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Recent advances in metal/metal-oxide nanoparticle-polymer nanohybrid for biomedical applications

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ABSTRACT

An increase in the application of metal/metal-oxide nanoparticle–polymer hybrid systems for biochemical purposes is due to their highly tunable porosity, large surface area and wide range of functional properties. These advanced materials exhibit exceptional biocompatibility, antibacterial properties, and controlled drug release characteristics, making them highly suitable for drug delivery, medical imaging, biosensing, and tissue engineering. The incorporation of metals and metal-oxide nanoparticles into the polymer matrix enhances the mechanical durability, chemical stability, and responsiveness of mesoporous polymers, broadening their applications in cutting-edge medical technologies. This study provides insight into the application of this hybrid system in medical imaging: MRI, CT scans, and fluorescence imaging. Targeted drug delivery: facilitating the controlled and sustained release of bioactive materials. Regenerative medicine, as bioactive scaffolds for tissue engineering, supports cell adhesion, proliferation, and differentiation. And therapeutic applications such as photothermal and photodynamic therapy. However, despite these advancements, challenges remain, including biocompatibility concerns, potential toxicity, and difficulties in large-scale manufacturing. This study highlights recent innovations, existing challenges, and prospects in metal/metal-oxide nanoparticle-polymer hybrid applications in next-generation healthcare systems.

1. Introduction

Polymers are the backbone of modern life, and this is due to their flexibility, durability, and indispensability. Ranging from synthetic plastics to natural proteins, their diverse forms and roles have been shown to drive advancements in technology and are probable catalysts for industrialization. Polymers with micro- and mesoporous structures play a crucial role in polymer chemistry. Microporous polymers have pores smaller than 2 nm, while mesoporous polymers feature pore sizes ranging between 2 and 50 nm. In contrast, macroporous polymers possess pores larger than 50 nm. These classifications help define the porous architecture of polymers, influencing their applications [1]. In recent years, polymers and their porous derivatives have attracted much attention in various scientific fields. That is, materials science, nanotechnology, and catalysis due to their remarkable structure and function properties. This is a result of its structural and functional characteristics. Great effort has been made in the last decade in the development and characterization of these novel materials. This resulted in their applicability in various fields of science and technology like gas separation, drug delivery systems, water treatment, and energy storage, among

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others [2–8]. The increasing number of technological applications of these materials because of their unique features, including large surface area combined with controllable pore size and chemical flexibility shown in Fig. 1. [9–11]. The pore size determines the value of surface area and pore volume, which are the determining factors for the final applications of the material; for example, size-selective permeability and selectivity of guest species [12,13]. Furthermore, the fundamental understanding of these materials provides insight into the structure and performance relationship and can be used to enhance their properties. The ability to modify its surface and functionalization also expands the horizons of its applicability for various purposes, such as metal ions sequestration, catalysis, and energy storage [14–19]. The pore size in mesoporous polymers depends on the choice of templates and synthesis conditions, thus offering an opportunity to create materials with desired characteristics. These features are most valuable under environmental remediation and sensing applications, for the detection and removal of pollutants or analytes in analytically complex matrices. As such, these characteristic positions it as an emerging multifunctional platform driving innovation in biomedical applications.

Umeh et al. reported the development of composite materials using corn silk infused with nickel oxide (NiO) and copper oxide (CuO) nanoparticles, which were used for the removal of ciprofloxacin from water [19]. These materials demonstrated excellent reusability over five cycles, maintaining removal efficiencies of 63.1 % and 66.9 %, respectively. In contrast, untreated corn silk showed a lower efficiency of 47.8 %. The primary method of contaminant removal involved electrostatic attraction, π–π interactions, hydrogen bonding, and hydrophobic forces, which enhanced the adsorption capacity of the modified corn silk compared to its unaltered form. Saini et al. [20] introduced new membranes by integrating guar gum (GG) along with poly(3,4-ethylenedioxythiophene)-poly(styrenesulfonate) (PEDOT:PSS) conductive polymer and bimetallic palladium-platinum (PdPt) nanoparticles. The production of PdPt nanoparticles followed a wet chemical approach. Gas separation tests conducted with hydrogen (H_2), nitrogen (N_2), and carbon dioxide (CO_2) revealed that membranes containing 20 % PEDOT:PSS/GG had the best performance while maintaining good mechanical strength. Results showed a 172 % increase in CO_2 permeability and a 138 % improvement in CO_2/H_2 selectivity. Additionally, incorporating PdPt nanoparticles further enhanced CO_2/H_2 selectivity by 197 %, due to the unique catalytic properties of the noble metal nanoparticles-polymer hybrid system.

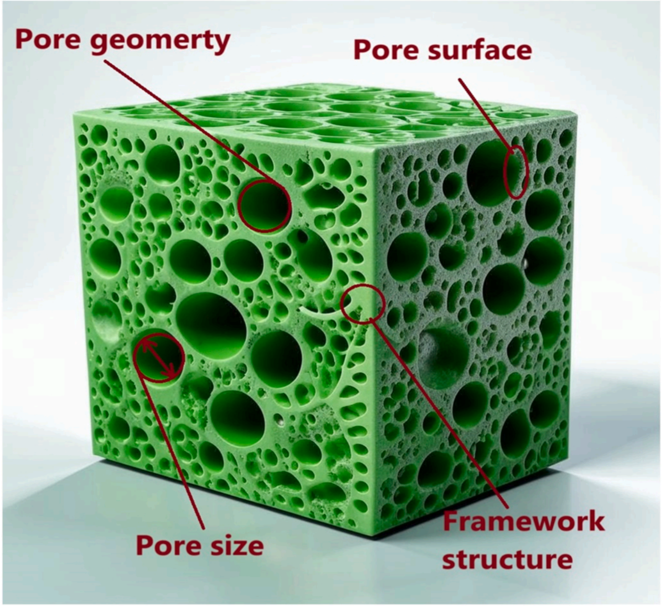


Fig. 1. Polymers matrix with micro- and mesoporous structure [1].

Khan et al. [21] described an enhanced potentiostatic strategy to enhance the energy storage features of polyaniline (PN) through the development of PN@ZnO (PNZ), PN@Fe_2O_3 (PNF) and PN@$ZnFe_2O_4$ (PNZF) hybrid electrodes using advanced porous structures. The PNZF electrode demonstrated the best specific capacitance values of 816 F g^{-1} at 5 mV s^{-1} scan rate and 791.3 F g^{-1} at a current density of 1.0 A g^{-1}. The material demonstrated both a high-power density level at 1058.4 W kg^{-1} and an energy density level at 136.4 Wh kg^{-1} with exceptional stability through 4000 consecutive cycles, where performance remained at 90 %. Researchers from Alghamdi et al. [22] developed $NiCo_2O_4$ NPs to add to polymeric structures when investigating optical, dielectric, magnetic and electrical conductivity properties. $NiCo_2O_4$ NP-reinforced polyacrylamide (PAM)/polyethylene oxide (PEO) composites were synthesized through the casting method by the researchers. $NiCo_2O_4$ NPs incorporated into PAM/PEO polymer blend increased its amorphous content thus enhancing performance attributes.

Furthermore, incorporating nanoparticles into a polymer matrix allowed for the grafting of catalytically active sites, which would considerably increase the efficiency of these materials in catalytic reactions and sensor applications, extending their uses in the environment and biomedical applications. A gas sensor for room temperature ammonia (NH_3) detection was developed through their Ag/Cu-doped polypyrrole hybrid nanocomposite system [23]. This sensor offers enhanced sensitivity and reliability, making it suitable for real-time monitoring of ammonia levels. An innovative hydrogen sulphide (H_2S) gas sensor was developed through the utilization of a nanocomposite made from reduced graphene oxide (rGO) and poly(o-toluidine) (POT) [24]. The sensor achieves high sensitivity and accuracy through the convergent use of electrical conductive POT with surface area-extensive rGO. Moreover, the possibilities to consciously adjust these chemical functionalities are highly significant when considering interactions at the molecular level, such as in the context of biosciences with applications in drug delivery and biosensing that highly rely upon the specificity and high sensitivity of molecular interactions.

Therefore, the roles of tunable chemical functionalities in polymers accord it a broad spectrum of uses depending on the extent of surface and chemical modification. Indeed, this tunability not only optimizes mesoporous polymer applications but also opens the pathway towards novel material type designs where control of target molecule interactions is paramount. Also, the incorporation of tunable functionalities improves polymer selectivity and sensitivity for sensor and catalytic process applications [25,26]. Despite significant advances in tunable mesoporous polymers and their hybrid for environmental and biomedical applications, there remains a critical gap in systematically correlating molecular-level functionalization strategies with real-time, multi-analyte sensing performance under complex environmental matrices, particularly for emerging contaminants, where selectivity, stability, and reusability are concurrently demanded.

Nanotechnology, which is the science of material synthesis has created new opportunities in the field of biomedicine, where metal and metal oxide NPs have received considerable interest because of their unique properties. These materials exhibit unique photoluminescence properties, biocompatibility and antibacterial properties, which have made them useful for cellular imaging, drug delivery and antimicrobial applications [27–33]. The size and morphology of these nanoparticles can be easily controlled to achieve desired functionalities suitable for required applications. For example, their application in water and wastewater treatment is due to their efficiency in the removal of pollutants from aqueous solutions [34,35], and their outstanding photocatalytic and antimicrobial activities, which enhance their usage in environmental cleaning and health care purposes [36–40].

This manuscript aims to systematically explore how strategic integration of tunable chemical functionalities and nanoparticle (metal/metal oxide) hybridization in micro- and mesoporous polymers can be leveraged to design next-generation multifunctional materials with enhanced selectivity, sensitivity, and efficiency for biomedical sensing applications.

2. Metal/metal-oxide nanoparticle-polymer composite?

Polymers and their composite material are adopted in biomedical science for tissue engineering and regenerative medicine, gene therapy, and drug delivery systems, as shown in Fig. 2. These polymers enable the controlled release of drugs while ensuring compatibility with biological systems such as cells, tissues, and bodily fluids [41–43]. The polymeric material should be safe, readily available, and capable of interacting with tissues without causing inflammation. Moreover, understanding the biochemical properties of these materials, in addition to their physical and chemical characteristics, is essential. The polymer's surface properties, including texture and water absorption, also influence biocompatibility. Excessive water absorption can weaken implants over time, which is particularly relevant for orthopedic and dental applications [44–46]. In tissue engineering, these polymers provide structural support for regenerating cells and tissues, with natural polymers due to their similarity to biological molecules. Polymers also enhance gene therapy by acting as carriers for DNA and serving as structural frameworks for tissue repair [47,48]. In drug delivery, they allow for controlled and sustained release of active pharmaceutical ingredients, ensuring targeted treatment and reducing post-surgical complications.

The main advantages of a metal/metal-oxide nanoparticles-polymer hybrid system include the following: (i) enhancing the surface area, (ii) achieving controlled release and (iii) providing better stability. The use of mesoporous polymers as the support matrix is highly advantageous because of its large surface area and the porosity of the material into which the metal and metal-oxide nanoparticles can be anchored. Due to the large surface area of the materials, a large number of the nanoparticles can be easily loaded, which in turn enhances their capacity for various applications.

The integration of metal and metal-oxide nanoparticles within mesoporous polymers enhances their ability to remain stable in the polymer matrix. Metals in nanoparticle form are usually prone to sintering and agglomeration, thus showing an initial loss of catalytic activity or functionality, especially for the delivery of drugs in drug delivery [49]. The mesoporous polymer matrix can offer physical and chemical protection against nanoparticle agglomeration through better dispersion and stabilization of nanoparticles. As such retain their high surface area and subsequently reactivity. More so, the nanoparticles can add further functionalities as a catalyst or mechanical strength. Such synergistic interactions between mesoporous polymers and metal/metal-oxide nanoparticles can lead to enhanced properties than each of the components. Thus, the combination of mesoporous polymers and metal/metal-oxide nanoparticles paves the way for the future advancement of new materials possessing superior characteristics and superior performance, which is directed towards enhancing the stability/durability of catalyst supports.

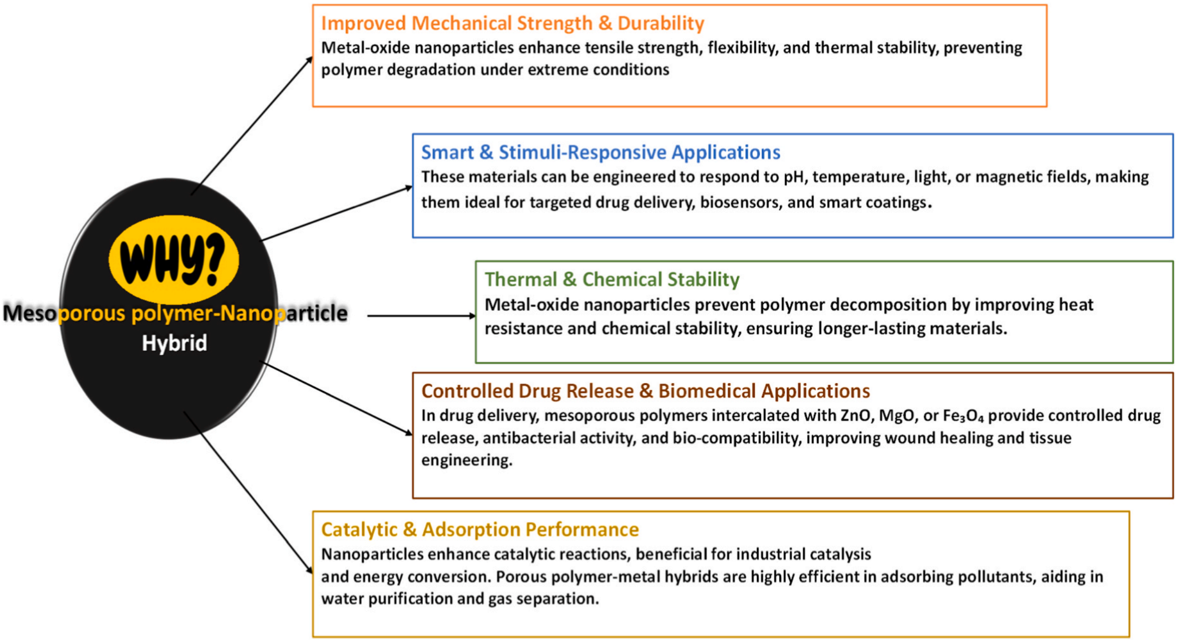
3. Synthesis and characterization of mesoporous polymers-metal/metal oxide nanoparticle hybrid

Mesoporous polymer-metal oxide hybrids have gained significant attention as versatile materials for catalysis, energy storage, and environmental remediation. By integrating the adaptability of polymers with the durability of metal oxides, these hybrids exhibit high surface area, adjustable porosity, and exceptional chemical stability. This section focuses on their synthesis techniques, followed by characterization. Which are imperative for their potential for a wide range of industrial and scientific applications.

3.1. Synthesis

Incorporating metal/metal oxide nanoparticles into a porous polymer matrix improves their properties for a range of applications. The two commonly used methods for achieving this are.

1. **Direct Mixing with Nanoparticles:** This method involves blending pre-made metal oxide nanoparticles into the polymer matrix during synthesis. The nanoparticles are evenly distributed within the polymer, leading to improvements in mechanical strength, heat resistance, and catalytic efficiency [50,51]. For example, incorporating TiO_2 nanoparticles into mesoporous polymers has been shown to enhance photocatalytic performance [52–54].
2. **Post-Synthetic Grafting:** In this approach, the polymer is modified after its initial formation to introduce metal oxide functionalities. Reactive groups on the polymer surface interact with metal precursors, forming metal oxide structures on the polymer's surface. This technique provides precise control over the amount and



Improved Mechanical Strength & Durability
Metal-oxide nanoparticles enhance tensile strength, flexibility, and thermal stability, preventing polymer degradation under extreme conditions

Smart & Stimuli-Responsive Applications
These materials can be engineered to respond to pH, temperature, light, or magnetic fields, making them ideal for targeted drug delivery, biosensors, and smart coatings.

Thermal & Chemical Stability
Metal-oxide nanoparticles prevent polymer decomposition by improving heat resistance and chemical stability, ensuring longer-lasting materials.

Controlled Drug Release & Biomedical Applications
In drug delivery, mesoporous polymers intercalated with ZnO, MgO, or Fe_3O_4 provide controlled drug release, antibacterial activity, and bio-compatibility, improving wound healing and tissue engineering.

Catalytic & Adsorption Performance
Nanoparticles enhance catalytic reactions, beneficial for industrial catalysis and energy conversion. Porous polymer-metal hybrids are highly efficient in adsorbing pollutants, aiding in water purification and gas separation.

Fig. 2. The essence of incorporating nanoparticles into a mesoporous polymer matrix.

placement of metal oxides, allowing the material to be customized for specific uses. For instance, post-synthetic grafting has been applied to increase the adsorption capacity of mesoporous polymers [55,56].

The method selection depends on the specific properties needed for metal oxide-incorporated mesoporous polymers as well as their intended applications. Different methods of synthesis demonstrate the integration of metal oxides into mesoporous polymers, mostly utilising pre-manufactured nanoparticles. Numerous examples of such materials have been developed, highlighting different fabrication approaches for these advanced hybrid materials. The methods for producing metal oxide-incorporated mesoporous polymers can be broadly categorized based on the synthesis route, which includes in-situ polymerization, impregnation, sol-gel processes, and templating methods. Below is an overview of the most common approaches.

3.1.1. *In-situ polymerization*

In-situ polymerization as reported by [57–59] is a flexible and effective approach for embedding metal oxides into porous polymers, resulting in hybrid materials as shown in Fig. 3a–b, with improved properties for uses like catalysis, energy storage, and environmental cleanup. This method involves forming the polymer structure and metal oxide nanoparticles at the same time, ensuring even distribution and close interaction between them. The process typically starts by dissolving or mixing a metal source, such as metal salts or metal alkoxides, into a solution containing monomers. These monomers then undergo polymerization through techniques like radical polymerization, sol-gel processes, or condensation reactions. As the polymer forms, the metal compounds are either reduced or broken down in place, generating metal oxide nanoparticles within the polymer network. By carefully controlling polymerization conditions, researchers can simultaneously develop the material's porosity and integrate metal oxides. Nourozi et al. reported a novel *in-situ* synthesis route for creating mesoporous silica-polypyrrole-Au nanoparticle composites for enhanced catalytic activity, highlighting the precision achievable with this method [60]. More so, this method offers benefits such as a customized pore structure, even metal oxide distribution, and strong material stability. The *In-situ* polymerization method produced high-performance supercapacitor electrodes from flexible polyaniline/MXene/CNF composite nanofibrous mats [61]. While Son et al., [62] work, as presented in Fig. 3b, on the synthesis of mesoporous PPy/MnO_2 composites using a simple in situ oxidative polymerization method.

