

Metals and Minerals in Pharmacy: Current Trends, Biomedical Applications, and Future Innovations

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Abstract

Metals and minerals have played important roles in medicine for centuries, ranging from the use of simple mineral powders in traditional therapies to the development of modern metal-based drugs and nanomaterials. In recent years, advancements in material science, nanotechnology and pharmaceutical engineering have expanded the biomedical relevance of inorganic materials far beyond their conventional use as excipients. This review highlights the growing integration of metallic and mineral systems into pharmaceutical formulations, therapeutic agents, imaging platforms, antimicrobial coatings and targeted drug delivery technologies. The discussion covers essential metals, noble metal nanoparticles, clay minerals, silica-based carriers, calcium phosphates, and metal–organic frameworks, with emphasis on their physicochemical properties, biological interactions and mechanisms of action. Special attention is given to toxicity considerations, regulatory requirements and long-term biocompatibility challenges. Recent trends such as green synthesis routes, AI-assisted material selection, multifunctional nanocarriers and emerging clinical applications are thoroughly analyzed. The review concludes by identifying promising future directions, including intelligent inorganic biomaterials, personalized metallodrugs and sustainable sourcing of pharmaceutical-grade minerals. Overall, metals and minerals continue to offer broad opportunities for innovative and impactful applications in pharmacy and biomedical science

Keywords: Metal-based therapeutics, Mineral excipients, Nanomedicine, Metal nanoparticles, Drug delivery, Biomedical applications, Biocompatibility

INTRODUCTION

Metallic elements and naturally occurring minerals have been integral to medical practice since antiquity, where raw mineral powders and metal salts were used in healing formulations and topical remedies. In contemporary pharmaceutical science these inorganic materials have evolved from passive excipients into active functional components—from metal-based anticancer agents and antimicrobial silver formulations to mineral carriers and inorganic nanocarriers for controlled drug delivery. This

transformation is driven by advances in materials synthesis, surface engineering, and nanotechnology that allow precise control over size, surface chemistry, porosity, and release kinetics, enabling minerals and metals to perform targeted biomedical roles previously accessible only to organic systems. [1, 2]

The graphical abstract provided below integrates the central scientific concepts of this review, illustrating the structural diversity, biomedical utilities, and innovative trends shaping the next generation of metal- and mineral-based pharmaceutical materials Figure 1.

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Received Date: December 08, 2025

Accepted Date: December 13, 2025

Published Date: December 25, 2025

Citation: Tushal Kyada, Monika Kyada. Metals and Minerals in Pharmacy: Current Trends, Biomedical Applications, and Future Innovations. International Journal of Minerals. 2025; 2(2): 12–24p.

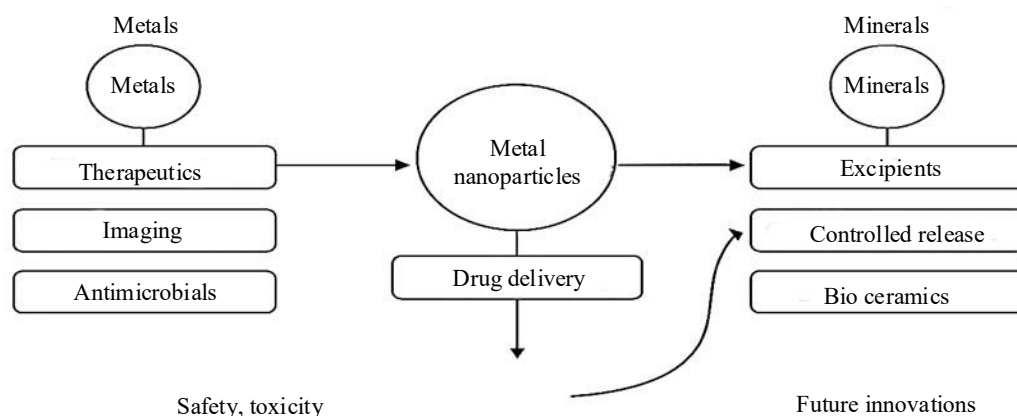


Figure 1. Graphical abstract illustrating the central theme of the study.

