanoparticle-based nanocomposites in biomedical application, Trends Biotechnol. 41 (12) (2023) 1471–1487.
[108] J. Sidhic, et al., Advancements in metal and metal oxide nanoparticles for targeted Cancer therapy and imaging: mechanisms, applications, and safety concerns, J. Drug Delivery Sci. Technol. 105 (2025) 106622.
[109] M. Halder, S. Jha, Medicinal plants and bioactive phytochemical diversity: A fountainhead of potential drugs against human diseases, in: Medicinal Plants: Biodiversity, Biotechnology and Conservation, Springer, 2023, pp. 39–93.
[110] M. Mabrouk, et al., Nanomaterials for biomedical applications: production, characterisations, recent trends and difficulties, Molecules 26 (4) (2021) 1077.
[111] K. Mortezaee, et al., Redox interactions and genotoxicity of metal-based nanoparticles: a comprehensive review, Chem. Biol. Interact. 312 (2019) 108814.
[112] S. Ramachandran, et al., Role of cytokines and chemokines in NSCLC immune navigation and proliferation, Oxid. Med. Cell. Longev. 2021 (1) (2021) 5563746.
[113] A.L. Saraswat, et al., Drug delivery challenges and formulation aspects of proteolysis targeting chimera (PROTACs), Drug Discov. Today 28 (1) (2023) 103387.

Aayasha Negi is a dedicated academic and innovative researcher currently serving as an Assistant Professor of Chemistry at IFTM University, Moradabad. Born on June 7, 1996, she hails from Pauri Garhwal, Uttarakhand, and holds a Ph.D. in Chemistry from Hemwati Nandan Bahuguna Garhwal University. Dr. Negi has established a distinguished research portfolio centered on the green synthesis of nanoparticles and nanocomposites using medicinal plants, with a focus on their biological efficacy and environmental applications, such as dye degradation and wastewater treatment. Her interdisciplinary approach integrates experimental techniques like XRD, SEM, TEM, and UV-Visible spectroscopy with computational tools, including DFT and molecular docking, to develop sustainable nanomaterials. With a strong publication record, she has authored 21 high-impact research articles in SCI and Scopus-indexed journals, contributed to 6 book chapters, and holds a patent, demonstrating her commitment to translating research into practical solutions. Her work has earned several accolades, including the Young Researcher Award (2024) and the Inspire Fellowship from DST India. An accomplished educator, Dr. Negi is proficient in advanced software like Gaussian and VESTA and actively mentors students, fostering a dynamic learning environment. Her consistent participation in international conferences and collaborations reflects her dedication to advancing green chemistry and nanotechnology.