The main advantage of this technique is excellent nanoparticle dispersion and small, confined particle sizes due to spatial confinement; the downsides include possible pore blocking and limited control of

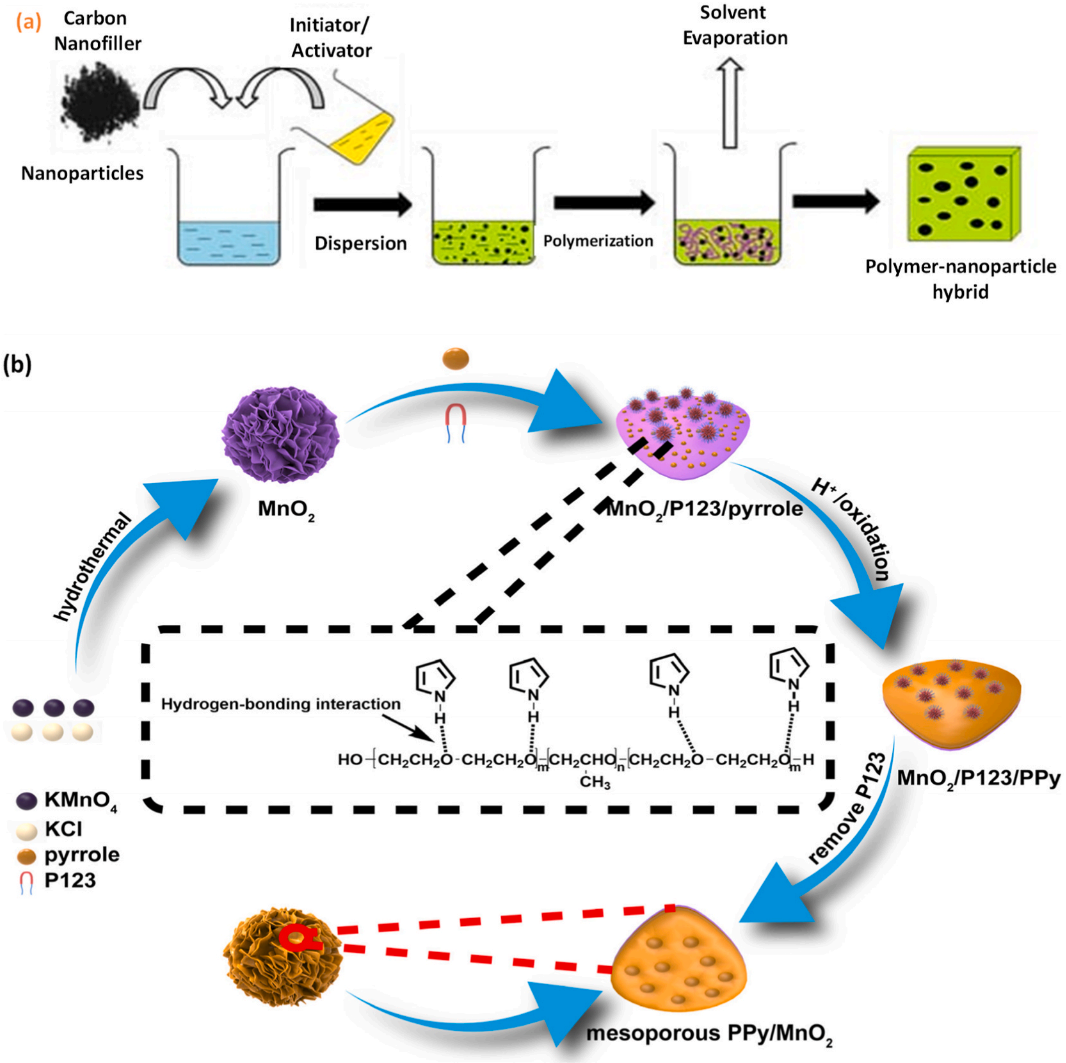


Fig. 3. Showing (a): The *in-situ* polymerization process [63] and (b): The synthesis of mesoporous PPy/MnO_2 composites using a simple *in-situ* oxidative polymerization method [62].

particle crystallinity if reduction conditions are not well chosen. Several biomedical and antimicrobial studies used impregnation in addition to in-situ reduction within mesoporous silica or polymeric matrices to create well-dispersed metal particles for antimicrobial activity [64].

3.1.2. *Impregnation method*

This is a commonly used technique for incorporating metal oxides into porous polymers because it is simple and adaptable. In this approach, a pre-made porous polymer is soaked with a solution containing metal compounds, such as metal salts or metal alkoxides. The solution seeps into the polymer's pores, allowing the metal compounds to settle inside. Afterwards, treatments like heating, hydrothermal processing, or chemical reduction transform these compounds into metal oxide nanoparticles, which spread throughout the polymer structure. This method is particularly useful for achieving a high concentration of metal oxides within the polymer [65,66]. However, challenges such as ensuring even distribution and preventing pore blockage can arise, depending on the amount of metal precursor used and the synthesis conditions. Its ease of use and adaptability make it suitable for different types of metal oxides. For instance, researchers developed novel fibrous cellulosic substrates that received *meta*-polybenzimidazole (PBI)- Hristo Penchev protected carbon nanotubes/zinc oxide through various ZnO weight percentage applications controlled with dimethylacetamide as dispersion media al [67].

3.1.3. *Sol-gel synthesis*

The sol-gel method is a flexible and effective way to create mesoporous polymers with embedded metal oxides, as reported by Refs. [68,69]. It involves using metal compounds, such as metal alkoxides or salts, which undergo chemical reactions called hydrolysis and condensation while polymerizable monomers are present. This simultaneous sol-gel reaction and polymerization result in a hybrid material where metal oxides are evenly spread throughout the porous polymer structure. By carefully adjusting key sol-gel process factors—such as temperature, reaction duration, precursor concentration, pH levels, and the type and amount of surfactants—it is possible to create mesoporous materials with different structures [70]. Metal nanoparticles find their placement within metal oxide pores by either reducing solution-based metal ions or running a sol-gel reaction. The production of these nanoparticles mainly occurs through colloidal methods, which require functionalization to stop clumping. Recovery of metal ions into nanoparticles through common reducing agents sodium borohydride, ascorbic acid and hydrazine, occurs simultaneously with stabilizer mechanisms from polyvinylpyrrolidone (PVP), thiols and surfactants, which prevent nanoparticle aggregation. Pre-made PVP-coated metal nanoparticles are mixed with a polymer solution before adding metal oxide precursors. This controlled nucleation and co-assembly of inorganic and organic materials help maintain nanoparticle sizes at the nanoscale.

The polymer-assisted approach allows for precise control over nanoparticle shape using different types of polymers, including homopolymers, double-hydrophilic polymers, and amphiphilic block copolymers [71–73]. During crystal formation, the polymer layer on the nanoparticles adjusts, ensuring that the nanoparticles stay well-dispersed while remaining flexible for controlled crystal growth. Additionally, photoreduction has been explored as an alternative to traditional chemical reduction, offering a way to fine-tune the shape and size of nanoparticles by encapsulating them in mesoporous oxides.

Sol-gel synthesis grants researchers exact control over material structures. This technique is especially useful for fabricating materials that can withstand high temperatures and harsh chemicals. Additional treatments, such as heating (calcination), can further improve the crystallinity of the metal oxides while preserving the polymer's porous nature. For example, Piotr Miądlicki et al., [74] worked on the synthesis of expanded polystyrene spheres (EPS) coated by SiO_2–TiO_2 or TiO_2 for application as a fluidized bed in the photocatalytic via sol-gel. This method is widely used for applications in catalysis, adsorption, and advanced nanohybrid, thanks to its high control over material structure and stability.

3.1.4. *Hard and soft templating method*

The hard templating method, also called the replication method, is a reliable technique for fabricating mesoporous polymers with embedded metal oxides while precisely controlling pore size and shape. A solution containing metal compounds and polymer-building molecules is introduced into the template's pores, where polymerization or sol-gel reactions take place. Once the material is formed, the template is removed using chemical etching or heating (calcination), leaving behind a mesoporous polymer with evenly distributed metal oxides [75] as shown in Fig. 4b. Structural control during synthesis reaches an exceptional level through this method, which allows materials to develop uniform pores and defined architectural frameworks. However, it can be time-consuming and requires careful template removal to prevent structural damage. While soft templating method, as shown in Fig. 4a, uses self-organizing soft templates, such as surfactants, block copolymers, or micelles, to guide the formation of porous structures [76–78]. Metal compounds and polymer-forming monomers are introduced into the system, where polymerization occurs around the self-assembled template. Once the soft template is removed using solvent extraction or heating (calcination), the final mesoporous polymer with evenly distributed metal oxides is obtained. This method allows for the development of materials with large surface areas, adjustable pore sizes, and uniform metal oxide dispersion. Unlike the hard templating approach, it does not require extra steps for template removal, making it more practical for large-scale production.

Furthermore, each templating approach presents distinct advantages and limitations. Hard templating employs rigid scaffolds such as silica or carbon to fabricate ordered porous frameworks with high structural fidelity. In contrast, soft templating relies on the self-assembly of surfactants or block copolymers, enabling tunable porosity and simplified synthesis, though often at the cost of reduced structural stability. A critical comparison of the above methods is presented in Table 1, highlighting their complementary features. Studies have shown that hard templates ensure structural rigidity and precise pore replication, while soft templates offer flexibility in morphology control, cost-effectiveness, and scalability. These different methods are highly application-dependent [80,81]. Table 1 provides more insight into the differences and uniqueness of both templating techniques.

3.1.5. *Electrochemical deposition*

This technique is an effective and precise method for the synthesis of mesoporous polymers with embedded metal oxides; this technique works by applying an electric voltage to deposit metal oxides directly onto the porous polymer framework from a solution containing metal compounds. The method transforms metal ions into metal oxide nanoparticles by using reduction or oxidation processes within the polymer's porous structure. Recent scientific investigations have proven this methodology to create electrochemical materials that possess superior functionality. For example, Mohammad Faraz Ahmer et al. [86] gave a report on Magnetic metal oxide-assisted conducting polymer nanohybrid as eco-friendly electrode materials for supercapacitor applications. While Esma Mutlu et al., [87] worked on a selective and sensitive molecularly imprinted polymer-based electrochemical sensor for detection of deltamethrin. This technique is widely recognized for its high precision and ability to produce uniform structures. The microwave instrument applies radiation energy to heat substances under rapid conditions which enhances both the synthesis rate and the yield numbers beyond traditional heating techniques. It is particularly useful for creating porous materials where precise control over pore size, surface area, and structure is essential. The findings involved investigating ZIF-8 nanoparticle concentration effects on the microwave-assisted synthesis of poly (vinyl alcohol)-co-acrylic acid copolymeric membranes and their fuel cell applications [88]. Research findings worked on

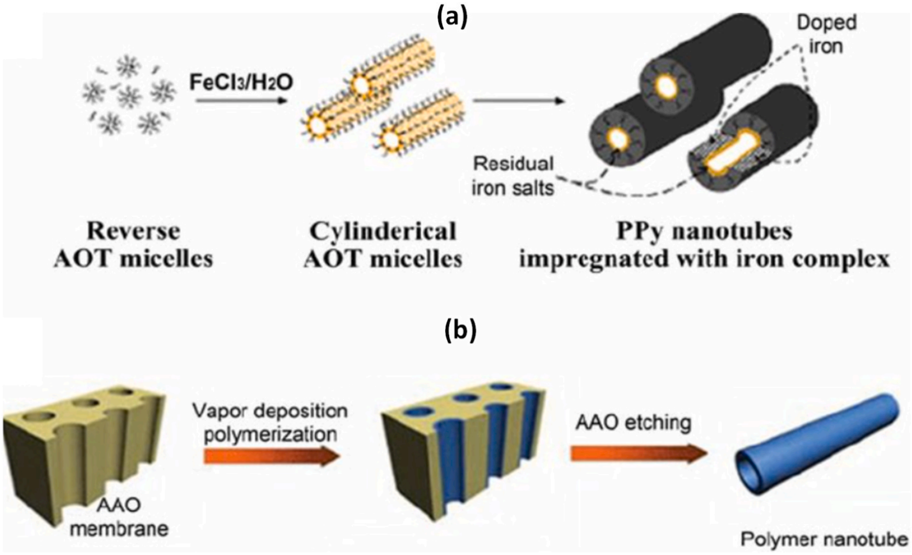


Fig. 4. The synthesis of polymer-nanomaterial hybrids uses two methods known as: the soft-template Method and the hard-template Method [79].

Table 1
Comparison between hard templating and soft templating [82–85].

Parameters	Hard Template Method	Soft Template Method
Templating type	Uses primarily inorganic materials such as silica, polymer microspheres, porous membranes, mesoporous carbon, anodic alumina oxide, or ion-exchange resins as templates.	It uses mainly organic molecules, including surfactants, block copolymers, flexible organics, or interfacial assemblies as templates
Synthesis approach	It basically relies on nanocasting processes that replicate the mesoporous structure of the template.	Based on cooperative self-assembly, true liquid crystal templating, or evaporation-induced self-assembly, typically fewer steps are required.
Template removal	It requires etching with HF or high-temperature calcination, which can potentially damage the nanostructure	Mild heat treatment is involved, combustion, or depolymerization; sometimes, template removal is unnecessary, preserving the nanostructure.
Surface tuning	Limited control over pore size and fixed morphology due to the rigidity of the preformed template	It offers tunable pore structure and morphology, allowing for controlled properties of the synthesized nanomaterial
Cost and Time	It is generally more expensive and time-intensive because of complex synthesis and template removal steps.	It is cost-effective and faster, with simpler procedures and easier template management

microwave-assisted synthesis produced ZnO@APTES quantum dots demonstrating strong antibacterial properties against methicillin-resistant staphylococcus aureus with no resistance development [89]. A scientific study designed Co_3O_4/RGO/$CoFe_2O_4$ hybrid system through multiple nanointerfaces to improve supercapacitor performance. This method enables precise control of metal oxides' thickness along with composition distribution, which can be achieved through modifications in voltage levels and current flow and electrolyte solution concentration adjustments. Additionally, it ensures strong bonding between the polymer and the metal oxide, improving the material's stability and overall performance. The rapid heating promotes the in-situ formation of metal oxide nanoparticles, which become embedded within the polymer network, forming a well-structured mesoporous material. The resulting hybrid materials exhibit enhanced stability, larger surface areas, and improved catalytic efficiency.

No single method universally optimizes metal oxide-polymer integration; rather, the choice must align with application-specific demands for precision, scalability, or performance. In-situ and sol-gel methods lead in structural control for catalysis and energy, while electrochemical and grafting approaches suit sensing. Soft templating and direct mixing offer industrial scalability. Furthermore, it is worth noting that the fabrication of metal/metal oxide-polymer nanohybrids, crucial for diverse applications spanning catalysis, energy storage, and biomedicine, relies on several distinct synthesis methodologies. Table 2 shows a systematic comparison of in-situ polymerization, impregnation, sol-gel synthesis, and templating methods as reported in this study, thereby revealing their unique advantages, limitations, and recent advancements [90,91].

3.2. *Characterization of mesoporous polymers-metal oxide hybrid*

Various analytical techniques are widely used in material science to characterize nanomaterials, as shown in Table 3. These techniques provide valuable insights into their structure, surface features, and chemical composition. To optimize the properties, it is crucial to thoroughly understand their characteristics. Accurate analysis helps determine their chemical makeup, mechanical strength, and structural features [99–107]. This knowledge enhances their performance for various purposes, such as biomedical applications, such as tissue engineering, and drug delivery. Understanding these properties fosters innovation and enables the development of materials with tailored properties to meet evolving technological and biomedical needs.

4. Biomedical applications

The metal/metal-oxide nanoparticles-polymers hybrid system has transformed biomedical research, providing new possibilities for drug delivery, tissue engineering, biosensing, and antimicrobial therapies. These hybrid materials have special features, including a large surface area, adjustable pore sizes, controlled drug release, and improved compatibility with biological systems, making them ideal for medical use. The metal and metal oxides offer antibacterial effects, magnetic properties, and light-driven reactions, supporting targeted drug delivery and medical imaging [108,109]. The porous structure of mesoporous polymers ensures the gradual and controlled release of drugs, enhancing treatment effectiveness while minimizing side effects. Additionally, these materials are vital in regenerative medicine by serving as bioactive scaffolds that help cells grow and repair tissues. As medical technology progresses, nanoparticle-polymer hybrid systems continue to drive the

Table 2
Comparative analysis of metal/metal oxide-polymer nanohybrid synthesis methods.

Method	Key Advantages	Limitations	Refs.
In-situ polymerization	Strong interfacial bonding - Uniform nanoparticle dispersion - Good morphology control	Risk of pore blocking, Limited crystallinity control if poorly optimized	[92,93]
Impregnation	Simple and versatile - High metal oxide loading achievable	Poor nanoparticle uniformity - Pore obstruction at high precursor concentrations	[94,95]
Sol-gel synthesis	Homogeneous nanoparticle distribution - Tunable porosity via reaction conditions - High thermal/chemical stability	Processing can be sensitive to pH, temperature, and drying conditions	[90,96]
Hard templating	Precise pore size and shape control - Highly ordered structures	Time-consuming, requires harsh template removal, risking framework damage	[90,97]
Soft templating	Cost-effective - Eco-friendly - Easy/mild template removal	Less structural stability - Limited long-range ordering	[98]

development of advanced healthcare materials.

4.1. Drug delivery systems

Controlled delivery of drugs to the precise location or target site while preventing harm to nearby healthy cells is the goal of a targeted drug delivery system. At the moment, the primary source of magnetic materials utilized to deliver anticancer drugs to specific regions is iron oxide nanoparticles, harnessing their magnetic properties for a proper guide of the drug to the required site [110]. Furthermore, a significant number of bioactive low-molecular-weight drugs, together with peptides/proteins, use polymer-controlled metallic nanoparticles as carriers for drug delivery under controlled delivery conditions. When compared to the delivery of parent-free drugs, the administration of pharmaceuticals coated with a polymer has proven to have significant advantages. These include better water solubility, increased bioavailability, decreased deactivation potential, decreased systemic toxicity, less antigenic propensity, and enhanced lesion site speeding up are all possible with polymer-coated medications [111].