A major factor behind the resurgence of interest in inorganic materials in pharmacy is their structural and chemical diversity. Metal–organic frameworks (MOFs), mesoporous silica, layered clays, calcium phosphates and metal nanoparticles (Au, Ag, Fe, ZnO, etc.) each provide distinct advantages — exceptionally high internal surface areas and tunable pore environments (MOFs and mesoporous silica), ion-exchange and intercalation for sustained release (clay minerals), osteoconductivity for bone delivery (calcium phosphates) and optical/magnetic properties useful for imaging and theranostics (gold and iron oxide nanoparticles).[3,4] These property-driven functions have been exploited in drug loading, controlled release, imaging contrast enhancement, localized hyperthermia, and antimicrobial surface coatings.[5] Safety and regulatory considerations provide necessary balance: while many inorganic materials demonstrate excellent performance in vitro, their translation to clinical use requires rigorous toxicological profiling, biodistribution studies, and standardized manufacturing practices. Nanometer-scale metals can induce oxidative stress, accumulate in organs, or trigger immune responses if not carefully engineered and tested; similarly, natural mineral sources vary in composition and impurity content, making pharmaceutical-grade standardization essential. Regulatory agencies increasingly demand detailed characterization, long-term safety data, and reproducible synthesis routes — especially for nanomaterials and novel metallodrugs. [6]

Recent reviews and high-impact studies highlight two converging trends accelerating innovation: (1) the design of multifunctional inorganic platforms that combine therapy, diagnosis, and responsive release (theranostics and stimuli-responsive carriers) and (2) the adoption of greener, more scalable synthesis routes (plant-assisted nanoparticle formation, solvent-minimizing MOF syntheses) coupled with computational and AI tools for material selection and property prediction. These directions aim to reduce environmental impact and improve translational potential while enabling personalized or precision metallodrug approaches. [7]

This review synthesizes recent developments across these areas — classification and properties of pharmaceutically relevant metals/minerals, their roles as excipients and active agents, nanostructured metal- and mineral-based delivery systems, diagnostic/theranostic applications, and the major safety/regulatory issues that frame clinical translation. We conclude by identifying knowledge gaps and future opportunities where inorganic materials can further contribute to safer, more effective pharmaceutical interventions. [8]

METALS AND MINERALS IN PHARMACEUTICAL SCIENCE

The integration of metals and minerals into pharmaceutical science spans from essential micronutrient supplementation to advanced inorganic carriers and nanomedicine platforms. In this context, the classification of metals and minerals based on their pharmaceutical relevance helps structure understanding and guides material selection for various applications.

Classification of Metals and Minerals Relevant to Pharmacy

Essential trace metals: Essential trace metals — such as iron (Fe), zinc (Zn), magnesium (Mg), copper (Cu), and selenium (Se) — play critical biological roles, acting as cofactors for enzymes, regulators of oxidative stress, modulators of immune responses, and mediators of metabolic and signaling pathways. For example, iron is crucial for hemoglobin formation and oxygen transport; zinc and copper are involved in enzymatic functions, DNA synthesis, and immune regulation; selenium is a known antioxidant cofactor; magnesium contributes to electrolyte balance and enzymatic reactions.[9,10]

Deficiency or imbalance of these trace metals is associated with a wide array of disorders, including impaired immunity, metabolic dysfunctions, chronic diseases, and increased susceptibility to infections. In pharmaceutical applications, these trace metals are used as dietary supplements, prophylactic agents, or supportive therapy to correct deficiencies — thereby improving immune functions, antioxidant defenses, and metabolic balance. Given their biological importance and safety when dosed appropriately, essential trace metals remain foundational in drug/nutraceutical design.

Therapeutic metals: Beyond supplementation, certain metals exhibit inherent therapeutic or pharmacological properties when formulated appropriately. Metals such as platinum (Pt), gold (Au), silver (Ag), and bismuth (Bi) — alone or in complexed/ionic/nanoparticle form -have been exploited for anticancer, anti-inflammatory, antimicrobial, and gastrointestinal therapies. For instance, platinum-based compounds remain widely used in chemotherapy regimens; gold complexes have been investigated for anti-inflammatory and antirheumatic effects; silver nanoparticles are known for strong broad-spectrum antimicrobial activity; bismuth salts are applied for gastrointestinal disorders.[11,12] Moreover, therapeutic metals may be incorporated into nanoparticulate systems or combined with organic/inorganic carriers to improve bioavailability, reduce toxicity, enable controlled release, or provide multifunctional (therapeutic + diagnostic) capabilities.[13]

Minerals: Minerals -particularly inorganic solids such as silica (e.g., mesoporous silica), calcium phosphates (e.g., hydroxyapatite), clay minerals (e.g., montmorillonite, smectite, kaolinite), carbonates, and various oxides - have long served as inert excipients in pharmaceutical formulations. Their roles include use as fillers, diluents, glidants, disintegrants, lubricants, thickening or suspending agents, and stabilizers in tablets, capsules, suspensions, and semi-solid preparations.[14]