Several studies have shown that metallic nanoparticles are apt to deliver medicine to a specified region. However, much like functionalization for metal oxide nanoparticles, which helps embed anticancer drugs inside nanoparticles or attach them to surfaces, the systems often require biocompatible polymer or gold coatings as shown in Fig. 5. After delivery, the drug/nanoparticle complex gets directed to a precise tumour location using an external metallic field. Alteration of certain parameters can be used to release the drug or bioactive material, which include changes in pH, temperature, osmolality, or enzyme activity from the vehicle [112,113].

4.1.1. Mechanisms of controlled drug release

The adoption of a metal oxide nanoparticle-polymer system for controlled drug release is a novel way to improve therapeutic efficacy while reducing negative effects in drug delivery systems. In practice, developers focus on developing zero-order delivery systems that release drugs gradually and systematically over extended periods. The therapeutic outcome becomes less effective when drug delivery exceeds appropriate limits, thus delaying the required time to get t the targeted site [115]. However, scientific studies focus on developing delivery systems that sense drug stimuli to trigger controlled medication pulsing. The following factors can impact drug release from polymer-supported nanoparticles: polymer swelling, polymer erosion or degradation, polymer degradation or erosion combined with drug diffusion through a polymer matrix, and so on [116,117]. Characterizing the polymer nanoparticle complex release phase is crucial to maximizing their effects because it differs from that of traditional drug delivery systems. Furthermore, when creating NPs, it's important to recognize and understand the special procedures and issues related to the release process, as well as to differentiate between them and understand their distinct qualities. One way to get a drug released from a carrier under control is to understand the following.

4.1.2. Diffusion-controlled release

The suitable technique for releasing drugs is diffusion control. The active content of the medicine diffuses through the polymer NP matrix to implement its controlled release functions during delivery. A drug release rate decreases as the active agent travels a longer distance longer distance [118,119]. Click or tap here to enter text. The substance conducts movement through the internal areas of the polymer matrix toward the release medium. Strands of polymers create a barrier that stops drug diffusion from taking place. The drug release through diffusion possesses a relationship with swelling. The mathematical definition of diffusion is provided by Fick's Law as shown in equation (1) which describes how substances move from regions of high concentration to low concentration [120–122]. In the context of polymer-based drug delivery systems, where polymer chains act as diffusion barriers and swelling affects diffusion.

$$J = -D\,\frac{dC}{dx} \tag{i}$$

Where J represents the diffusion flux, D indicates the diffusion coefficient, C stands for drug concentration and x indicate spatial position. This equation demonstrates that drug molecules diffuse along a concentration gradient, with the polymer matrix governing the release rate by influencing DD, which can vary with swelling. As swelling occurs, polymer chain mobility increases, allowing for enhanced diffusion. In contrast, when the polymer network remains unswollen, it acts as a more effective barrier, limiting drug movement. Fick's law parameters require specific assumptions for their determination including drug particle dimensions that are smaller than the polymer matrix diffusion length and media conditions that remain in sink conditions during the release process along with drug particle pseudo-steady state maintenance.

Drug molecules will spread across the full extent of the polymer matrix because matrix systems contain no diffusion-blocking membrane barriers. The initial drug release phase will begin at a high rate yet it will gradually decrease according to the solution medium distance traveled by drug molecules. The diffusion coefficient shows direct proportionality to the release rate so an increase in diffusion coefficient results in a parallel increase in the release rate [123,124]. Diffusion-controlled release remains the most promising strategy for polymer-based drug delivery due to its simplicity and tunability via polymer design and swelling. Challenges include predicting non-ideal release kinetics under non-sink conditions and heterogeneous matrix swelling. The field is moving toward smart, stimuli-responsive polymers that dynamically modulate diffusion coefficients (D) in response to pH, temperature, or enzymes, enabling precise spatiotemporal control beyond passive Fickian models. Emerging focus includes multi-scale modeling and real-time release monitoring to overcome assumptions of steady state and ideal diffusion.

4.1.3. The swelling-controlled release

The release of drugs from the polymer matrix occurs through media penetration and subsequent chain breakdown of the polymer. The polymer expands before degradation [110]. The density of polymer

Table 3
Characterization techniques for Mesoporous Polymers incorporated with Metal/Metal-oxide Nanoparticles.

S/n	Methods	Application
1	Scanning Electron Microscopy (SEM)/Transmission Electron Microscopy (TEM)	The SEM generates highly detailed images for effective examination of nanoparticles' distribution and their morphology and porosity in the polymer matrix. TEM provides detailed information about the dimensions and distribution patterns of nanoparticles embedded in mesoporous polymers. The TEM technique gives exceptional usefulness in studying the internal framework and structure of hybrid materials.
2	Atomic Force Microscopy (AFM)	This analytical instrument measures surface roughness, material texture, and mechanical properties for nanoscale investigation of nanoparticle distribution in polymer matrixes together with material pore structure and distribution patterns.
3	Brunauer-Emmett-Teller (BET)	The BET analysis measures surface area as well as both pore size and pore volume quantities of composite materials. This analysis enables crucial examination of material porosity combined with absorption capabilities and stability metrics for optimal property development through the management of material pore composition and elevated surface area detections.
4	X-ray Diffraction (XRD)	The XRD analysis method reveals material crystallinity as well as identifies phase composition and detects structural properties. XRD provides information about crystalline phases in addition to nanoparticle measurements and structural defect detection. The XRD technique confirms both proper material creation and phase purity and stability which proves essential for maximizing performance in catalysis and energy storage and sensing operations. The method shows how materials change between specific phases while determining how alterations in solvent types or concentration levels as well as nanoparticle incorporation influence hybrid material structure.
5	Nuclear Magnetic Resonance (NMR) Spectroscopy	NMR provides insights into polymer-metal interactions, functional group modifications, and structural stability. Solid-state NMR is particularly useful for studying heterogeneous materials, offering detailed information on atomic-scale arrangements and bonding environments.
6	Energy-Dispersive X-ray Spectroscopy (EDS or EDX)	EDS analysis determines where metal/metal-oxide nanoparticles exist within polymers as well as their chemical composition. This technique helps identify the presence, concentration, and spatial dispersion of the nanoparticle, by ensuring uniform incorporation. It is crucial for material optimization in catalysis, energy storage, and environmental applications by confirming successful metal intercalation and/or incorporation.
7	Inductively Coupled Plasma Optical Emission Spectroscopy (ICP-OES) and Inductively Coupled Plasma Mass Spectrometry (ICP-MS)	ICP-OES and ICP-MS serve as established analytical methods to detect metal composition in polymers-metal/metal nanohybrids. ICP-OES detects and quantifies multiple elements based on their emitted light spectra, while ICP-MS provides higher sensitivity by measuring ionized metal species. These methods ensure precise elemental composition analysis, aiding in quality control, optimizing synthesis processes, and evaluating material performance.
8	Thermogravimetric Analysis (TGA)	TGA examines the material's thermal stability and the detection of decomposition behaviours during tests. TGA uses the relationship between weight loss and temperature to detect degradation temperatures and determine moisture content and residual metal oxides. TGA helps determine the thermal endurance of polymer-nanoparticle composites, optimizing their performance for high-temperature applications such as catalysis and energy storage. Additionally, it provides insights into the interactions between polymer matrices and embedded nanoparticles, aiding in material design and stability enhancement.
9	Fourier-Transform Infrared (FTIR) Spectroscopy/Attenuated Total Reflectance-Fourier Transform Infrared Spectroscopy (ATR-FTIR)	The purpose of FTIR or ATR-FTIR is to analyze the chemical structure and functional groups present in the nanohybrid system. ATR-FTIR provides valuable information on molecular interactions, bonding characteristics, and surface modifications by detecting vibrational modes of chemical bonds. This technique is particularly useful for studying polymer-metal oxide interactions, functionalization, and stability. Its advantages include minimal sample preparation, surface-sensitive analysis, and the ability to analyze both solid and liquid samples with high accuracy.
10	X-ray Photoelectron Spectroscopy (XPS)	XPS identifies elemental composition, oxidation states, and chemical bonding, providing insights into surface interactions, functionalization, and stability, which are crucial for optimizing catalytic, electronic, and adsorption properties. This examines how molecules vibrate and detect specific chemical groups in the hybrid system. It helps determine the structure and makeup of the polymer, before and after the formation of the hybrid.
11	**UV–Visible Spectroscopy (UV–Vis)**	UV–Vis spectroscopy examines both optical properties along electronic structural elements. It helps determine the bandgap energy, absorption behaviour, and light-harvesting efficiency, which are crucial for photocatalysis, sensors, and optoelectronic applications. Additionally, it provides insights into nanoparticle dispersion and interactions within the polymer matrix.
12	**Photoluminescence Spectroscopy (PL)**	PL examines the electronic properties and charge carrier dynamics of metal/metal-oxide nanoparticles in mesoporous polymers. It is particularly useful for analyzing defect states, recombination rates, and emission behavior, which influence photocatalytic efficiency and optoelectronic performance. More so, it studies the electronic structure and charge carrier dynamics in photocatalytic applications.
13	**Dynamic Mechanical Analysis (DMA)**	DMA evaluates nanocomposite mechanical properties by studying these materials under different combinations of stress levels, temperature changes and frequency ranges. The test equipment uses three key measurements to analyze viscoelastic behavior and phase transitions while evaluating thermal stability conditions. DMA helps in understanding how metal or metal-oxide incorporation affects the mechanical strength, flexibility, and durability of the polymer, making it crucial for optimizing materials used in energy storage, sensors, and coatings.

chains, degree of swelling, and hydrophilicity all influence diffusion. Active material delivery happens through simultaneous degradation of the polymer structure combined with diffusion during non-Fickian swelling of the matrix. The relaxation constant determines the device geometries, including slabs, spheres and cylinders, because drug release speed affects the significance of relaxation constant values. The geometries related to these systems remain unaffected by changes in the diffusion constant value. The release process appears best described by the Weibull model. The Weibull model is more suited for figuring out the drug release profile of swellable PNPs in vivo and seems adaptable enough to take into consideration the impact of system parameters on the release process [125,126].

The Weibull model is the most promising strategy for modeling drug release from swellable PNPs, effectively capturing non-Fickian kinetics and parameter sensitivity in vivo. Key challenges include precisely controlling polymer swelling, degradation rates, and geometry-dependent relaxation dynamics. The field is moving toward predictive, multi-parameter models that integrate material properties (hydrophilicity, chain density) with in vivo behavior, enabling tailored nanocarrier design. Geometry independence from diffusion constants simplifies design, but real-world variability demands adaptive, biologically informed models beyond empirical fits.

4.1.4. Erosion and degradation-controlled release

Diffusion, swelling, and dissolving are all aspects of polymer erosion. Polymers can erode in two different ways: homogeneously, which happens when they erode consistently across the matrix, and heterogeneously, which happens when they erode from the outermost layer to the innermost core. The breakdown of polymers stems from water absorption as well as media pH, polymer volume, enzyme presence, and media characteristics. The release of medicine depends on four main factors, including polymer type and internal bonding as well as adjuvant

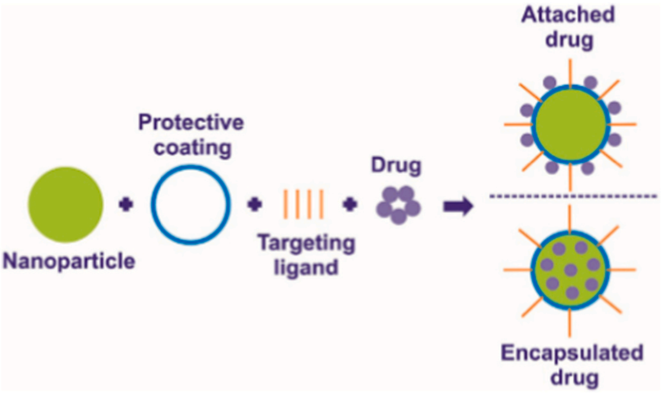


Fig. 5. Diagram illustrating Drug-loading alternatives for focused drug delivery [114].

components and NP size and shape [123]. Small-sized NPs increase polymer breakdown rates by their effect on crystallization domain size together with the length of water diffusion distance. The polymer may exhibit indications of bulk deterioration but not typical surface erosion. Because components may be safely eliminated from the body without causing harm over time, biodegradable polymeric systems are recommended. At the target tissues, the pharmaceutical drug-polymer conjugates are released through enzymatic or hydrolytic cleavage. The cleavage rate controls the drug release kinetics [127]. Homogeneous erosion and small NP design are most promising for controlled drug release, enhancing diffusion and crystallinity modulation. Heterogeneous erosion remains challenging due to unpredictable core degradation. The field is advancing toward enzyme-responsive, pH-sensitive biodegradable polymers with tailored NP size/shape for precise spatiotemporal release. Hydrolytic cleavage dominates, but enzymatic targeting offers greater specificity. Key challenges include balancing degradation rate with therapeutic demand and ensuring complete, non-toxic byproduct clearance.

4.1.5. Stimuli-controlled release

Integrating metal/metal-oxide nanoparticles into polymer matrixes enables the controlled release of bioactive compounds, significantly improving drug delivery and medical treatments. These advanced materials function as controlled drug delivery systems because they respond to external signals including pH changes and temperature variations along with light intensity, magnetic forces and redox effects. The drug release mechanism of metal oxides depends on targeted conditions including tumour acid environment and near-infrared (NIR) light exposure. Additionally, magnetic nanoparticles like Fe_3O_4 facilitate remote-controlled drug release using magnetic fields [128]. These intelligent delivery systems enhance treatment effectiveness, minimize side effects, and enable targeted therapies, making them ideal for cancer treatment, tissue regeneration, and antimicrobial applications. The adaptability of these stimuli-sensitive mesoporous polymer-nanoparticle systems is advancing personalized medicine and innovative nanomedical technologies.

Both internal and exterior triggers can be used to release drugs. Internal stimuli have been demonstrated to enhance the selectivity of therapeutic action since they target sick tissue directly. This necessitates adding the proper materials to polymer-nanoparticles (PNPs) hybrid systems that are stimulated by specific endogenous triggers. PNPs and the tumour microenvironment (pH, redox, etc.) both provide tumour-targeting selectivity and efficiency. Ultrasonic waves, electromagnetic and magnetic fields, and temperature are examples of external stimuli that are applied. This approach has the benefit of precisely administering medications to the intended location while reducing adverse effects [118,128]. Stimuli-responsive polymer-nanoparticle systems (pH, NIR, magnetic) enable precise, targeted drug release with minimal off-target effects—ideal for cancer and antimicrobial therapy. Key challenges: reproducible synthesis, long-term biocompatibility, and scalable manufacturing. Field is moving toward multifunctional, hybrid systems integrating diagnostics (theranostics) and AI-driven stimulus tuning for personalized medicine, with growing focus on endogenous triggers (tumor microenvironment) to enhance selectivity over external controls.

4.2. Imaging and Diagnostic Applications: MRI, CT scans, and fluorescence imaging

Metal-oxide nanoparticle-polymer systems are transforming medical imaging and diagnostics by boosting contrast, sensitivity, and biocompatibility. These cutting-edge materials enhance imaging methods like MRI, CT scans, and fluorescence imaging as shown in Fig. 6 by offering clearer signals and precise targeting. Their large surface area and adjustable properties support accurate drug delivery and real-time disease tracking. Consequently, they are becoming essential for early diagnosis, non-invasive monitoring, and personalized medicine, driving advancements in next-generation healthcare solutions.

4.2.1. Magnetic resonance imaging (MRI)

The synergy of metal oxide nanoparticles and polymer to form metal oxide nanoparticle-polymer hybrid materials is gaining attention for MRI applications in biomedical engineering due to their enhanced contrast properties, biocompatibility, and multifunctionality [129]. The medical imaging method MRI operates with established power by activating proton spin through external magnetic field radio frequency pulses to create detailed soft tissue images of high resolution and contrast. It employs non-ionizing radiation and radiotracers, though limitations include high cost, longer imaging times, and artifacts from motion or implants. Contrast agents further enhance lesion detection in clinical settings [130].

Although, studies have shown that hydrogen protons play a key role in MRI, aligning spins under a magnetic field. A radiofrequency pulse disturbs this alignment, leading to T1 and T2 relaxation, which are used by contrast agents. T1 agents like chelated gadolinium create positive contrast; T2 agents like SPIO create negative contrast. Hydrogen protons, aligning under magnetic fields, are essential for MRI, with radiofrequency pulses deflecting and then relaxing their spin. T1 and T2 relaxation times are key, and contrast agents—paramagnetic for T1 (positive contrast) and superparamagnetic for T2 (negative contrast)—enhance imaging [125]. More so, dual-weighted contrast agents, like gadolinium oxide nanoparticles (Gd_2O_3), enable both T1 and T2 imaging.

Furthermore, nanoparticles make it possible to perform MRI imaging at the gene, protein, cell, and organ levels. When optimizing images, the targeting strategy for nanoparticles must be taken into account. Surface labelling is essential for the biodistribution of nanoparticles in active targeting. To diagnose tumours, certain peptides, ligands, and antibodies have been employed as surface markers [131]. The size of the nanoparticle, which can vary from several nanometers to hundreds of nanometers, is the most crucial factor for passive targeting. The EPR effect has been exploited by this method in tumour imaging. Several applications utilize non-specific cellular absorption to perform blood pool contrast imaging along with inflammatory imaging, cancerous lymph node detection, mesenchymal stem cell tracking and islet transplantation monitoring.

More so, the brain, muscles, heart, and cancer cells are among the internal organs that can be observed during an MRI using radio waves and magnetic fields [132]. Compared to other imaging methods, this procedure typically finds differences between different bodily soft tissues. However, it might occasionally be challenging to find tiny tumours. In that instance, the application of MRI contrast-enhancing drugs is necessary. However, with the right polymer coating, to produce a nanoparticle-polymer hybrid system, the toxicity of metallic cations can significantly be lowered., thereby guaranteeing a prolonged duration of blood circulation in addition to raising contrast. The explicit ligands of the probe can link to different polymer systems with polylysine, poly (l-glutamic acid)-cystamine, PEG, poly (lactic acid), PEG-poly (L-lysine), PEG-b-poly(N-(N-(2-aminoethyl)-2-aminoethyl) (aspartame)), polysilsesquioxane, dextran, and L-cystine bisamide copolymer, serving as examples for Gd chelate conjugation. These polymers are widely utilized in the manufacturing of compounds that enhance MRI contrast [133,134]. When Gd-DTPA-polylysine was applied, it was seen that the signal intensity in the pulmonary arteries of healthy lungs increased by 118 %, whereas the signal intensity in the lungs with injury was revealed to increase by 121 % (Fig. 7) [135–137]. This shows that these hybrids combine the high magnetic susceptibility of metal oxides (e.g., iron oxide) with the flexibility and stability of polymers, enabling better imaging resolution and reduced toxicity [138]. Research highlights their use in targeted imaging and theranostics, improving diagnostic accuracy and treatment monitoring [139]. Recent advances also explore surface modifications to optimize stability and minimize aggregation in biological environments [57]. Such hybrids represent a breakthrough in non-invasive diagnostics and personalized medicine.

Metal oxide-polymer hybrids show great promise for MRI by combining high relaxivity with polymer-enhanced biocompatibility, prolonged circulation, and targeted delivery via ligands. More so, dual T1/T2 agents enable multifunctional imaging, while EPR-driven passive targeting and active ligand binding improve tumor and inflammation detection. However, the major roadblock remains controlling nanoparticle aggregation, ensuring long-term toxicity profiles, and achieving consistent biodistribution. However, the development of smart, stimuli-responsive systems with surface-engineered polymers for theranostics, real-time monitoring, and personalized diagnostics, particularly in oncology and neuroimaging, is driving clinical translation beyond conventional gadolinium agents.

4.2.2. CT scans

Computed tomography (CT) imaging plays a vital role in medical diagnostics, enabling high-resolution imaging of internal structures. The two different types of CT contrast agents are categorized according to their nanoparticle composition. Iodine-based contrast agents belong to the first group because they have a long-standing presence in clinical imaging studies. Core-shell structures serve as vectors to carry iodine while maintaining its traditional placement. As with liposomal iodine, iodine is loaded into the core of the nanoparticle [140,141]. CT contrast agents fall into two categories, with the second group using metals as the basis for developing nanoparticles. The list of materials available in this category includes tantalum oxide together with zirconium dioxide and gold metals. The different platforms of MRI imaging nanoparticles consisting of fundamental, core-shell and vector designs replicate similar structural elements found in metal-based nanoparticle systems. The basic structure of gold nanoparticles makes them the most commonly used entity in CT imaging applications of translational research. Nanometer-sized CT contrast agents demonstrate valuable properties such as strong attenuation and targeting abilities which allow their application in several medical settings. Research has used gold nanoparticles that red blood cells accept to image blood flow through the human body. The assessment of tumour blood vessels relies on liposomal iodine as it maintains a long residence time and produces a strong CT signal enhancement. Research has shown that prostate cancer visualization occurs through the use of gold nanoparticles which incorporate aptamer alongside prostate-specific membrane antigens. Lastly, tumour imaging and medication distribution tracking have been achieved through the deposition of zirconium dioxide nanoparticles [140,142,143]. Metal components function either as components of a core-shell structure or as a shell or core material. New nanostructures exist with zirconium dioxide in their shell and PPy and doxorubicin inside the core structure together with gold nanosphere core and indocyanine-loaded mesoporous silica shell nanotopographies. The metal components act as surface materials for vector drawings while poly(acrylic acid)bridged gadolinium nanoparticles with gold surface elements serve as a prime illustration of this design [135].

The use of metal-oxide nanoparticles incorporated into mesoporous

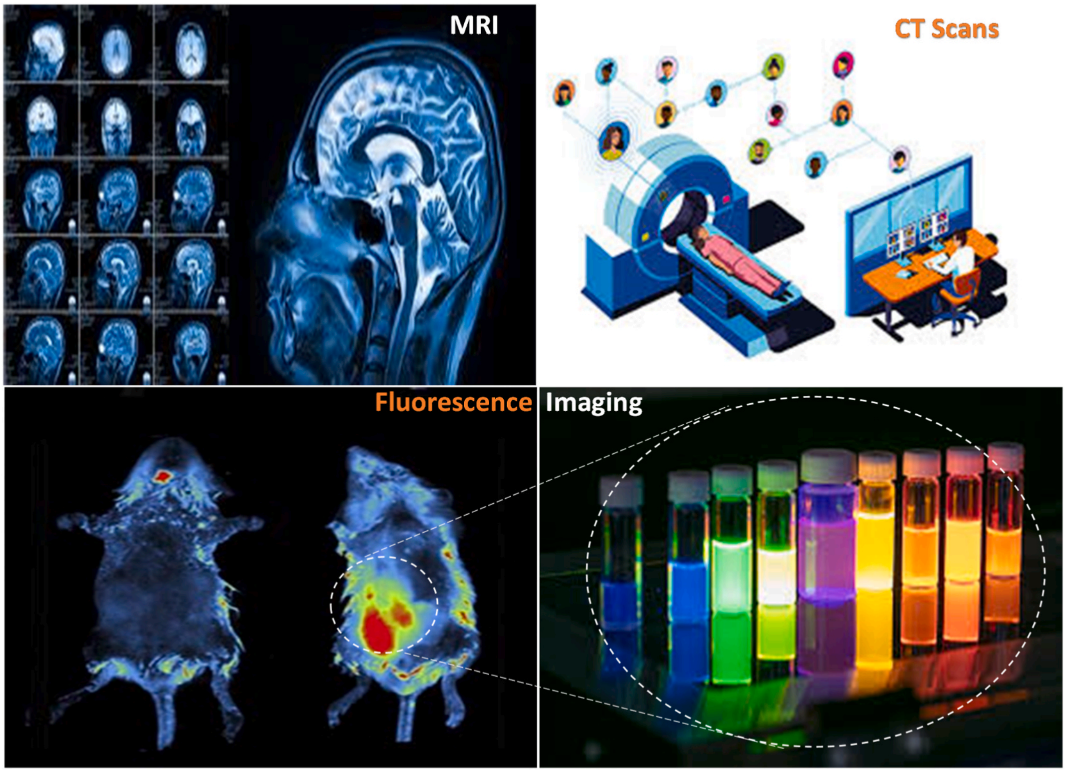


Fig. 6. Imaging and Diagnostic Applications of polymer-metal oxide nanoparticle Hybrid.

polymers has emerged as an innovative approach to enhancing CT contrast agents and improving imaging quality while addressing concerns related to toxicity and biocompatibility. The incorporation of metal oxides into mesoporous polymers leads to the development of stable biocompatible imaging agents with high contrast. These materials offer enhanced X-ray attenuation, controlled porosity for drug loading, and improved circulation time in the bloodstream. Recent advancements focus on multifunctional mesoporous polymer-metal oxide composites that combine imaging with therapeutic functionalities, such as drug delivery or tumour targeting [144–146]. These hybrid materials enable dual-modal imaging, combining CT with other imaging techniques like MRI or fluorescence imaging for more precise diagnostics. Additionally, their controlled porosity enhances biocompatibility and clearance, reducing long-term toxicity.

Additionally, polymer-templated mesoporous TiO_2 was investigated for its ability to enhance pseudocapacitive charge storage, which is essential for hybrid imaging systems [147]. These findings demonstrate the growing potential of mesoporous polymer-metal oxide hybrids in advancing CT imaging for precise, high-resolution diagnostics. Recent developments also highlight biodegradable polymer-coated metal-oxide nanoparticles that enhance biocompatibility while reducing toxicity risks, making them ideal for real-time in vivo imaging [148–150]. These advancements demonstrate the growing potential of mesoporous polymer-metal oxide hybrids in next-generation CT imaging technologies, offering higher precision, improved safety, and multifunctionality.

Iodine-based agents remain clinically dominant but lack targeting; metal-based NPs (gold, ZrO_2, Ta_2O_5) offer superior attenuation and functionalization potential. Gold NPs lead in translational research for vascular and tumor imaging, while zirconium dioxide enables theranostic applications [151,152]. The most promising strategies involve mesoporous polymer-metal oxide hybrids, combining high X-ray attenuation, drug delivery, and biodegradability—with emerging dual-modal (CT/MRI/fluorescence) capabilities.

4.2.3. Fluorescence imaging

Fluorescence imaging of nanoparticles enables the simultaneous execution of gene detection alongside protein analysis, enzyme activity assessment, element tracing, cell tracking, early disease diagnosis, tumour-related research and real-time therapeutic effect monitoring. In particular, near-infrared fluorescence imaging offers the best spatial resolution available for microscopic disease diagnostics using fluorescence imaging technologies. The advantages of non-invasive radiofrequency over visible light include less non-specific tissue autofluorescence and deeper tissue penetration. Even yet, the penetration depth is still restricted, and the scattering and auto-fluorescence characteristics in different tissues continue to impede the therapeutic utility. Furthermore, low sensitivity for identifying abnormalities may result from limited fluorescence in the target lesion as well as possible blink and photobleaching effects. Metallic oxide nanoparticles are the most widely utilized nanoparticle design for fluorescence imaging in preclinical research [153].

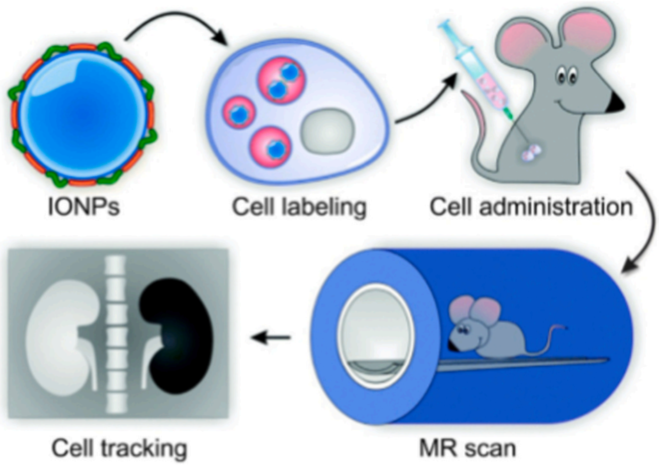


Fig. 7. Design factors to be taken into account while creating polymer-coated iron oxide nanoparticles for stem cells [136].

The most frequently utilized design employs surface-labeled fluorophores attached to vectors. A plasmonic/magnetic nanoparticle linked with the Cy3-modified S6 aptamer represents an example design. The nanoparticles provide increased local concentrations through both passive and active targeting, while the fluorescent dye provides imaging [154] as shown in Fig. 8. Another design, referred to as a "core-shell" structure, labels the outer shell of the nanoparticles with peptides, ligands, and antibodies while loading a fluorescent dye into the centre of the particles. Micelles, dendrimer and Qdot quantum nanoparticles, and multi-layered nano matryoshka are a few examples of core-shell structures. These designs have the advantage of solubilizing hydrophobic fluorophores and shielding interior fluorophores from excretion and quick degradation [130].

The possible drawbacks of fluorescence imaging can be circumvented by using the advantageous qualities of nanoparticles. For example, more signals can be produced by loading more fluorescent dye molecules into nanoparticles. Furthermore, the nanoparticles can be shaped or altered to avoid possibly dampening NIR fluorescence when necessary. Moreover, the local lesion concentration of fluorescent dye can be raised by employing both active and passive techniques to raise the concentrations of nanoparticles in lesions. More absorption in the target lesions is also made possible by the comparatively lengthy stay in circulation. Among the strategies to minimize photobleaching along with blink effects in nanoparticles is their engineering to change low-energy photons into high-energy photons.

Furthermore, the integration of metal-oxide nanoparticles into polymers has made notable advancements in fluorescence imaging, especially for medical imaging and disease detection. These hybrid materials provide strong light stability, adjustable emission properties, and excellent biocompatibility, making them well-suited for real-time imaging and improving image contrast. The combination of these three metal oxide nanoparticles Fe_3O_4 TiO_2 and CeO_2 with polymers offers enhanced capabilities for fluorescence imaging and magnetic resonance imaging [155–160] These have the propensity to improve deep-tissue imaging while reducing light-induced damage These innovations emphasize the increasing importance of mesoporous polymer-metal oxide composites in advanced imaging and medical technology, Improving contrast and specificity in imaging is important for personalized medicine as well since it allows for the development of customized treatments based on in-depth imaging of the diseases of specific patients [161]. In addition, the most promising strategies involve core-shell nanoparticles and polymer-metal oxide hybrids which enhance brightness, stability, and multi-modal imaging while mitigating photobleaching and improving deep-tissue penetration via NIR fluorescence. More so, active/passive targeting boosts lesion accumulation, enabling precise diagnostics and therapy monitoring.

4.3. Regenerative medicine

The metal/metal-oxide nanoparticles-polymers hybrid has shown great potential for regenerative medicine research according to studies [162]. Hybrid materials that combine properties of mesoporous polymers provide a special set of advantages by increasing material compatibility and enabling controlled drug delivery while promoting better cell-cell interactions. At the same time, the metal NPs can impart electrical conductivity, magnetic targeting, and antimicrobial properties, to the composites [163–165]. This makes them ideal for various biomedical applications.

4.3.1. Scaffold design using mesoporous polymers for tissue engineering

Tissue engineering aims to develop biomimetic scaffolds that support cell growth, differentiation, and regeneration. Mesoporous polymer scaffold design for tissue engineering is a state-of-the-art method in regenerative medicine. These scaffolds offer the structural support required for cell adhesion, development, and differentiation, which results in tissue formation. They are designed to resemble the extracellular matrix. The ultimate goal of tissue engineering, a cutting-edge, quickly expanding field based on chemical, biological, and engineering concepts, is to avoid organ transplantation. The primary objectives of tissue engineering include tissue regeneration, organ function restoration, and the enhancement and repair of tissues that have been damaged due to a variety of circumstances, including disease, injury, and congenital anomalies [166–168]. It has the potential to regenerate nearly all human organs and tissues. Three general strategies can be identified in tissue engineering: implantation and replacement of cells into the organism; delivery of substances that induce tissue growth, such as cytokines; and positioning of cells on or within different matrices and growth factors [166]. Additionally, tissue engineering techniques are primarily divided into two categories: Soft tissue engineering regarding skeletal muscle, tendon, nerve, cardiac patch, and blood vessels and secondly, bone-related hard tissue engineering [169–171].

The first step in the tissue engineering process is to identify and isolate isolated and cultivated cells under carefully regulated conditions that enable cell division and population growth. To continue proliferating, the cells are also placed in a reactor after being implanted on or inside a substrate or scaffold. Ultimately, the scaffold is going to be reinserted into the host tissue. Synthetic extracellular matrix, or scaffold, is an essential component of cell support and offers a transient structural framework for developing tissue [166]. A scaffold design must satisfy fundamental needs including biodegradability, biocompatibility, serializability, the capacity to promote nutrition delivery into the scaffold and support cell attachment, as well as appropriate mechanical qualities that match the native tissue. Thus, it is essential to have a larger surface area and a connected three-dimensional (3D) porous structure. The most important factor in the implantation, cell proliferation, and creation of new 3D tissue for various organs is polymeric scaffolds.

Numerous natural polymer scaffolds, including hyaluronic acid, collagen, alginate, chitosan, and fibrin, have been effectively used in a variety of tissue targets. Mesoporous polymers are a useful vehicle for drug administration because of their specific and distinctive characteristics, which include biodegradability, biocompatibility, very low toxicity, and non-immunogenicity [131,172]. Mesoporous polymers are extremely biocompatible; they break down in tissues into non-toxic amino sugars and do not cause allergic reactions or rejection. One benefit of using chitosan nanoparticles as drug carriers is that they

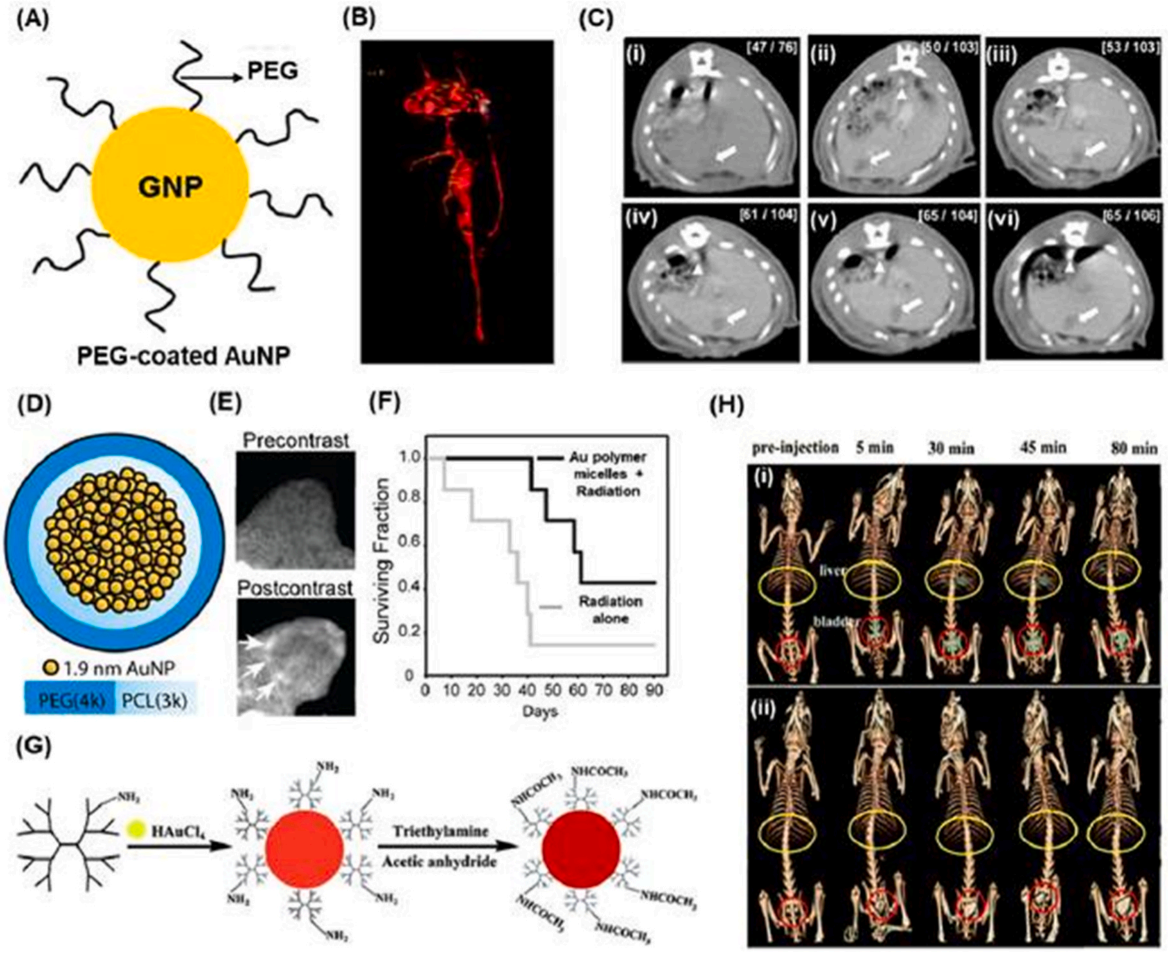


Fig. 8. (A) A visual diagram showing PEG-coated gold nanoparticles (AuNPs); (B) A live CT scan image of the heart and major blood vessels of a Sprague-Dawley rat, taken 10 min after injecting PEG-coated AuNPs (140 mg/mL); (C) A series of CT scan images of a rat liver tumour model after injecting PEG-coated AuNPs (100 mg/mL) at different time points: (i) before injection, (ii) 5 min, (iii) 1 h, (iv) 2 h, (v) 4 h, and (vi) 12 h after injection; (D) A simplified diagram showing the structure of gold-loaded polymeric micelles; (E) Live CT scan images of nude mice with HT1080 tumours before and 24 h after injection. ; (F) A Kaplan-Meier survival graph showing the lifespan of tumour-bearing mice treated with gold-loaded polymeric micelles and radiation therapy; (G) A simplified diagram explaining the process of making PAMAM-reduced AuNPs; (H) Live CT scan images taken after injecting PAMAM-AuNPs into the bloodstream (0.47 mmol of gold per kg of body weight). (i) a CT scan of PAMAM-AuNPs and (ii) a CT scan taken using the same amount of Omnipaque, based on iodine concentration [154].

release the drug gradually and under control, increasing the drug's stability, and efficacy, and lessening its toxicity. To lessen the reticuloendothelial system's quick removal of the particles from circulation, nanoparticles are typically composed of biocompatible polymers. Natural polymers have advantages, but they also have drawbacks, such as low mechanical stability, high rates of degradation, the potential to spread disease, and immunogenicity. Synthetic polymers with controlled degradation rates, the capacity to form complex shapes, enhanced cell attachment, and the ability to deliver soluble molecules such as polyethylene glycol (PEG), PGA (Polyglycolic Acid), Poly (lactic-co-glycolic acid) (PLGA), Polycaprolactone (PCL), and poly (propylene fumarate) have been widely used as scaffolds for tissue engineering [166,173,174]. Several 3D scaffolding techniques have been improved [132]. Rapid prototyping techniques have enabled researchers to produce 3D MBG scaffolds through different primary approaches leading to various outcomes as shown in Table 4.