Recent research goes beyond inert excipient roles: porous inorganic materials such as mesoporous silica, calcium phosphate nanoparticles, and clays are being actively developed as drug carriers. Their high surface area, tunable porosity, ion-exchange capacity, and structural stability make them attractive for controlled or sustained release, improved solubility of poorly soluble drugs, enhanced drug loading, and targeted delivery.[15]

Clay minerals in particular (montmorillonite, smectite, kaolinite, halloysite, etc.) have gained renewed attention: they offer biocompatibility, low toxicity, layered structures, ion exchange, adsorption capabilities, and ability to form nanocomposites (e.g., with polymers) — enabling stable, controlled, and efficient drug delivery systems.[16]

As a result, mineral-based carriers are increasingly considered for oral, topical, and parenteral drug delivery, or even tissue engineering scaffolds and regenerative medicine — broadening the conventional definition of “excipients.” [17]

Nanometals: Advancements in nanotechnology have facilitated the use of metal nanoparticles — such as gold, silver, iron oxide (Fe₃O₄), titanium dioxide (TiO₂), etc. — as functional entities in pharmaceuticals. These nanometals bring properties absent in their bulk counterparts: unique optical characteristics (plasmonic resonance in gold/silver), magnetic behavior (iron oxide), high surface-to-volume ratio, tunable surface chemistry, and improved interaction with biological systems.

Table 1. Classification of metals and minerals for pharmaceutical use.

Category	Examples	Key roles / properties in pharmacy
Essential Trace Metals	Fe, Zn, Mg, Cu, Se	Nutritional supplementation; enzyme cofactors; immune modulation; antioxidant defense; metabolic support. [10,19]
Therapeutic Metals	Pt, Au, Ag, Bi	Chemotherapy (Pt), anti-inflammatory (Au), antimicrobial (Ag), GI therapy (Bi). [20]
Mineral Excipients / Carriers	Silica, calcium phosphates, clay minerals (montmorillonite, kaolinite, halloysite, smectite), carbonates, oxides	Excipients (fillers, diluents, lubricants, disintegrants); drug carriers with controlled release; increased bioavailability; carrier for poorly soluble drugs. [15]
Nanometals / Inorganic Nanoparticles	Au-NPs, Ag-NPs, Fe ₃ O ₄ -NPs, TiO ₂ -NPs	Drug delivery, diagnostics, imaging, antimicrobial coatings, theranostics, responsive or targeted delivery.[18]

Such metal and metal-oxide nanoparticles have been applied in drug delivery, diagnostics and imaging, photothermal or photodynamic therapy, antimicrobial coatings, and theranostic (therapy + diagnostics) platforms. For example, iron oxide nanoparticles serve as MRI contrast agents; gold nanoparticles enable photothermal therapy; silver nanoparticles provide antimicrobial effects; and titanium dioxide is explored for drug delivery, photocatalysis-based therapies, or surface modifications.[18]

Moreover, combining nanometals with mineral carriers (e.g., embedding metal nanoparticles inside porous silica or clay matrices) can mitigate toxicity, improve stability, and allow controlled release — merging advantages of both classes of materials. To clearly distinguish the functional roles of these materials, a structured classification of metals and minerals used in pharmaceutical applications is presented in Table 1.

Physicochemical Properties that Make Them Useful

The functionality of metals, metal oxides, and mineral materials in pharmaceutical applications is fundamentally governed by their distinct physicochemical properties, which determine their interactions with drug molecules, biological environments, and formulation components. These properties influence critical processes such as drug loading, encapsulation, release kinetics, bioavailability, biocompatibility, and targeting efficiency. Understanding these characteristics is therefore essential for rational material selection and the design of effective drug delivery systems.

Surface charge and zeta potential

Surface charge plays a central role in electrostatic interactions between inorganic carriers and drug molecules. Minerals such as montmorillonite, halloysite, and mesoporous silica possess tunable surface charges that determine drug adsorption, colloidal stability, and cellular uptake. A positive surface charge often enhances interaction with negatively charged biomolecules (DNA, proteins) and improves cellular internalization, whereas negative surfaces may improve stability and dispersibility in aqueous media. Zeta potential also dictates aggregation behavior of nanoparticles, thus influencing their pharmacokinetics and systemic circulation. Studies show that surface charge engineering enhances drug loading efficiency and prevents premature release. [21–22]

Solubility and dissolution behavior

The solubility profiles of metal ions and minerals significantly influence their pharmaceutical utility.