This necessitates the adoption of Metal-oxide nanoparticles incorporated into mesoporous polymers. The role of metal-oxide nanoparticles in tissue engineering is because these materials exhibit superior activity, a wide surface area, and zeta potential. The adoption of Metal-oxide nanoparticle-polymers hybrid systems has gained significant attention due to their biocompatibility, structural stability, and tunable porosity, which allow controlled drug release, mechanical reinforcement, and bioactive functionalities.

The designing of nanocomposite scaffolds that replicate the extracellular matrix remains the current research focus because these scaffolds help cells both attach and proliferate. More so, metal-oxide nanoparticles are widely used in bone regeneration, wound healing, and neural tissue engineering due to their: Antibacterial properties (ZnO, CeO_2) [181,182], Osteoinductive potential [183] and Controlled drug delivery capabilities [59,184].

Demir et al. [185] studies present the assembly of mesoporous iron oxide nanoparticles (meso-MNPs) with cryogel scaffolds made of chitosan and gelatin. Meso-MNPs with particle sizes ranging from 2 to 50 nm, a surface area of 140.52 $m^2\ g^{-1}$ and a pore volume of 0.27 $cm^3\ g^{-1}$ were achieved through the synthesis of mesoporous nano-particles on a SiO_2 template using PEG 6000 followed by SiO_2 leaching. The research integrated multiple ratios of meso-MNPs effectively into chitosan: gelatin cryogels at total polymer content levels. The number of MNPs had a direct effect on the cryogels' morphological structure and physicochemical qualities. The VSM curves revealed that all composite cryogels could be magnetized by applying a magnetic field. In terms of the safety of magnetic cryogel scaffolds for use in biomedicine, it is important to note that all values are less than the static magnetic field exposure limit, and cytotoxicity data show that scaffolds containing meso-MNPs are nontoxic, with cell viability ranging from 150 to 275 %. In addition, microbiological investigation using gram-negative and gram-positive bacteria revealed that the scaffolds were active against these bacteria. Yahay et al. [186] reported this study used evaporation-induced self-assembly and sacrificial foamy templates to create zinc silicate hybrid scaffolds with hierarchical meso/-macroporous architectures. F127 triblock copolymer as well as polyurethane (PU) foam served as scaffold templates to create mesoporosity and macroporosity features. The performance evaluation of these scaffolds took place in an in vitro environment through the assessment of degradability along with apatite-forming ability and cytocompatibility testing. When cultured with MG-63 human osteosarcoma cells, scaffolds calcined at 750 °C displayed improved apatite production and cytocompatibility.

Furthermore, Fazli Wahid et al. [187] reported that cross-linking polymer materials using metal ions or combining polymer hydrogels with nanoparticles (metals and metal oxides) is a simple yet effective method for creating multi-functional materials. Various metals and metal oxides, including silver (Ag), gold (Au), zinc oxide (ZnO), copper oxide (CuO), titanium dioxide (TiO_2), and magnesium oxide (MgO), have been incorporated into hydrogels for antimicrobial applications.

A finding produced a multi-purpose composite hydrogel system that aids diabetic wound healing processes through controlled drug delivery and fights against infections, as reported by Ye Wu et al. [188] A hydrogel system exists from cellulose-based materials, which form when POMC containing phenylboronic acid groups is cross-linked with PVA. The material demonstrates self-healing capabilities and allows for easy injection-dependent delivery. The hydrogel system receives enhancement through rhCOL1 type I collagen, which promotes cell growth and angiogenesis combined with zinc oxide mesopores for antimicrobial and anti-inflammatory protection.

Additionally, Xhamla Nqoro et al. [189] reviewed polymeric wound dressings containing bioactive agents, such as metal-based nanoparticles, as effective treatments for infected wounds. Metal-based nanoparticles, including silver, gold, magnesium oxide, and zinc oxide, have demonstrated strong antimicrobial properties. The study found that zinc oxide-loaded dressings were more effective against Gram-positive bacteria, while silver nanoparticle-based dressings showed stronger activity against Gram-negative bacteria.

It is worth nothing that the most promising strategies in tissue engineering involve mesoporous polymer scaffolds functionalized with metal-oxide nanoparticles which combine biomimetic porosity, controlled drug delivery, mechanical reinforcement, and bioactive functionalities—particularly for bone regeneration and infected wound healing. However, challenges remain in achieving precise spatial control of pore architecture, long-term in vivo stability, immune evasion, and scalable manufacturing. Furthermore, there is a spontaneous advancement towards the innovation and adoption of multifunctional, stimuli-responsive nanohybrids that integrate 3D printing, smart drug release, and immunomodulation—shifting from passive scaffolds to "active" regenerative platforms. More so, natural polymers offer biocompatibility but lack mechanical strength; synthetics provide tunability but risk immunogenicity. Future success hinges on optimizing hybrid designs that mimic native ECM dynamics while enabling clinical translation through standardized, reproducible fabrication.

4.3.2. *Incorporation of nanoparticles for enhanced biocompatibility and functionality*

Kumar et al. [190] reported that polymer-coated gold nanoparticles offer significant advantages over silica or amino-based coatings for biomedical applications, including improved biocompatibility, flexibility, and tunability of surface properties. The medical imaging field uses polymer-gold nanohybrid effectively as contrast agents for MRI, CT and photoacoustic imaging and surface-enhanced Raman spectroscopy (SERS). The integration of polymers with gold nanoparticles has enabled the development of multimodal imaging probes, theranostic platforms, and targeted imaging approaches. Similarly, Barani et al. [191] described their research about the biological activity and physicochemical properties of *Moringa peregrina* extract-based green copper oxide nanoparticles (CuO NPs) prepared with graphene oxide (GO) and CuO-GO composite. SEM analysis showed that the nanocomposite displayed polygonal CuO NPs together with thin wrinkled GO sheets along with a hybrid composition of CuO NPs and GO. Evaluation by EDS showed the presence and positioning of different elements. X-ray diffraction found the monoclinic crystalline structures in both CuO NPs and GO and CuO-GO compositions with observable distinct peaks. DLS size distributions showed CuO NPs as having the most defined distribution compared to the other materials. BET surface analysis showed that all materials were mesoporous but the nanocomposite achieved higher surface area values and larger pore volume measurements. CuO-GO demonstrated superior cytotoxicity toward cancer cell lines MCF-7 and NIH/3T3 but displayed no adverse impact on regular cells so exhibited selective cell damage properties. The antibacterial tests showed that *Pseudomonas aeruginosa* and *Staphylococcus aureus* bacteria were effectively inhibited by CuO-GO. The synergistic mechanism of the composite material resulted in better microbial inhibition because its inhibitory concentration minimum value exceeded that of its isolated

Table 4
The production of 3D scaffolds occurred through a combination of rapid prototyping methods with ceramic MBG materials.

Scaffold Type	Organic Polymer (Binder Agent)	Scaffold Modification	Effects	Ref.
$G_{RIF}MG_{LEV}PVA_{VAN}$	PVA	Antibiotic loading (Rifanpicin, Levofloxacin, Vancomicin)	Multidrug scaffolds release	[175]
[(b)]4Zn-doped MBG*	PCL/Gelatine crosslinked using GA	Antibiotic loading (Levofloxacin, Rifanpicin, Vancomycin and Gentamicin)	The solution demonstrates both Staphylococcus biofilm elimination and Escherichia biofilm eradication together with quick bacterial growth blockage	[176]
[(a)]MGHA (Magnesium-doped Hydroxyapatite)	Hydroxy methylcellulose (HPMC)	Nano HA embedded with amine functionalization	Improved preosteoblast adhesion, proliferation and differentiation	[177]
MBG/PCL (Mesoporous Bioactive Glass/ Polycaprolactone)	PCL	PBS particles	Enhanced microporous, Increased bioactivity and neovascularization	[178]
MBG/PCL	PCL	Zoledronic acid loaded	Antiresorptive and avoids inflammatory response	[179]
[(b)]4Zn- doped MBG*	PCL/Gelatine crosslinked GA	Osteostatin	Osteogenic	[180]

[(a)] The organic binder system was eliminated through 700-degree Celsius thermal processing or.
[(b)] Followed by GA gelatin application with cross-linking.
[*] This research involved MBG with 4 % added zinc oxide.

components. This study demonstrated cancer treatment and antimicrobial medicine applications of CuO NPs GO and their nanocomposite as well as their potential to function as advanced nanomaterials.

Magnetic nanoparticle (MNP) assemblies possess significant promise for biomedical use because of their tunable magnetic behavior and cooperative functions. Among various fabrication methods, polymer-assisted assembly is particularly advantageous, as it integrates the magnetic responsiveness of inorganic nanoparticles with the flexibility and biocompatibility of polymers, enabling hybrid structures with improved diagnostic and therapeutic performance [192] Precise control over interparticle interactions and spatial organization through polymer guidance allows fine manipulation of the physical, chemical, and biological properties of these nanoassemblies. Zare et al., [193] reported that poly(lactic-co-glycolic acid) (PLGA) stands out for its excellent biocompatibility and biodegradability. The study affirms that incorporating metal-based nanostructures (MNSs) into PLGA matrices enhances structural integrity and introduces antimicrobial and labelling functionalities. Similarly, Omidiya et al. noted that light-activated antimicrobial nanoparticle–polymer composites can integrate photothermal (PTAs) and photodynamic agents (PDAs) to generate heat or reactive oxygen species under illumination, producing synergistic antibacterial effects for coatings on implants, catheters, wound dressings, and related devices [194].

Futhermore, polymer-coated gold nanoparticles are highly promising for multimodal imaging and theranostics due to superior biocompatibility and tunability, driving clinical translation. In contrast, CuO-GO nanohybrids show strong potential in targeted cancer therapy and antimicrobial applications via synergistic cytotoxicity, but face challenges in long-term toxicity and scalable synthesis [195]. The field is moving toward hybrid, multifunctional nanoplatforms—combining targeting, imaging, and therapy, while prioritizing biodegradability and regulatory safety. Green-synthesized materials like CuO-GO offer eco-friendly advantages but require standardized characterization for clinical adoption.

4.4. Therapeutic approaches

The development of a metal/metal-oxide nanoparticle-polymer hybrid system emerged through recent nanotechnology advancements for biomedical functions. These hybrid materials offer unique properties, such as enhanced stability, controlled release, and targeted delivery, making them promising candidates for various therapeutic approaches [196,197]. Therefore, integrating metal/metal-oxide nanoparticles into mesoporous polymers represents a significant advancement in nanomedicine, potentially revolutionizing healthcare and improving patient outcomes. These innovative therapeutic approaches are.

4.4.1. Photothermal therapy

Metal/metal-oxide nanoparticles-polymers hybrid offer a promising approach to photothermal therapy (PTT) [198]. PTT is a minimally invasive cancer treatment that utilizes near-infrared (NIR) light to induce localized heating in tumour tissues, leading to cell death as reported by Thirumurugan et al. [199]. Kumar et al. stated that the PTT requires two key components: a photothermal agent (PTA) and NIR radiation [200]. It has superior advantages such as enhanced photothermal conversion, and targeted drug delivery, the polymer can be designed to be biocompatible and biodegradable with minimal side effects, improved stability and dispersion, and multimodal imaging for both diagnosis and therapy [198,201]. Moreover, Yin et al. [202] described the ZnO/PdO-x series by developing palladium particles in situ followed by precursor nano-ZIF-8 calcination for creating a homogeneous nano heterojunction accumulation structure which enhanced ppm level ammonia absorption paths within exhaled gases. ZnO/PdO_2 sensors exhibit maximum sensitivity because they produce a response of 5.56–100 ppm NH_3 at 160 °C together with a detection threshold of 0.75 ppm. The sensor detects authentic exhaled patient gas from liver and renal patients with precise numeric results. Successfully understanding the relationship between MOF template in situ loading during sensing might lead to rational metal-oxide sensor design methods which offer an effective approach for clinical detection.

Furthermore, Sukumar et al. studies showed that $CS@GO/Fe_3O_4$ has the potential to be a superior drug delivery method, and they describe the nanoparticles made from chitosan (CS), graphene oxide (GO), and magnetite (Fe_3O_4), as well as their **nanohybrids.** [203]. These were used to improve the loading and release efficiency of camptothecin (Fig. 9a). Nanostructures were studied using image microscopy, FT-IR, and X-ray diffraction, with an average crystallite size of 5.5 nm. Camptothecin binding percentages were 70 % for CS, 81 % for $CS@Fe_3O_4$, 58 % for CS@GO, and 74 % for $CS@GO/Fe_3O_4$. At pH 5.0, CPT release ratios were 87 %, 80 %, 88 %, and 90 %, while at pH 7.4, they were 84 %, 72 %, 89 %, and 87 %. The MTT assay was used to determine cytotoxicity in HepG2 and SMMC-7721 cancer cells. $CPT-CS@GO/Fe_3O_4$ showed the maximum survival at 5 μM and 12.5 μM doses, making it the most effective nanocarrier for camptothecin administration. Metal/metal-oxide-polymer hybrids system presents a great potential in improving PTT and theranostics due to enhanced photothermal conversion, targeted delivery, and biocompatibility. However, the major challeneges include long-term toxicity, scalable synthesis, and precise tumor targeting. These challeneges can however be mitigated through the development of MOF-derived nanoplatforms integrating therapy, diagnostics, and real-time monitoring, with rational design guided by heterojunction engineering and stimuli-responsive polymers.

4.4.2. *Photodynamic therapy*

Photodynamic therapy (PDT) uses light-sensitive agents to selectively eliminate abnormal cells. With its accuracy and minimal invasiveness, PDT shows great potential in treating cancer, skin conditions, and other medical challenges. Metal/metal-oxide nanoparticles-polymers hybrid has shown to be of great importance in PDT [204]. This strategy leverages the unique properties of both components to improve the efficacy and selectivity of PDT [204,205]. It has the combined advantages of enhanced ROS generation, improved drug delivery, reduced side effects, and multimodal therapy with potential applications for cancer and antimicrobial therapies with wound healing [201,204,206].

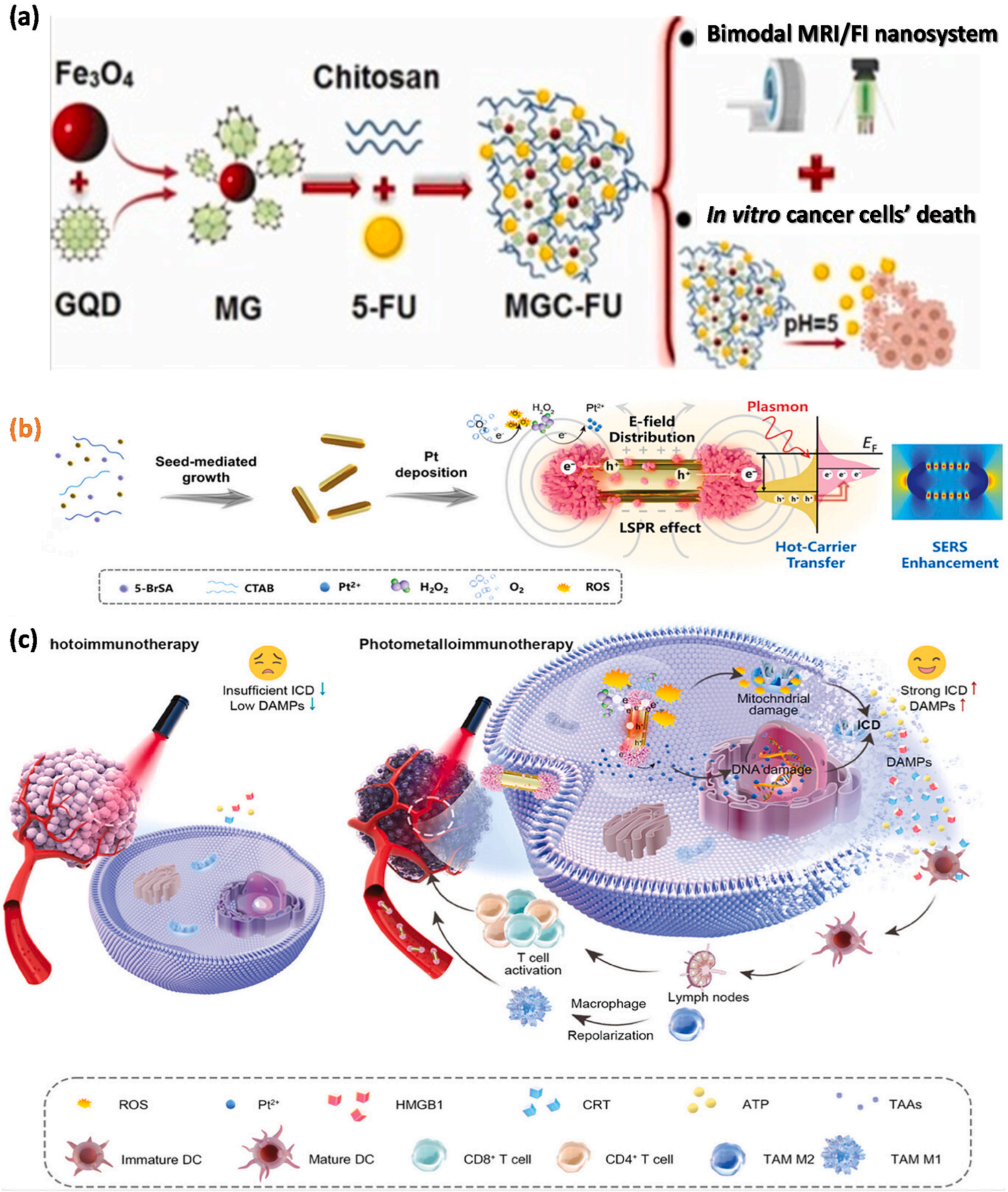


Fig. 9. (a) Chitosan-coated iron oxide/graphene quantum dots as a potential multifunctional nanohybrid for bimodal magnetic resonance/fluorescence imaging and 5-fluorouracil delivery [209] (b) Schematic illustration of PMIA design through multi-dimensional regulation of heteroepitaxial multi-site Pt growth on Au NRs. PMIA enhances efficient electron-hole spatial separation and intensifies the local electron enrichment field under NIR laser irradiation, thereby promoting ROS generation and Pt2+ ions release. (c) PMIA induces intranuclear DNA damage and amplifies immunogenic cell death (ICD), eliciting robust antitumor immune responses. As well as, PMIA exhibits resilience against NIR attenuation, synergizing the strengths of both photoimmunotherapy and metalloimmunotherapy (Bian et al., 2024).

Adam et al. studied a TiO_2 material prepared from Saussurea costus natural sources. Researchers examined the antibacterial properties of therapeutic compounds consisting of HLAm, $Cu(LAm)_2$, TiO_2/ZnO, $Cu(LAm)_2$, and $Cu(LAm)_2@TiO_2/ZnO$ against various food-related bacteria and fungi. The growth of bacteria and fungi showed maximal inhibition from $Cu(LAm)_2$ and $Cu(LAm)_2@TiO_2/ZnO$ [207]. The combined $Cu(LAm)_2$ and $Cu(LAm)_2@TiO_2/ZnO$ showed better behaviour than HLAm and TiO_2/ZnO because the Cu^{2+} ions contributed to Schiff base coordination compounds through Tweedy's chelation effect. Electrophoresis methods analyzed the DNA-binding properties of the tested materials. Further studies should evaluate $Cu(LAm)_2$ and immobilized $Cu(LAm)_2$ on TiO_2/ZnO nanoparticles for potential use as a biomedical candidate because of their antibacterial behaviour.

Furthermore, Bian et al. developed a new PMIA agent that overcomes the existing limitations of photoimmunotherapy while improving NIR light-activated cancer treatment [208] as shown in Fig. 9b and c. PMIA contains a dumbbell-shaped heterostructure of AuPt with starry nanoclusters that the researchers optimized for plasmonic catalysis. NIR laser irradiation of the engineered design separates electron-hole pairs so that it produces strong ROS while releasing Pt^{2+} ions. The combination of these effects leads to DNA damage within the cell nucleus while simultaneously promoting the synergistic immunogenic cell death mechanism in metalloimmunotherapy. PMIA creates conditions that attract T-cells while activating immune responses to effectively treat both main tumours and remote sites along with preventing cancer metastasis in animal testing. The research presents a pioneering method for dual-mode ICD amplification which unites photoimmunotherapy techniques with metalloimmunotherapy to create efficient cancer photometalloimmunotherapy.

4.5. Mechanistic insights into metal/metal-oxide nanoparticle-polymer nanohybrids

The polymer component plays a pivotal role in modulating critical aspects such as nanoparticle stability, controlled drug release, and targeted biodistribution [90,91]. Polymer coatings prevent nanoparticle aggregation and degradation, enhancing colloidal stability and extending functional lifespan in complex biological environments. Furthermore, the polymer matrix dictates drug release kinetics through tailored degradation rates and diffusion pathways, enabling precise and sustained therapeutic delivery. This control over surface chemistry and architecture also governs biodistribution, facilitating targeted accumulation and minimizing off-target effects, thereby optimizing therapeutic efficacy and diagnostic precision in advanced nanomedicine applications. The fundamentals of the mechanistic insight of the incorporation of metals or the oxides counterpart include modulation of the nanomaterial or particle, influence of drug release kinetics and the biodistribution of the drug in the biological system, and interfacial charge transfer, among other parameters. All these could affect the bioavailability of the dispersed/encapsulated drug or material. The impact of these parameters is further explained below.

- **Modulation of Nanoparticle Stability**: Polymer matrices are instrumental in enhancing the colloidal and chemical stability of embedded nanoparticles, effectively mitigating aggregation and preserving their structural integrity in complex environments. The judicious selection of polymer type, its molecular architecture, and the nature of its interaction with the nanoparticle surface are paramount. Strong chemical bonding or robust physical encapsulation by the polymer shell prevents agglomeration and safeguards against degradation, thereby extending the functional lifespan of the nanoparticles [90] For instance, polymer encapsulation has been shown to significantly improve the cycling stability of metal oxide-based materials in energy storage applications [Akhtar et al., 2025]. In biological contexts, polymer coatings act as a protective barrier, shielding nanoparticles from enzymatic degradation and non-specific protein adsorption, which is crucial for maintaining their colloidal stability in vivo and prolonging systemic circulation [210]. Recent investigations underscore how specific polymer designs can influence long-term chemical stability and prevent the undesirable leaching of metal ions, a critical consideration for therapeutic and diagnostic applications [90].
- **Influence on Drug Release Kinetics**: The polymer matrix serves as a sophisticated control element for dictating the drug release kinetics from nanohybrid systems, enabling precise and sustained therapeutic delivery. The physicochemical properties of the polymer, including its molecular weight, degradation rate, hydrophilicity, and the method of drug encapsulation, collectively govern the release profile [211]. Drug release mechanisms typically involve surface dissolution, diffusion through the polymer network, or polymer degradation. Smart polymers, responsive to specific physiological stimuli such as pH or temperature, can be engineered to trigger drug release in targeted pathological microenvironments, like acidic tumour sites or inflammatory regions [211]. Furthermore, the polymer's crosslinking density and porosity are key parameters that can be finely tuned to achieve desired release rates, ranging from rapid burst release to prolonged, zero-order kinetics [212].
- **Impact on Biodistribution:** Polymer coatings profoundly influence the biodistribution of metal/metal-oxide nanoparticles within biological systems, thereby determining their accumulation in target tissues and subsequent clearance pathways. Polyethylene glycol (PEG) functionalization, or PEGylation, remains a cornerstone strategy to minimize non-specific uptake by the reticuloendothelial system (RES) and to extend systemic circulation time, facilitating passive targeting to tumours via the enhanced permeability and retention (EPR) effect [210,213]. Beyond passive mechanisms, active targeting ligands, such as antibodies or peptides, can be covalently attached to the polymer surface. This enables specific recognition and binding to receptors overexpressed on target cells, significantly improving therapeutic efficacy and reducing off-target effects [211]. More so, Yu et al. reported that the polymer's surface charge, overall hydrophilicity, and the hydrodynamic size of the nanohybrid critically modulate cellular internalization pathways and organ-specific accumulation patterns [213].
- **Interfacial Charge Transfer:** The performance of metal/metal-oxide nanoparticle-polymer nanohybrids in advanced applications, including photocatalysis, electrochemistry, and sensing, is fundamentally governed by efficient interfacial charge transfer (ICT). Strong interactions at the polymer-nanoparticle interface are crucial for optimizing electron and ion mobility, thereby dictating the overall efficiency and responsiveness of these composite systems [91,214]. Mechanistically, the polymer matrix acts as a sophisticated mediator, facilitating charge separation and transport. When a metal or metal-oxide nanoparticle is photoexcited or subjected to an electrochemical potential, electron-hole pairs are generated. The polymer, through tailored functional groups or its inherent electronic structure, can effectively scavenge charge carriers from the nanoparticle surface, preventing recombination and promoting their directed movement [214]. This optimized electron/ion mobility across the interface significantly enhances photocatalytic activity by increasing the lifetime of reactive species, boosts electrochemical performance by improving charge storage and kinetics, and sharpens sensing capabilities through more efficient signal transduction [215,216]. Recent studies highlight how precise control over interfacial bonding and polymer chain conformation can create preferential pathways for charge migration, leading to unprecedented performance enhancements in next-generation devices [98].

5. Challenges, future perspectives, and emerging trends

5.1. Challenges

5.1.1. Biocompatibility, toxicity, and translation challenges

The combination of metal/metal-oxide nanoparticles with mesoporous polymers encapsulates enormous biomedical potential because of their distinctive qualities, which include large surface area and adjustable pore dimensions as well as adjustable release properties. The successful medical implementation of these materials faces strong obstacles because of their compatibility issues and toxicity concerns. More so, their clinical translation requires careful consideration of cytotoxicity, biodegradation, and regulatory perspectives.

- **Biocompatibility Challenges:**

The biocompatibility of these materials depends on certain factors, which include surface properties, particle size and shape, release kinetics, and long-term stability. The surface properties of metal/metal-oxide NPs, such as charge, hydrophobicity, and ligand density, can influence their interaction with biological systems [217]. Non-biocompatible surfaces can trigger immune responses, inflammation, and cell death. The size and shape of nanohybrids can significantly impact their biodistribution, cellular uptake, and toxicity [218]. A size below a certain unit measure increases their surface area exposure while boosting their chemical reactivity potential. The controlled (kinetic) release of bioactive molecules from mesoporous polymers is crucial for achieving desired therapeutic effects [217]. Manuja et al. [219] reported that the physical state of metal/metal oxide NPs critically influences their toxicity, with metal oxides showing lower stability and greater susceptibility to dissolution and ion release in biological environments, leading to reactive oxygen species production and oxidative stress. However, premature or uncontrolled release can lead to reduced efficacy and increased toxicity. The long-term stability of metal/metal-oxide NPs in biological environments is essential for their safe and effective use. Degradation or aggregation of NPs can alter their properties and potentially lead to adverse effects [219]. Biodegradable polymers such as poly(lactic co glycolic acid) (PLGA) enable safe clearance of nanoparticles through hydrolytic or enzymatic pathways, while non-degradable coatings such as PEG may persist in vivo, raising long-term safety issues [232]. Iron oxide polymer hybrids benefit from natural iron metabolism pathways, where degraded particles integrate into ferritin or hemoglobin, enhancing their clearance compared to non-biodegradable gold polymer constructs [233]. Therefore, according to Ameida et al. and Zhang et al. [220,221], successful biomedical implementation required comprehensive surface modification strategies, including biocompatible coatings and functionalization with active biomolecules, to achieve safe interaction with biological systems.

- **Toxicity Challenges:**

Metal/metal-oxide NPs lead to ROS production that triggers oxidative stress, along with the consequent damage to cellular components [222]. The contact of NPs with immune cells activates inflammation, which causes tissue destruction that ultimately hurts organ functionality [223]. Multiple studies have uncovered DNA-damaging properties of metal/metal-oxide NPs that might enhance cancer development rates. Batîr-Marin et al., [224] reported that these NPs can induce oxidative stress through overproduction of ROS, leading to cellular dysfunction, inflammation, apoptosis, and genotoxicity. Furthermore, Jabeen et al. and Zhou et al. reported that the high surface area and reactivity of metal oxide NPs contribute to their biological effects, making them effective as anticancer agents but also potentially harmful to human cells [225,226]. Similarly, Luo reported that high atomic number metal NPs used as radiosensitizers can amplify radiation effects and cause DNA damage through enhanced dose deposition and ROS generation [227]. While green synthesis methods have been developed to reduce toxicity compared to chemical synthesis approaches, according to Zhou et al., [226]The oxidative stress mechanisms and genotoxic potential of these nanomaterials remain significant concerns for their clinical translation and widespread use. NPs can directly damage cells by disrupting cell membranes, interfering with cellular processes, or inducing apoptosis. Furthermore, Ogungbesan et al. reported that molybdenum oxide–doped tungsten oxide polymeric nanohybrids, although exhibiting strong antibacterial activity, showed dose-dependent cytotoxicity in vitro, highlighting the importance of careful dose optimization and surface engineering to minimize toxicity [228]. This affirms that polymeric nanohybrids containing metal oxides produced significant reductions in cell viability at higher concentrations, confirming that the nanoparticle–polymer interface strongly influences biocompatibility outcomes.

- **Clinical Translation Barriers**

Despite promising preclinical findings, few nanoparticle polymer hybrids have advanced to human trials. One key challenge is the heterogeneity of in vivo responses. As Truong et al. emphasized, biological outcomes depend not only on material composition but also on size, surface charge, and protein corona formation, which complicates reproducibility. Scale-up synthesis and reproducibility of polymer coating are additional barriers [234]. For ZnO and TiO_2 hybrids, batch-to-batch variability in nanoparticle size alters both therapeutic efficacy and safety [230].

- **Regulatory Perspectives**

From a regulatory standpoint, hybrid nanomaterials fall under complex frameworks that vary between regions. The U.S. FDA considers nanoparticle polymer hybrids as combination products, requiring evaluation of both drug and device aspects [229]. In Europe, the EMA requires extensive toxicological profiling and environmental impact assessments. Importantly, as Nguyenova et al. highlighted, long-term persistence of gold-based hybrids raises questions about cumulative toxicity, which regulators treat as a significant barrier [231]. These challenges underscore the gap between laboratory-scale promise and real-world clinical adoption.

5.1.2. Scalability and commercialization

The integration of metal/metal-oxide NPs into mesoporous polymers has opened up exciting avenues in biomedical applications and promising advancements in drug delivery, imaging, and therapy. However, the transition from laboratory-scale research to large-scale production and commercialization faces significant challenges.

Recent advancements in biomedical applications of metal/metal-oxide nanoparticles incorporated into mesoporous polymers have been significantly influenced by factors like scalability of synthesis, uniform dispersion and stability, toxicity and biocompatibility, regulatory hurdles, and cost-effective production. The scalability of synthesis processes is crucial for large-scale production, ensuring consistent quality and reducing costs. Uniform dispersion and stability of nanoparticles within the polymer matrix are essential for optimal performance and controlled release of therapeutic agents. Toxicity and biocompatibility are paramount concerns, necessitating careful selection of materials and synthesis methods to minimize adverse effects. Regulatory hurdles, including stringent safety and efficacy evaluations, can delay the clinical translation of these nanomaterials. Finally, cost-effective production is vital for widespread adoption and affordability, requiring optimization of synthesis techniques and material sourcing.

5.2. Future direction and potential solutions

Future developments in metal-oxide nanoparticle-polymers hybrid focus on personalized medicine, intelligent drug delivery, and bioactive scaffolds. Advancements in biodegradable polymers and multifunctional **nanohybrids** will enhance biocompatibility and treatment accuracy, addressing challenges including toxicity, durability, and precise nanoparticle release in biomedical settings. The under-listed points give more insight, providing a workable solution to mitigate imminent challenges.

- **Scalability of Synthesis:** To obtain controlled synthesis, it is critical to ensure consistent size, shape, and surface properties of NPs at a large scale. Developing efficient and scalable synthesis methods like continuous flow or microfluidic reactors can address this. Establishing rigorous quality control measures and standard operating procedures is essential for reproducibility.
- **Uniform Dispersion and Stability:** Preventing NP agglomeration within the polymer matrix is vital for optimal performance. Surface functionalization with suitable ligands can enhance dispersion and stability. Tailoring the polymer's properties, such as porosity and surface chemistry, can improve NP dispersion.
- **Toxicity and Biocompatibility:** Comprehensive toxicological studies are crucial to assess the long-term effects of NPs and polymer composites. Employing biodegradable polymers can minimize potential environmental and biological risks. Modifying the NP surface to reduce toxicity and enhance biocompatibility.
- **Regulatory Hurdles:** Navigating complex regulatory frameworks for nanomaterials, including safety assessments and clinical trials, is time-consuming and costly. Developing standardized testing protocols for NP-based products can streamline the regulatory process. Fostering collaboration between scientists, engineers, regulatory experts, and clinicians can facilitate regulatory approval.
- **Cost-Effective Production:** Optimizing synthesis techniques to reduce costs while maintaining quality. Investing in dedicated facilities for large-scale production can lower costs. Developing efficient purification and characterization methods can reduce production time and costs.
- ***In vitro* and *in vivo* testing**: Testing metal/metal-oxide nanoparticles embedded in mesoporous polymers needs extensive laboratory and animal studies to confirm their biological tolerance, effectiveness and chemical safety. In vitro studies can provide valuable insights into cellular interactions, uptake mechanisms, and potential adverse effects. In vivo studies, such as animal models, can evaluate systemic distribution, biodistribution, and therapeutic efficacy. By conducting comprehensive preclinical studies, researchers can identify potential safety concerns, optimize formulations, and develop strategies to mitigate toxicity. These rigorous testing protocols are crucial for ensuring the safe and effective translation of NP-based therapies into clinical applications, ultimately accelerating their commercialization and benefiting patients.

5.3. Emerging trends

Metal/metal-oxide nanoparticles inside mesoporous polymers function as an emerging platform for biomedical trends as shown in Fig. 10. These materials contain a combination of high surface area and tunable pore size together with excellent biocompatibility characteristics.