Calcium phosphate, for example, exhibits pH-dependent solubility, dissolving in acidic environments such as tumor tissues or intracellular lysosomes.

Silica-based carriers are known for slow, controlled dissolution into non-toxic silicates, making them suitable for long-acting delivery.

This tunable solubility enables environment-responsive (pH-triggered) release, improving targeting precision and reducing systemic toxicity. [23]

Ion-exchange capacity

Layered silicates such as montmorillonite and smectite exhibit high cation-exchange capacity (CEC), enabling replacement of inherent ions (Na^+ , Ca^{2+}) with protonated drug molecules. This mechanism provides: high drug-loading capacity, stabilization of labile molecules and controlled release through reversible ion exchange. Ion-exchange also minimizes burst release and enhances mucoadhesion in oral formulations. [24–25]

Adsorption capacity and surface area

High-surface-area materials such as mesoporous silica (MCM-41, SBA-15), activated clays, and metal–oxide nanoparticles exhibit strong adsorption capabilities due to: large pore volume, high internal surface area ($>1000 \text{ m}^2/\text{g}$ in some cases) and unique pore geometry. These properties make them ideal for loading poorly water-soluble drugs, increasing dissolution rate and bioavailability. Several studies demonstrate that mesoporous silica enhances solubility of BCS Class II drugs by stabilizing them in amorphous form. [26–27]

Catalytic and redox activity

Metals such as iron, platinum, silver, and gold exhibit intrinsic catalytic or redox activity, which can be exploited for biomedical and pharmaceutical applications: Iron oxide (Fe_3O_4) drives Fenton-like reactions for chemo-dynamic therapy, Gold nanoparticles facilitate photothermal or catalytic drug activation and Silver ions catalyze antibacterial oxidative stress. These redox-based mechanisms provide theranostic (therapy + diagnostics) capabilities and selective action at disease sites. [28]

Mechanical strength and structural stability

Minerals such as hydroxyapatite, silica, and titanium dioxide offer mechanical stability essential for: protection of sensitive drugs, sustained release matrices, implant coatings and scaffolds in tissue engineering applications. Their ability to resist dissolution or deformation ensures predictable, long-term release and enhances mechanical integrity in tablets and implantable therapeutic systems (29).

Optical, magnetic, and multifunctional properties

Many metals and minerals provide additional functional advantages: Magnetic iron oxide nanoparticles enable MRI imaging and magnetically triggered drug targeting, Gold and silver nanoparticles exhibit surface plasmon resonance, useful for imaging and photothermal therapy and Titanium dioxide exhibits photocatalytic activity relevant in antimicrobial coatings. These multifunctional properties extend their utility beyond drug delivery into imaging, biosensing, antimicrobial applications, and cancer therapy. [30]

PHARMACEUTICAL APPLICATIONS OF METALS

Metals have played a pivotal role in modern drug development, with applications ranging from therapeutic agents to imaging tools, antimicrobial components, and precision-medicine platforms. Their unique physicochemical properties—including redox activity, coordination chemistry, catalytic potential, and nanoparticle behavior—enable functionalities not easily achievable with purely organic molecules. This section reviews major pharmaceutical applications of metals, focusing on small-molecule metal complexes, metal-based drugs, and nanometal systems currently shaping biomedical innovation.

Metal-Based Therapeutics

Metal-based pharmaceuticals constitute a major class of therapeutic agents used across oncology, infectious diseases, inflammation management, and gastrointestinal disorders.

Platinum-based chemotherapeutic agents

Platinum complexes-including cisplatin, carboplatin, and oxaliplatin-remain some of the most widely used chemotherapeutics worldwide. These compounds exert cytotoxicity via DNA crosslinking, which disrupts replication and induces apoptosis in rapidly dividing cancer cells. Cisplatin revolutionized cancer treatment and remains frontline therapy for testicular, ovarian, lung, and bladder cancers. [31] Carboplatin and oxaliplatin were later developed to reduce toxicity and improve tumor selectivity. [32] Despite side effects such as nephrotoxicity and neurotoxicity, platinum drugs continue to be indispensable, with ongoing research exploring nanoparticle-assisted delivery and next-generation Pt(IV) prodrugs to improve pharmacokinetics and reduce systemic toxicity. [33]