1. Targeted Drug Delivery

Veiga et al. reported the development of multifunctional nanoparticles with targeting ligands to deliver drugs specifically to diseased cells or tissues [235]. Li et al. emphasized that combination drug delivery through nanoparticles serves as a crucial method for developing novel therapeutic agents to address multiple human disorders from cancer to cardiovascular conditions and inflammatory diseases [236]. The combination therapy benefits from nanoparticle-based drug delivery systems because these systems enable precise drug delivery with sustained drug release together with enhanced drug stability. They also argued that combination therapy could lead to synergistic effects, reduced administration dose, decreased toxicity, and alleviated drug resistance, making it a promising approach for treating various clinical illnesses [236]. Furthermore, Li et al. developed a core/shell nanocarrier consisting of acid-dissolvable magnetic superparticle cores covered by the redox-degradable polymer poly(methyl acrylic acid-co-N,N-bis (acryloyl)cystamine)(P(MAA-Cy)) through distillation-precipitation polymerization-based synthesis, allowing dual loading of different guest molecules. This sequential pathological condition degradation properties of the microsphere shell and core match the conditions present in the cancer cell cytoplasm. This development stage produced the MSP-FITC@P(MAA-Cy)-Rho microspheres, which contained fluorescein isothiocyanate (FITC) dyes in their core and rhodamine in their shell. Researchers tested these microspheres using HeLa cell and HEK 293T cell cultures to demonstrate selective degradation in HeLa cells, releasing the rhodamine and FITC dyes one after the other. Research showed that nano-drug MSP-TXL@P(MAA-Cy)-DOX released drugs from its core and shell regions better than free medications at equal dosages, thus demonstrating its value in stimulus-based drug release programs [237].

2. Bioimaging

Metal NPs function as contrast agents to improve imaging capabilities of magnetic resonance imaging (MRI) computed tomography (CT) and fluorescence analysis. Das et al. created water-soluble, biocompatible, noncytotoxic, sugar-functionalized MIM-capped superparamagnetic ultrasmall Fe_3O_4 NPs that exhibit bright-NIR emission for targeted multimodal imaging. The incorporation of dual-functional stoppers that use an unsymmetrical NIR squaraine dye within macrocycles forms MIMs that show better durability and NIR fluorescence performance. The axle features two separate function-bearing stoppers that include TPP+, which binds to mitochondria, and a dopamine group that binds to Fe_3O_4 NPs. Magnetic NPs of ultrasmall size can be transported to mitochondria by Fe_3O_4 NPs, which contain surface-bound targeted NIR rotaxanes. The macrocycle of MitoSQRot-(Carb-OH) receives two carbohydrate groups through a click chemical reaction to enhance its water solubility and biological behaviour. Water-soluble, rotaxane-capped Fe_3O_4 nanoparticles. The water-soluble Fe_3O_4 NPs capped with rotaxanes allow researchers to perform targeted live-cell mitochondria-based NIR fluorescence confocal imaging, as well as 3D and multicolour examinations and T2-weighted MRI on a 9.4 T scanner which shows a high relaxation rate of 180.7 $mM^{-1}s^{-1}$. The combination of biocompatible properties with noncytotoxicity, as well as ultrabright NIR emission, makes rotaxane-capped superparamagnetic ultrasmall monodisperse Fe_3O_4 NPs a good candidate for targeted multimodal imaging applications [238].

Incorporating fluorescent dyes or quantum dots into the polymer matrix for enhanced imaging contrast. The research by Momina et al. unfolds through the synthesis of a magnetic Na alginate biocomposite system containing carbon dots (CDs) for dealing with pollution from organic dyes and metallic contaminants. The cost-effective eco-friendly biocomposite production method enhances the adsorption together with regeneration properties through CD integration. Various techniques confirmed that the composite displayed good dispersion and abundant functional groups and superior adsorption capability. The combination of Response Surface Methodology allowed optimization of adsorption process variables which led to an optimized adsorption capacity reaching 232.44 mg/g. The Artificial Neural Network (ANN) model showed superior results than other models by predicting adsorption capacity. The physical model with a statistical basis explained dye molecule binding behaviour and orientation patterns on this surface which calculated a predicted uptake of 467.57 mg/g. The composite demonstrated effective performance in column adsorption experiments that confirmed its capability to adsorb dyes with good desorption traits. A complete financial assessment showed the manufactured composite to

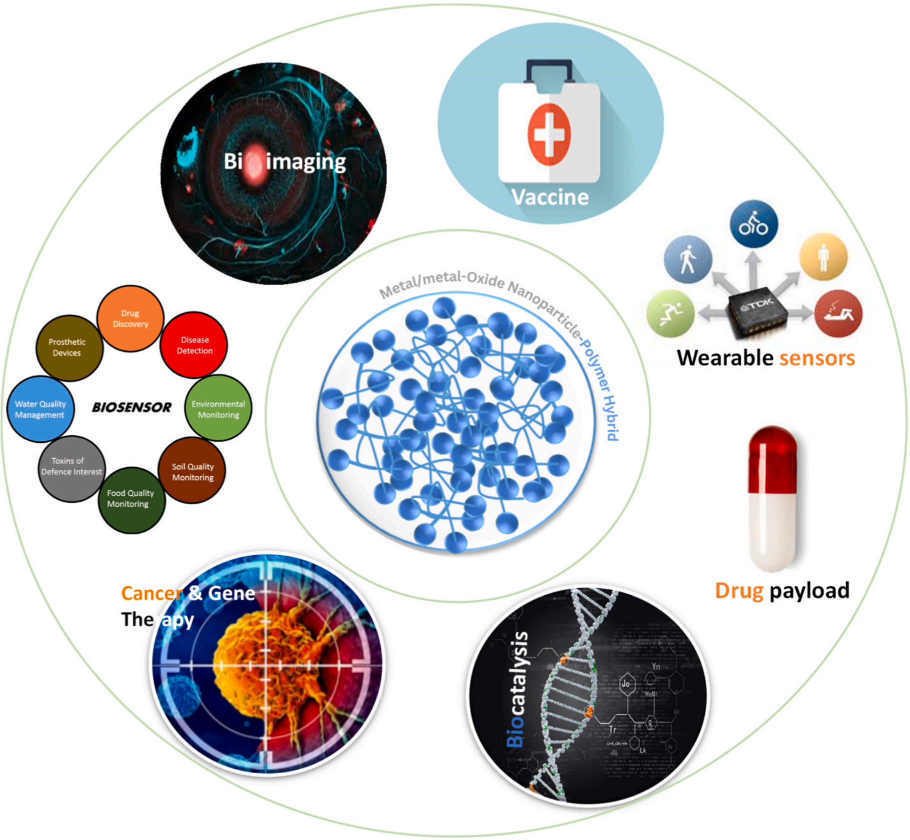


Fig. 10. Emerging trends in the application of metal/metal oxide nanoparticle-polymer hybrid system.

be economically attainable for practical usage [239].

3. Biosensing

The development of sensors requires capabilities for precise biomolecule detection including proteins DNA together with small molecules. The growing statistic in mortality accrued to cancer together with increasing cancer treatment neccesiates a continuous research for new cancer diagnostic tools as well as medicinal approaches [240,241]. Although, several recent scientific research has led to the development of cancer therapies and diagnostics systems built with G derivative structures. G derivatives solve both genetic damage and immune responses of viral vectors when used as carriers to deliver treatments against cancer. The material characteristics, including large surface area, photoluminescence properties, and economy-based functionalization, along with the optical properties and stability of graphene, make this substance promising. G-based **nanohybrids** demonstrate promising abilities to offer treatment combined with third-party imaging functionality. G-based **nanohybrid systems** with tumour ligands binding to their surface show better capabilities of delivering specific medications targeted for cancer cells. **Nanohybrids** based on graphene possess suitable functionalized or coated surfaces, which enable their use as a nanoplatform across cancer detection and treatment applications. The safety of G-based **nanohybrids** depends on biocompatibility tests because they lead to serious health complications [242].

The application of metal NPs as catalysts in electrochemical and optical sensing. The study authors presented their work that demonstrated the promising use of green-synthesized CuO NPs for sensing and dye degradation operations. An environmentally friendly green method produced Copper oxide nanoparticles (CuO NPs). The green-generated CuO NPs underwent structural characterizations while optical, morphological and electrochemical assessments were performed using various technique methods. The X-ray diffraction analysis showed a monoclinic crystal structure for CuO NPs that possessed the $C2/c$ space group. Glucose detection required the use of cyclic voltammetry as an electrochemical measurement method. The catalytic properties of green-generated CuO NPs were found to be effective in electrochemical detection devices as well as photochemical applications. The CuO NPs possessed high detection precision and glucose measuring accuracy because their detection sensitivity reached 370 μA $mM^{-1}cm^{-2}$ alongside a detection limit of 1.0 μM. The degradation performance of CuO NPs achieved 84 % dye removal in a period of 150 min [178].

4. Antimicrobial Applications

Metallic nanoparticles particularly silver and copper exhibit antimicrobial properties for the development of antibacterial coatings and wound dressings. Measurement studies from Nuti et al. showed that multidrug-resistant bacteria endanger the worldwide health situation. During their investigation, the researchers examined the antibacterial characteristics of silver and gold nanoparticles which had mesoporous silica coating applied to different-sized grains. Research has shown that silver nanoparticles demonstrated antibacterial properties against all types of bacteria as larger nanoparticles proved more effective in destroying *Salmonella enterica.* Functionalizing the nanoparticles with terminal amine groups to reverse the surface charge significantly enhanced their antibacterial activity. Furthermore, incorporating these nanoparticles into polyurethane films significantly improved the antimicrobial properties of the material. Their findings highlight the potential of mesoporous silica-coated silver nanoparticles as a promising strategy to combat multidrug-resistant bacteria in healthcare and food industry applications [243].

Antimicrobial surfaces that can clean themselves will help prevent infection. The study by Reshna et al. introduces a dual-step manufacturing process for generating hydrophobic glass coatings that mimic rose petal wetting behaviour. Superhydrophobic glass surfaces were manufactured by applying two sequential processes to glass slides. The hydrophobicity came first from ZnO nanorod coatings grown through hydrothermal epitaxial methods followed by MTMS coating which transformed the glass surface into superhydrophobic. The scientific analysis focused on the three aspects of dosage, surface topology, structural chemistry and the testing process for antibacterial properties with quantitative and qualitative outcomes. The developed self-cleaning glass slides successfully combined exceptional antibacterial properties with superior bacterial-repellent performance. The combination of ZnO nanorod properties and MTMS coating enables ZOMS hybrid surfaces to deliver superior water repellency and autonomous cleaning functions, and exceptional antibacterial strength. The hybrid surface demonstrates notable potential for exterior along interior usages because it suits healthcare needs and optical devices, architectural design and also the automobile industry [244].

5. Cancer Therapy

Loading anticancer drugs into nanoparticles for targeted delivery to tumour cells. Kazemi et al. reported that the Zn-MOF-74 nanoparticles (d < 100 nm), synthesized at room temperature, were functionalized with polydopamine (PDA) to enhance their drug delivery capabilities. When loaded with doxorubicin (DOX), RA-MOF-74 exhibited a higher drug loading capacity (19.6 %) and efficiency (96.5 %) compared to RN-MOF-74. The uncoated form of RA-MOF-74, along with PDA-coated RA-MOF-74 displayed faster drug release at acidic pH conditions, although uncoated RA-MOF-74 showed an enhanced increase of 24.3 %. The MDA-MB-231 breast cancer cells showed increased sensitivity to treatment with RA-MOF-74 formulations containing DOX compared to pure DOX at 400 μg/mL according to biological testing. This tested formulation demonstrated better cancer-inhibiting effects than unmodified DOX. Both delivery methods also showed a low potential to damage blood cells. Additional in vivo research needs to be conducted, given the promising findings about Zn-MOF-74 nanoparticle potential for biomedical applications.

The use of metal nanoparticles functions as a photothermal agent for destroying cancer cells. A new approach to raise MPTT involved Li et al.'s development, which minimized both heat shock response and autophagic mechanisms. Researchers have created TF-CQ@mPdPt as a nanosystem that combines chloroquine (CQ)-loaded mesoporous PdPt material with tannic acid-iron ion metal-organic framework coating for enhanced MPTT by blocking autophagy and the heat shock response pathway. The photothermal properties, together with peroxidase (POD) mimicking the activity of TF-CQ@mPdPt appear satisfactory. The POD-mediated endogenous hydrogen peroxide decomposition creates reactive oxygen species, which cause mitochondrial damage, thus reducing ATP availability while stopping the expression of heat shock proteins during MPTT treatment, thus making tumour cells heat-sensitive. During MPTT CQ production by TF-CQ@mPdPt inhibits cell autophagy, therefore interrupting the self-recovery mechanisms of tumour cells. The therapeutic effect of MPTT treatment was enhanced through the use of TF-CQ@mPdPt because the system decreased 4T1 tumour progression in mice [245].

6. Gene Delivery

Gene therapy needs nanoparticles, which serve as carriers to transport genetic material throughout cell structures. The unique silica–metal-organic framework hybrid nanoparticle (SMOF NP) described by Wang et al. [183] exhibits exceptional features, including high payload efficiency and stability with efficient delivery of a broad range of material types, including hydrophilic small molecule drugs (e.g., doxorubicin hydrochloride) and nucleic acids (e.g., DNA and mRNA) and genome-editing machines (e.g., Cas9-sgRNA ribonucleoprotein (RNP) as well as RNP combined with donor DNA (e.g., RNP + ssODN)). The SMOF NPs exhibit superior drug delivery and gene transfection as well as genome-editing performance through their controlled pH-release mechanism and endosomal escape mechanism achieved by imidazole moieties in the SMOF NPs. The silica component of SMOF NPs allows straightforward modifications through PEGylation and ligand conjugation to incorporate different functional groups on the surface. Research using subretinal injections showed that SMOF NPs containing RNP successfully performed genome editing functions on murine retinal pigment epithelium tissue. This demonstrates their capability to deliver different hydrophilic therapeutic agents using these nanoplatforms.

The research development of new non-viral gene carriers seeks to achieve better performance quality and improved security standards. A study established that modifying Non-viral carriers produces essential advancements in achieving stable complexes with targeted delivery, along with enhanced transfection performance. The field of gene therapy research includes diverse investigations of multiple non-viral carrier systems. The chemical structure and surface features of non-viral carriers, along with their numerous alterations, help cells penetrate extracellular and intracellular barriers for successful gene delivery [246].

7. Vaccines

The process involves adding antigens to nanoparticles to improve both vaccine immunological response and overall efficiency. Ibrahim and their colleagues created a vaccine against salmonellosis through their work. The zoonotic disease affects humans and chickens through the use of ferrous iron oxide (FNPs), silicon dioxide (SiNPs), carboxymethyl chitosan (C.CS NPs) and FNPs-chitosan (FCNPs) nanocomposite as immunological adjuvants. Studies demonstrate silicon dioxide SiNPs have potential as a vaccine delivery platform since they enhance Salmonella immunity in chickens. Research results revealed that vaccinations containing SiNPs as adjuvants and nanoparticles increased protection levels to 93.3 % above the 83 % defense rate of the local vaccine [247].

The research moves toward creating immune response-enhancing adjuvant devices employing metal NPs. Various nanomaterials, which serve as effective vaccine adjuvants, are described in detail by Ahmed et al. Research indicates that chitosan-aluminum nanoparticles prove superior to chitosan nanoparticles as vaccine adjuvants. Gold nanoparticles exhibit critical functions for immune reactions besides inflammatory cytokine development, yet researchers have established how particle dimensions, together with morphology, affect these processes. Both inactivated in vitro tests and active in vivo tests verify that PLGA nanospheres work as well as Alum does to stimulate vaccine responses. The release of cytokines and cellular uptake is increased by carbon-based nanomaterials [248].

8. Diagnostics

Metal NPs function as diagnostic indicators for both lateral flow assays and point-of-care devices. According to Bahamondes Lorca et al., nanoparticles (NPs) can function as biosensing detectors for biological specimens while bonding with diverse biomolecules. During the COVID-19 pandemic, researchers mostly relied on gold-NP-based lateral flow assays (LFAs) as the primary application of this tested method. Their findings establish that new plasmonic NPs with titanium nitride cores (TiN) and copper cores coated with gold shells (Cu@Au) match or outperform gold nanoparticles in terms of performance. This discovery matters due to gold's high price and its global scarcity. The new nanoparticles developed after this procedure achieved excellent testing conditions for LFAs through strong signaling capabilities, high specificity and the ability to detect signals without additional tools. The synthesis costs of Au NPs during commercial kit production determine their main expenses, yet the authors present success using Cu@Au and TiN NPs from laser-ablation fabrication, which shows promise for building affordable plasmonic nanomaterials across biological applications. The biodetection method using TiN material outperformed Au material in terms of accuracy, according to our machine learning research [249].

Scientific experts create biosensors to improve diagnostic procedures while ensuring both efficiency and high precision. The synthesis of nanorod-shaped Ni_3(HITP)2c-MOFs occurred using straightforward processes while dopant cobaltosic oxide (Co_3O_4) NPs generated bimetallic NiCo(HITP) c-MOF **hybrid** through a decoration procedure. The Co_3O_4NPS/NiCo(HITP) bimetal c-MOFs nanostructure possesses a massive specific surface area with high electrical conductivity and numerous active sites of desired nanostructures which enable quick electron transfer and efficient antigen-antibody binding operations. Different amounts of Au nanoparticles applied to the Co_3O_4NPS/NiCo (HITP) **nanohybrids system** functioned to improve the electrochemical properties. The designed Au@ Co_3O_4NPS/NiCo(HITP) electrochemical immunosensor demonstrates optimal detection features regarding HBsAg while operating across a broad linear detection range starting from 1 pg mL^{-1} and extending to 100 ng mL^{-1} with a minuscule detection threshold at 15 fg mL^{-1} (S/N = 3). The electrochemical immunosensors show excellent performance regarding selectivity reproducibility and stability when produced as manufactured devices. The quantitative method for detecting HBsAg leads to effective real-sample analysis results. Their research presents an effective method for designing sensitive electrochemical immunosensors based on hybrid c-MOF nanomaterials and shows potential application in early hepatitis B disease detection [250].

9. Biocatalysis

Metal/metal-oxide nanoparticles can be immobilized in mesoporous polymers to create biocatalysts with enhanced activity and stability, enabling applications in biomedicine, energy, and environmental sciences. Mirsalami et al. reported that enzyme stabilization on permeable scaffolds is a key technique for increasing enzyme stability and activity. Covalently attaching enzymes to support surfaces can increase the endurance and performance of immobilized biocatalysts. Modifying the structure and formulation of mounted enzymes with polymers can improve enzyme stability and create a diverse platform for biocatalytic processes [251].