Gold compounds

Gold-based therapeutics have long been studied for anti-inflammatory and antirheumatic properties. Compounds such as auranofin have demonstrated efficacy in rheumatoid arthritis through immunomodulation and thiol-reactive mechanisms. [34] In recent years, gold complexes have re-emerged as promising anticancer agents, thanks to their ability to inhibit mitochondrial respiration, induce redox imbalance, and target thioredoxin reductase pathways. Furthermore, gold nanoparticles (AuNPs) enhance tumor selectivity and enable combined photothermal-chemotherapeutic approaches. [35]

Silver salts and silver nanoparticles

Silver is one of the oldest metallotherapeutic agents, widely recognized for its broad-spectrum antimicrobial activity. Silver ions and silver nanoparticles (AgNPs) disrupt bacterial membranes, generate reactive oxygen species, and bind to DNA and proteins, leading to microbial death. Today, AgNPs are incorporated into: wound dressings, burn therapies, topical antimicrobial creams and coating materials for medical implants.

Their nanoscale dimensions increase surface reactivity, enabling enhanced antimicrobial potency even against multi-drug-resistant organisms. [36]

Bismuth compounds

Bismuth-based drugs are non-systemic agents with excellent safety profiles. Bismuth subsalicylate and bismuth subcitrate remain widely used for gastrointestinal disorders, including peptic ulcers and diarrhea. Notably, bismuth compounds are key components of quadruple therapy for *Helicobacter pylori* infection due to their antibacterial, anti-inflammatory, and mucosal-protective properties. [37]

Biological Roles of Metal Ions

Metal ions serve critical physiological functions that form the basis for their pharmaceutical relevance. Their deficiencies often require therapeutic supplementation.

Iron (Fe)

Iron is essential for oxygen transport via hemoglobin and for mitochondrial electron transport. Iron deficiency leads to anemia, cognitive impairment, and reduced immunity. Numerous oral and intravenous iron formulations exist to correct deficiency states. [38]

Zinc (Zn) and copper (Cu)

Zinc plays indispensable roles in: immune modulation, protein synthesis, wound healing and antiviral and antioxidant pathways.

Copper contributes to mitochondrial energy production, superoxide dismutase activity, and connective tissue development. Controlled supplementation of Zn and Cu is common in nutraceuticals and supportive treatments to correct immune and metabolic dysfunctions. [39]

Magnesium (Mg)

Magnesium participates in more than 300 enzymatic reactions, including ATP metabolism, DNA repair, neuromuscular function, and cardiovascular regulation. Mg supplements are widely used in managing arrhythmias, migraine, preeclampsia, and metabolic imbalance. [40].

Metal-ion supplementation remains a cornerstone of preventive and therapeutic medicine due to the irreplaceable roles of metal cofactors in human physiology.

Nanometals and Their Biomedical Significance

Nanostructured metals and metal-based nanomaterials have transformed modern pharmaceuticals due to their superior surface-to-volume ratio, tunable optical properties, magnetism, bioreactivity, and functionalization potential.

Magnetic nanoparticles (Fe_3O_4 , $\gamma-Fe_2O_3$)

Magnetic nanoparticles enable: magnetic hyperthermia for cancer therapy, MRI contrast enhancement, magnetically guided drug targeting and biosensing. Their controllable magnetic response allows localized heating of tumor tissues and real-time imaging support (31).

Gold nanoparticles (AuNPs)

Gold nanoparticles exhibit unique surface plasmon resonance, allowing: photothermal therapy, enhanced imaging (CT, OCT), targeted drug delivery and gene delivery.

Their biocompatibility and surface-functionalization flexibility make them excellent carriers for chemotherapeutics and biomolecules (35).

Silver nanoparticles (AgNPs)

In addition to their antimicrobial properties, AgNPs are explored for antiviral coatings, disinfectants, and responsive drug delivery systems. Their high reactivity provides strong activity at low doses (36).

Metal-organic frameworks (MOFs)

MOFs are hybrid crystalline materials with extraordinary porosity and tunable chemistry. In pharmaceuticals, MOFs are used for: controlled and sustained drug release, co-delivery of multiple agents, gas delivery (e.g., NO-release systems) and imaging when combined with metals such as Fe, Zr, or Gd. Their high loading capacity and modular design make them next-generation drug carriers. [32]