Cardoso et al. [252] stated that Nanozymes, nanomaterial-based enzyme mimics, offer stability, cost-effectiveness, and tunability over natural enzymes. Their diverse compositions, sizes, and shapes enable a wide range of enzyme-like activities, making them promising candidates for biosensing. While limitations like selectivity and catalytic efficiency exist, surface modification, particularly with molecularly imprinted polymers (MIPs), can enhance these properties. They further reported that researchers have developed biomimetic sensors by combining MIPs with enzymes with improved selectivity and catalytic performance. Such multimodal platforms, responsive to various microenvironments and stimuli, hold significant potential for diverse biosensing applications.

10. Wearable Sensors

Flexible and wearable sensors can be fabricated using mesoporous polymers and metal/metal-oxide nanoparticles to monitor vital signs and other physiological parameters.

The Ni–Cu coatings underwent electrolytic production using baths containing various Cu^{2+}:Ni^{2+} ratios to establish and build high-performance, quick low-cost nonenzymatic glucose monitoring equipment, which employed porous Ni–Cu nanosheet deposition on 3D laser-induced graphene substrates. A performance evaluation for the biosensor electrodes took place through glucose detection tests performed in an artificial sweat solution, which represents the biological fluid for real-time monitoring applications. The sensor achieved successful analytical performance through its wide detection range with high sensitivity levels (11,012.73–15,286.66 μA/mM.cm^2) and a detection threshold of 0.0062 μM. When measuring interfering compounds, the sensor maintained a stable tracking ability. The laboratory results confirmed that the Ni–Cu-LIG sensor can identify glucose content in artificial sweat solutions, making it suitable for deployment as a wearable detection device [253].

Tian et al. reported that an HHTP@CuxS NCBs sensor prototype was simulated to detect NH3 with a consistent response because Ammonia (NH_3) sensing is simultaneously required with high selectivity, stability, low detection limit, and wide concentration range detection for monitoring NH_3 leakage, but has been difficult through Copper sulphide (CuxS) hollow nanocubes functionalized with 2,3,6,7,10,11-hexahydroxytriphenylene molecules (HHTP@CuxS NCBs) were developed to improve NH_3 sensing performance at room temperature. Copper Oxide NCBs served as the starting materials through five processing stages starting with partial sulphidization and core dissolution that finished in HHTP-functionalized processing. Studies of functionalized HHTP molecules on the CuxS surface show the existence of numerous floccules after completion of the process. The sensing response of HHTP@CuxS NCBs increases by 126 times when examining 1000 ppm NH_3 concentrations in comparison to CuxS NCBs. The sensor prototype achieves detection within the 0.3–10000 ppm detection range with a detection limit of 0.3 ppm and maintains excellent repeatability features alongside 33 days-long room temperature stability. Such superior NH_3 sensing performance happens through two key elements: the abundant π-conjugated sites on HHTP molecules, along with the hollow structure of NCBs [254].

Furthermore, fabric is a traditional yet excellent material for adding nanoparticles to create multifunctional features. Nanoparticle-treated fabrics can serve different purposes, such as repelling water and oil, preventing static buildup, fighting bacteria, and blocking ultraviolet light. They can also react to electrical, chemical, mechanical, heat, light, and magnetic signals [14]. Since textiles are polymeric materials, Metal-oxide nanoparticle-integrated mesoporous polymers are increasingly being used in wearable sensors due to their enhanced electrical, mechanical, and chemical properties. These hybrid materials enable the development of flexible, stretchable, and durable sensors for various applications, including health monitoring and environmental sensing, as shown in Fig. 11 nanoparticles can be incorporated or embedded in its matrix to produce wearable textile materials because they do not change the natural feel and flexibility of the fabric. Additionally, conductive nanoparticles can be added to fibers, yarns, and fabrics for large-scale production. Various metal nanoparticles, including copper, gold, nickel, silver, and aluminum, have been used to create e-textiles [14]. More recently, carbon materials like graphene and carbon nanotubes (CNTs) have become popular for use in electronic textile manufacture.

11. Advanced Biomedical Implants and Drug Delivery

The synergy between the field of nanotechnology, pharmacy, and medicine has revolutionalized medicine and drug delivery systems, through the development of biomedical implants and drug delivery, providing safer and more efficient therapeutic outcomes. Metal and metal oxide nanoparticles demonstrate enhanced biocompatibility when coated with polymers, minimized cytotoxic effects, and superior integration with host tissues [256]. These hybrid constructs not only strengthen the mechanical function of implants but also serve as vehicles for localized and sustained drug release, thereby lowering systemic toxicity and improving treatment outcomes. In drug delivery, polymer–nanoparticle hybrids enable precision targeting through stimuli-responsive mechanisms, including variations in pH, temperature, or enzymatic activity. Moreover, their design can incorporate controlled degradation, aligning with natural tissue regeneration pathways. Together, the interplay of nanomaterials and polymer science is driving the development of next-generation implants that merge mechanical resilience with multifunctional therapeutic potential, offering promising avenues for regenerative medicine, targeted cancer therapy, and long-term biomedical device innovation [256,257].

12. Enhanced catalysis for renewable energy

Furthermore, metal oxide–polymer hybrid composites are emerging as versatile catalysts in renewable energy research, offering unique structural and electronic synergies. Their mesoporous architectures and tunable surface chemistry enable precise control over catalytic microenvironments, thereby improving reaction kinetics, selectivity, and product yield [215]. In green hydrogen production, these hybrids accelerate water-splitting reactions through enhanced charge transfer and stability under operational conditions. Similarly, in CO_2 conversion, the integration of metal oxides with functional polymers facilitates efficient adsorption, activation, and reduction pathways, transforming CO_2 into value-added fuels and chemicals [215,258]. For biofuel synthesis, these composites promote cleaner, more efficient transformations of biomass-derived intermediates. By bridging structural durability with molecular adaptability, metal oxide–polymer hybrids represent a promising platform for scalable, sustainable catalytic technologies in the renewable energy sector [90,215].

13. 3D-Printable Polymer-Nanoparticle Hybrid Materials for Biomedical Applications

The frontier of regenerative medicine has been significantly advanced by 3D-printable polymer-nanoparticle hybrid materials, specifically tailored for the additive manufacturing of custom biomedical implants and tissue scaffolds. These composites are meticulously engineered to optimize rheology and printability, ensuring precise fabrication of patient-specific geometries with enhanced mechanical and biological properties [259]. Nanoparticles, including metal oxides and metal-organic frameworks, are strategically incorporated to impart crucial functionalities such as radiopacity, antimicrobial characteristics, or osteoinductivity, thereby elevating the therapeutic efficacy of implants [259,260]. Furthermore, these hybrid systems facilitate the fabrication of sophisticated tissue scaffolds that effectively mimic the native extracellular matrix. Nanoparticles within these scaffolds promote cellular adhesion, proliferation, and differentiation, and enable controlled release of growth factors, which is paramount for successful tissue regeneration [260,261]. The emphasis on biodegradable polymers combined with biocompatible nanoparticles ensures safe integration and eventual degradation in vivo, minimizing long-term complications and advancing the next generation of temporary implants and regenerative therapies [262].

6. Comparative analysis of metal, metal-oxide nanoparticles, and polymer hybrids

A direct comparison of metal and metal-oxide NPs highlights the complementary advantages and limitations of each category in biomedical applications. According to Truong et al., metal nanoparticles, particularly gold (Au) and silver (Ag), are distinguished by their surface plasmon resonance properties, which enable applications in high-resolution imaging and photothermal therapy [234]. Similarly, Karnwal et al. emphasized that AuNPs are widely explored for theranostic applications, whereas AgNPs are frequently studied for antimicrobial interventions due to their potent ion-mediated activity [263]. Oxides like Fe_3O_4, TiO_2, and ZnO provide magnetic, photocatalytic, and redox functionalities. Their divergent biocompatibility profiles are largely shaped by differences in ion release, ROS generation, and surface chemistry. In contrast, metal-oxide nanoparticles offer functionalities rooted in their magnetic and photocatalytic behaviours. For example, Meng et al. reported that Fe_3O_4 NPs remain central to MRI because of their superparamagnetic characteristics and biodegradability into systemic iron pools [229]. Likewise, Chandoliya described how ZnO and TiO_2 NPs are gaining traction for their photocatalytic, antibacterial, and UV blocking properties, making them valuable not only in biomedical contexts but also in environmental remediation [264].

Collectively, these studies show that while metal nanoparticles excel

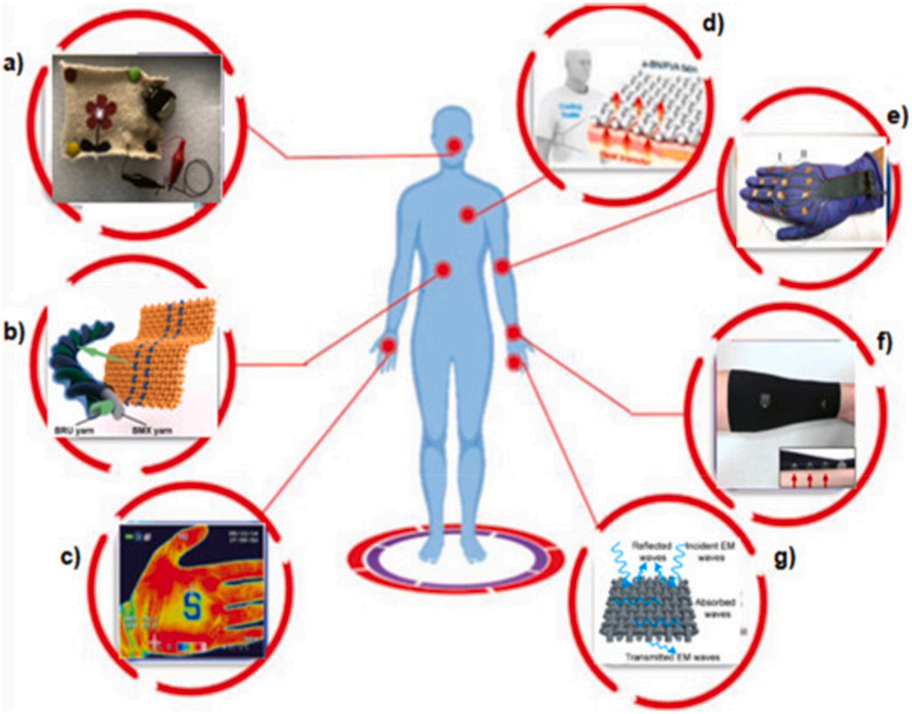


Fig. 11. Showing different Nanoparticle-integrated textiles (polymer) flexible, stretchable, and durable sensors (a) Wireless power transfer; (b) Fabric-based supercapacitors for energy storage; (c) Heated gloves coated with nanomaterials; (d) Temperature-regulating textiles; (e) Stretchable sensors for detecting movement; (f) Wearable sensors for heart (ECG) and muscle (EMG) monitoring, and (g) Textiles designed to block electromagnetic waves [255].

in optical-driven applications, metal oxide nanoparticles (MNOPs) dominate in magnetic and redox-driven biomedical uses, underscoring the complementary nature of both classes. Nanoparticle polymer hybrid systems have emerged as a next-generation strategy to overcome the intrinsic drawbacks of bare metal and metal-oxide nanoparticles, such as aggregation, short circulation times, and dose-dependent cytotoxicity. In these constructs, inorganic nanoparticles are coated, encapsulated, or functionalized with synthetic or natural polymers (e.g., chitosan, dextran, gelatin), thereby improving their colloidal stability, biocompatibility, and drug delivery efficiency [229,230,233].

Metal oxide nanoparticles are increasingly being integrated into biomedical practice as antibacterial and wound healing agents, biosensors, anticancer therapeutics, and imaging contrast agents. According to Negrescu et al. several MONPs such as zinc oxide (ZnO), cerium oxide (CeO_2), iron oxide (Fe_2O_3), silver oxide (AgO), magnesium oxide (MgO), titanium dioxide (TiO_2), nickel oxide (NiO), zirconium oxide (ZrO), and cadmium oxide (CdO) stand out as promising candidates due to the large volume of in vitro and in vivo data supporting their biological activity [265].

- **Zinc Oxide Nanoparticles/Polymer Hybrids (ZnO NPs)**

ZnO NPs are considered biocompatible and relatively nontoxic, although their properties are strongly influenced by size, morphology, and synthesis method. As highlighted by Negrescu et al. [265]. ZnO NPs are already present in commercial products such as sunscreens, ointments, food packaging, and cosmetics [265]. They display potent antibacterial effects, with activity varying by dose and exposure time [39]. Importantly, ZnO NPs also possess inherent anticancer activity; Truong et al. reported that the FDA has approved ZnO based formulations as antitumor therapies, largely due to their ability to generate ROS and disrupt zinc-dependent protein homeostasis in malignant cells [234]. However, several studies including Karnwal et al. warn of toxic effects on normal cells and organisms, suggesting the need for further safety evaluation before broad clinical adoption [263]. ZnO NPs are widely studied for antibacterial and anticancer activity through ROS generation and Zn^{2+} release. When combined with polymers like chitosan or PLGA, they show synergistic antimicrobial effects and reduced cytotoxicity. Nqoro et al. demonstrated ZnO chitosan dressings with superior wound healing, though systemic toxicity remains a concern due to dissolution and ion release [230].

- **Cerium Oxide Nanoparticles/Polymer Hybrids (CeO_2 NPs)**

CeO_2 NPs are widely recognized for their antioxidant and anticancer properties through redox cycling activity (Ce^{3+}/Ce^{4+}). Their activity is based on the redox cycling between Ce^{3+} and Ce^{4+} states, which allows them to act as ROS scavengers [265]. Meng et al. emphasized that this redox flexibility underlies their use in tissue regeneration and anticancer therapies [229]. Interestingly, these nanoparticles may also exhibit pro-oxidant effects under acidic conditions or at high concentrations, as demonstrated by Truong et al., raising concerns about cytotoxicity depending on dosage and synthesis method [234]. Polymer functionalization broadens their stability under variable pH and ionic conditions. Meng et al. noted their promise in wound healing and radioprotection, though pro-oxidant behaviour may occur at high doses or low pH, requiring careful formulation [229].

- **Titanium Dioxide Nanoparticles/Polymer Hybrids (TiO_2 NPs)**

TiO_2 NPs have gained attention primarily in bone and tissue engineering due to their ability to enhance cell migration, adhesion, and osseointegration [265]. They also function as antibacterial agents, particularly effective under UV irradiation via ROS production [264]. Furthermore, their ROS-generating capacity has been harnessed in anticancer applications, making TiO_2 one of the most versatile MONPs in biomedical contexts.

Polymer functionalization with PLGA or gelatin improves cell adhesion and reduces off-target ROS. Kim et al. synthesized polymer-coated TiO_2 composites with enhanced biocompatibility, though ROS under UV activation can still damage host tissues [232].

- **Iron Oxide Nanoparticles (Fe_2O_3 NPs)**

Among MONPs, Fe_2O_3 nanoparticles are especially valued for their magnetic properties. Meng et al. described their use as drug-delivery carriers, where external magnetic fields or ligand conjugation can enable targeted release [229]. They are also used as MRI contrast agents and in cell labeling, allowing non-invasive monitoring of therapeutic efficacy [234]. This dual role in therapy and diagnostics (theranostics) makes Fe_2O_3 NPs a cornerstone in clinical nanomedicine research. Polymer functionalization enhances stability and reduces immune clearance. Meng et al. highlighted their role in theranostics, while Lomphithak et al. reported that high dose exposures can still induce autophagy-dependent ferroptosis, even with polymer coatings [229, 233].

- **Magnesium oxide (MgO NPs) and Nickel oxide (NiO NPs)**

Negrescu et al. reported that MgO NPs are a relatively non-toxic and soluble nanomaterial. MgO NPs are applied in antibacterial wound dressings and as drug delivery vehicles in anticancer therapy, with the advantage of minimal tissue accumulation [265]. Similarly, according to Chandoliya, NiO NPs possess antibacterial, antifungal, and anticancer properties, though their long-term biosafety remains a subject of debate [264]. AgO NPs, zirconium oxide (ZrO NPs), and cadmium oxide (CdO NPs): These are less extensively studied compared to ZnO or Fe_2O_3 but demonstrate antimicrobial and biosensing applications. However, Karnwal et al. noted that their potential toxicity and environmental persistence may limit clinical translation unless safety issues are resolved [263].

7. Conclusion

The excellent characteristics of metal/metal-oxide nanoparticle-polymer hybrid systems as reported in this study are due to their high surface area, adjustable pore sizes, and flexible chemistry. This enables precise drug release, better compatibility with the body, and targeted treatments. More so, the incorporation of metal nanoparticles and their oxide derivatives into the polymer matrix produces a hybrid system with enhanced antibacterial activities, improved durability, and surface functionality. Moreover, the introduction of nanoparticles improved the imaging properties of the nanoparticle-polymer hybrid for CT scans, MRI and fluorescence imaging, resulting in better contrast effects and improved sensitivity. These novel materials offer enhanced bioactive scaffolds for biomedical engineering, promoting cell growth and regeneration. Despite the immense potential of metal/metal-oxide nanoparticle-polymer hybrid, the study shows that toxicity, biocompatibility, and scalability remain key limitations to the full adoption of this material. In conclusion, metal/metal-oxide nanoparticle–polymer hybrid systems offer remarkable potential in biomedical engineering, combining multifunctionality with biocompatibility. Their innovative applications promise to enhance diagnostics, targeted therapies, and regenerative medicine, shaping the future of healthcare technologies.

CRediT authorship contribution statement

Abayomi Bamisaye: Writing – review & editing, Visualization, Validation, Supervision, Methodology, Conceptualization. **Monsuru Adewale Adekola:** Writing – review & editing, Visualization, Investigation. **Shakirudeen Modupe Abati:** Writing – review & editing, Writing – original draft, Visualization, Resources. **Nelson Oshogwue**

Etafo: Writing – review & editing, Writing – original draft, Visualization, Validation, Data curation. **Okewole Samson Ademola:** Writing – review & editing, Writing – original draft, Visualization, Validation. **Philips Tosin Joseph:** Writing – review & editing, Writing – original draft, Visualization, Validation. **Oreniyi Samuel:** Writing – review & editing, Visualization, Resources. **Olumuyiwa Olufisayo Ogunlaja:** Writing – review & editing, Visualization, Validation, Resources. **Henrietta Langmi:** Writing – review & editing, Validation, Resources. **Mopelola Abidemi Idowu:** Writing – review & editing, Visualization, Validation, Supervision, Resources.

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.

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Data availability

All data used have been included in this article

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