PHARMACEUTICAL APPLICATIONS OF MINERALS

Minerals as Excipients

Minerals play a crucial role as excipients due to their chemical inertness, thermal stability, and cost-effectiveness. Widely used minerals—such as talc, kaolin, silica, bentonite, and magnesium stearate—are incorporated in solid dosage forms as glidants, lubricants, diluents, stabilizers, and disintegrants. Their performance is strongly influenced by particle size distribution, surface morphology, crystallinity, and impurity content, which determine powder flow, compressibility, lubrication efficiency, and interaction with APIs. For example, talc improves blend flowability, whereas magnesium stearate reduces die-wall friction during compression. Modern pharmaceutical manufacturing emphasizes stricter quality-by-design (QbD) approaches, especially regarding heavy-metal impurities and mineral source variability, to ensure consistent product quality. [41]

Minerals in Drug Delivery

Minerals are increasingly being engineered as drug delivery carriers because of their tunable surface chemistry, adsorption capacity, and biocompatibility. Layered silicates like montmorillonite provide interlayer spaces and high surface areas, enabling drug intercalation, controlled release, and stabilization of sensitive molecules. Similarly, mesoporous silica materials (MCM-41, SBA-15) possess

well-ordered pores that allow encapsulation of antibiotics, proteins, and hydrophobic drugs, offering precise control over loading and release kinetics through pore-size modification or surface functionalization. In biomedical applications, calcium phosphates, especially hydroxyapatite, are preferred for bone-targeted delivery, combining osteoconductivity with the ability to immobilize therapeutic agents. These minerals offer multifunctional capabilities—drug release, structural support, and bioactivity—making them valuable in regenerative medicine. [42]

Traditional Medical Use of Minerals

Traditional medical systems such as Ayurveda, Siddha, and Unani utilize minerals in the form of bhasmas, which are produced through repeated purification and calcination processes. These processes are believed to enhance safety, digestibility, and bioavailability while reducing toxicity. Recent advances in analytical techniques—including XRD, SEM/TEM, FTIR, and ICP-MS—have provided deeper insights into the nano-scale structure, chemical transformations, elemental composition, and stability of mineral-based therapeutic preparations. Scientific evaluation now focuses on establishing standardization protocols, toxicity thresholds, and mechanisms of therapeutic action to integrate these traditional formulations with evidence-based medicine. [43]

METAL- AND MINERAL-BASED NANOMATERIALS IN BIOMEDICAL APPLICATIONS

Drug Delivery

Metal- and mineral-based nanomaterials have emerged as versatile drug delivery platforms due to their tunable physicochemical properties, high loading capacities, and ability to enhance drug stability and bioavailability. Metallic nanoparticles—including gold, silver, and iron oxide—can be surface-functionalized with polymers, antibodies, peptides, or aptamers to achieve targeted delivery, reduce off-target toxicity, and improve therapeutic efficiency. [44] Their ability to respond to external stimuli such as light, magnetic fields, or pH gradients further enables stimuli-responsive drug release.

Mineral-based nanocarriers such as mesoporous silica nanoparticles (MSNs) and layered double hydroxides (LDHs) offer structural stability, large surface areas, and controlled-release behavior. These carriers can protect sensitive therapeutic agents—including peptides, siRNA, and enzymes—from degradation while ensuring sustained release at the target site. [45]. In addition, metal–organic frameworks (MOFs), composed of metal ions bridged by organic linkers, exhibit exceptionally high porosity and tunable pore architecture, allowing efficient encapsulation of both small molecules and biological macromolecules. Their capacity for ligand modification, pH-triggered degradation, and coordinated drug–carrier interactions makes them promising candidates for precision nanomedicine. [46]

Diagnostic and Imaging Applications

Metal- and mineral-based nanomaterials significantly enhance diagnostic accuracy due to their unique optical, magnetic, and electronic properties. Superparamagnetic iron oxide nanoparticles (SPIONs) are widely used as contrast agents in magnetic resonance imaging (MRI) due to their ability to alter local magnetic fields and improve soft tissue contrast. [47]. Gold nanoparticles (AuNPs) exhibit tunable surface plasmon resonance, enabling their use in computed tomography (CT) enhancement, photoacoustic imaging, and photothermal imaging. Their biocompatibility and ease of functionalization make them suitable for molecular diagnostics and imaging-guided therapy. [48]

Additionally, quantum dots (QDs)—nanocrystals typically composed of semiconductor metals—offer high fluorescence intensity, photostability, and narrow emission spectra, making them ideal for cell tracking, biosensing, multiplexed imaging, and real-time molecular diagnostics. [49] Their ability to emit light at specific wavelengths allows sensitive detection of biomolecules even at very low concentrations.

Antimicrobial and Antiviral Benefits

Metal and metal oxide nanoparticles have demonstrated strong broad-spectrum antimicrobial and antiviral properties, driven by mechanisms such as generation of reactive oxygen species (ROS),

membrane disruption, protein inactivation, and interference with microbial DNA replication. Zinc oxide (ZnO) and copper oxide (CuO) nanoparticles, in particular, exhibit potent activity against bacteria, fungi, and viruses, making them suitable for wound dressings, antimicrobial coatings, personal protective equipment, and implant surfaces. [50]

Silver nanoparticles (AgNPs), long known for their antimicrobial efficacy, continue to be incorporated into catheters, bandages, dental materials, and topical formulations due to their ability to disrupt microbial cell walls and inhibit biofilm formation. [51] Their antiviral activity against enveloped viruses has also led to applications in preventive medical devices. The development of mineral-based antimicrobial systems—such as clay–metal oxide hybrids—offers additional advantages, including reduced resistance development and enhanced sustained antimicrobial action. [52]

SAFETY, TOXICITY, AND REGULATORY PERSPECTIVES

The increasing integration of metals, minerals, and nanomaterials into pharmaceutical and biomedical applications necessitates a rigorous understanding of their toxicity profiles, biodistribution pathways, and long-term biological interactions. Although many metallic and mineral-based agents provide therapeutic benefits, they may also pose risks such as heavy metal toxicity, oxidative stress induction, genotoxicity, organ accumulation, or unexpected immunological responses when administered without proper control. [53] Toxic manifestations depend on factors such as particle size, surface charge, solubility, oxidation state, and dosage, which ultimately dictate their interaction with biological membranes, proteins, and nucleic acids. A key concern with metal-based nanomaterials is their potential to generate reactive oxygen species (ROS), leading to mitochondrial damage, lipid peroxidation, and inflammatory cascades. Some nanoparticles, particularly those containing cadmium, nickel, and certain metal oxides, may cross biological barriers—including the blood–brain barrier—raising questions regarding long-term neurotoxicity and systemic accumulation. [54] Similarly, mineral-based carriers such as silica or alumina require careful evaluation of biodegradation kinetics to prevent chronic accumulation or granulomatous responses.

From a regulatory standpoint, agencies including the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) mandate comprehensive assessments covering acute, sub-chronic, and chronic toxicity, biocompatibility, immunotoxicity, carcinogenicity, genotoxicity, and reproductive toxicity before clinical approval. [55] For metal-based therapeutics, specific attention is given to metal ion release, oxidation behavior, and potential off-target interactions. Nanomaterials are subject to even stricter regulatory scrutiny because of their unique size-dependent properties. Regulatory frameworks now require detailed characterization of parameters such as particle size distribution, shape, surface chemistry, agglomeration tendency, dissolution rate, and *in vivo* degradation patterns. Emerging guidelines emphasize the need for long-term pharmacokinetic and biodistribution studies, environmental impact assessments, and evaluation of nano–bio interactions under physiologically relevant conditions. [56] Furthermore, international regulatory bodies are converging toward establishing standardized testing protocols for nanomedicines, including updated ISO standards and OECD test guidelines. These efforts aim to ensure safety, reproducibility, and transparency in the development and clinical translation of metal- and mineral-based pharmaceutical materials. [57]

RECENT TRENDS

The field of metal- and mineral-based pharmaceuticals is rapidly evolving, driven by innovations that enhance safety, precision, and multifunctionality. Several emerging research directions are reshaping drug development, diagnostics, and biomaterials science.

Green and plant-mediated synthesis of metal nanoparticles has gained significant attention due to its environmental sustainability and reduced chemical toxicity. Botanical extracts, microbial cultures, and polysaccharides act as natural reducing and stabilizing agents, enabling the ecofriendly synthesis of gold, silver, zinc oxide, and iron oxide nanoparticles with enhanced biocompatibility. [58] These green-synthesized nanomaterials often exhibit improved biological activity due to surface-bound phytochemicals that enhance antimicrobial and anticancer properties.

Another advancing frontier is the AI-driven prediction of metal-ligand interactions, where machine learning models enable rapid screening of metallodrug candidates, prediction of binding affinities, and optimization of structural properties. [59] Artificial intelligence accelerates the discovery of metal-based therapeutics by providing insights into toxicity patterns, redox behavior, and coordination chemistry, significantly reducing experimental workload and development timelines.

The rise of hybrid organic-inorganic drug carriers represents a convergence of material science and pharmacology. These systems—such as polymer-coated metal nanoparticles, silica–lipid hybrids, and metal-organic nanocomposites—offer enhanced drug loading, tunable release kinetics, and improved biological stability. [60] Hybrid carriers overcome limitations associated with purely organic or inorganic materials, enabling synergistic functionalities such as dual drug delivery, imaging, and therapeutic action within a single platform.

The application of rare-earth metals such as gadolinium, europium, and terbium in advanced imaging technologies continues to expand. Their unique luminescent and paramagnetic properties support high-resolution MRI, fluorescence imaging, and multimodal diagnostic systems. [61] Engineered rare-earth nanostructures are now being explored for real-time tracking of drug distribution, tumor mapping, and image-guided therapy.

Finally, the pharmaceutical field is moving toward personalized metallodrug development, driven by precision medicine principles. Individual genetic, metabolic, and proteomic profiles are increasingly used to tailor metallodrug formulations—such as platinum-based chemotherapeutics or metal ion supplements—to maximize therapeutic outcomes and minimize adverse effects. [62] This trend marks a shift from generalized treatment toward personalized regimens guided by biomarkers and computational modeling.

FUTURE INNOVATIONS

Future innovations in metal- and mineral-based pharmaceutical technologies are expected to transform both therapeutic and diagnostic landscapes. One promising direction is the development of smart nanocarriers capable of responding to physiological triggers such as pH, temperature, redox gradients, enzymatic activity, or external magnetic/light stimuli. These advanced carriers enable on-demand release, real-time therapeutic adjustment, and minimized systemic toxicity, offering precise and personalized treatment options. [63] Smart nanosystems integrating metals such as gold, iron oxide, and titanium dioxide are already under investigation for controlled chemotherapy, immunomodulation and theranostics.

Another emerging frontier involves biodegradable metallic implants, particularly magnesium-, zinc-, and iron-based alloys. These materials degrade safely within the body while supporting tissue regeneration, eliminating the need for secondary surgical removal. Their mechanical strength, corrosion behavior, and biocompatibility are being engineered at the nanoscale to create implants for cardiovascular stents, orthopedic screws, and bone fixation devices. [64] Future designs may integrate drug-eluting capabilities and biosensing functions.

Mineral-based 3D printing materials represent a transformative direction for personalized medicine. Calcium phosphates, bioactive glasses, and silica-based composites are being optimized for additive manufacturing of patient-specific scaffolds, enabling precise anatomical matching and localized drug or growth factor delivery. [65] These materials hold immense potential for regenerative medicine, dental reconstruction, and orthopedics.

Sustainability is an increasingly important focus for the pharmaceutical sector. The sustainable sourcing of pharmaceutical-grade minerals aims to reduce environmental impact, ensure traceability, and improve global supply chain resilience. Efforts include green mining technologies, recycling of rare metals, and development of synthetic mineral analogues with reduced ecological footprint. [66]

Finally, the convergence of metals and minerals with nanorobotics and bioelectronics offers radical future possibilities. Metal-based nanorobots capable of targeted navigation, biosignal sensing, and micro-scale drug deployment are under active development. Integration with soft bioelectronic interfaces may enable real-time physiological monitoring, implantable diagnostic systems, and smart therapeutic feedback loops, marking the next generation of precision healthcare. [67]

CONCLUSION

Metals and minerals continue to play a critical and evolving role in modern pharmaceutical science, offering unique physicochemical and biological attributes that enable diverse therapeutic, diagnostic, and biomaterials applications. From traditional uses as excipients and mineral formulations to advanced metallodrugs, nanometals, and engineered mineral carriers, these materials provide functionalities that cannot be achieved with purely organic systems. Recent progress—including green nanoparticle synthesis, AI-assisted drug design, hybrid organic–inorganic platforms, and rare-earth-based imaging agents—has significantly expanded their biomedical relevance.

At the same time, safety, toxicity, and regulatory evaluation remain essential, particularly for nanostructured materials whose biological behavior differs fundamentally from their bulk counterparts. Comprehensive assessment of biocompatibility, degradation, organ accumulation, and long-term interactions will determine the successful clinical translation of next-generation metal- and mineral-based technologies.

Looking forward, innovations such as stimuli-responsive nanocarriers, biodegradable metallic implants, mineral-based 3D-printed scaffolds, and nanorobotic–bioelectronic systems are expected to redefine precision medicine and personalized therapeutics. Sustainable sourcing and responsible manufacturing will further shape the future landscape, ensuring that advanced materials are both effective and environmentally conscious. Ultimately, the integration of metallomics, nanotechnology, artificial intelligence, and materials engineering positions metals and minerals at the forefront of future pharmaceutical breakthroughs.

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