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# Metal Nanoparticles as Novel Drug Delivery Systems: A Review of Current Challenges and Opportunities

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**Abstract**

Nanotechnology's intriguing characteristics have attracted a lot of study in recent years. Nanomaterials, nanoelectronics, and nanobiotechnology are all subfields of nanotechnology that share a great deal of common ground. The possibility for metal nanoparticles **(MNPs)** to completely transform treatment is what has made them so remarkable. In addition to avoid antibiotic resistance and improving medication delivery, MNPs have been shown to raise the efficacy index of medicines. Additionally, MNPs have applications in in vitro and in vivo tests, improved biodegradable substance production, and nutraceuticals. Improved targeting at the necessary target location is one major benefit of using metallic nanoparticles for drug delivery systems due to their improved durability and half-life in circulation. Bio-nanotechnology is expanding into the new field of green synthesis of MNPs, which is more environmentally friendly than traditional chemical and physical synthesis techniques. Focusing on environmentally friendly approaches to the preparation, surface modification, and applications of various MNPs like silver, gold, platinum, palladium, copper, zinc oxide, metal sulfide, and nanometal organic frameworks, this review seeks to present current insights into the challenges and perspectives of MNPs in drug delivery systems.

## Introduction

Nanotechnology is currently regarded as one of the most recent and essential disciplines. Its exceptional advantages for the welfare of humankind have appeared as a result of its theory and practical significance. Nanomedicine is one of the most significant applications of nanotechnology, if not the most important. This is due to its immediate relationship to human existence and wellbeing. Nanotechnology's recent advancement has aided in changing the medical norms used in illness prevention, diagnosis, and treatment. Nowadays, the age of nanomedical technology is being lived in, whereby novel methods for transporting medicines inside the human body that can target specific

cells are provided [1]. One of the top objectives for study in the area of nanomedicine is drug transport to tissues, which is based on the production of exact nanometer materials that increase drug absorption. This means that the pieces of the medicine are in the right place in the body, which is where they work best. Because of this, the number of times people take medications, the bad effects they have, and the total cost of therapy all go down [2], [3]. Researchers in pharmaceutics keep making nano polymer-based ways to deliver medicines to the same biological cells. This objective is critical because many illnesses are caused by defects within the cell itself. Furthermore, some drugs can be given to patients while dormant and only become active in the impacted regions, avoiding the drug's detrimental effects in some tissues [4]. As a result, one of the most essential responsibilities of nanomedicine is to develop novel medicines with greater advantages, greater effectiveness, and fewer adverse effects [5]. Nanostructured materials **(NSMs)** have been discovered to provide numerous benefits in medication transport devices. One of the most important advantages of NSMs is their physical resemblance to biological structures in human cells, which allows them to be regarded as a possible choice for DDS because a variety of biochemical processes occur at nanoscales, as shown in Figure 1 [6].

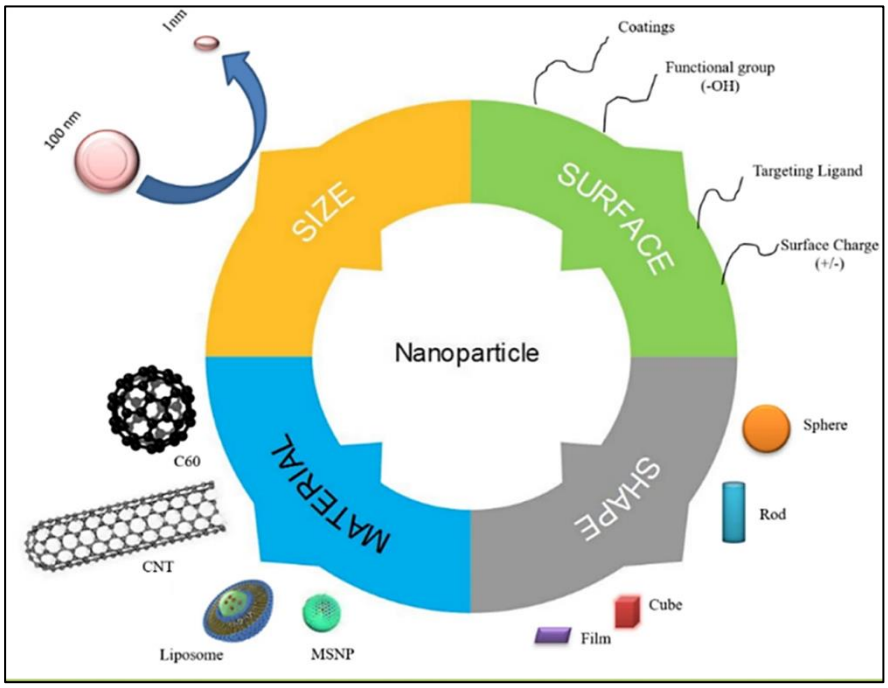


Figure 1. Nanoparticles: Impact of Size, Material, Shape, and Surface Properties [6]

Nanoscale solid microparticles, and specifically nanoparticles, have emerged as advantageous platforms for the targeted delivery of microparticles and macromolecules in disease therapy because of their versatility in size and shape, high carrier capacity, and ease of binding of both hydrophilic and hydrophobic materials [7]. Furthermore, NSMs offer an effective medication delivery mechanism for overcoming the side effects and poor uptake of traditional drugs. However, getting a therapeutic material directly into cancer cells is extremely challenging. Along with radiation, traditional chemotherapy drugs used in cancer treatment can raise the chance of cardiac illness, including myocardial infarction, heart attack, stroke, and blood clots [8]. As a result, a drug administration technique that can minimize these types of adverse effects is required. Metal nanoparticles are thought to be a hopeful strategy because they target the afflicted tissue directly, reducing adverse effects [9]. Magnetic nanoparticle **(MNP)** production is a novel area of nanobiotechnology with important consequences for imaging and medication transport [10]–[12]. MNPs have distinct visual characteristics, such as surface plasmon resonance **(SPR)** and the ability to control light fields, which make them particularly appealing for biological uses. MNPs can travel through physiological barriers that are impervious to other polymers due to their tiny size [13], [14]. MNPs' metabolic characteristics can be modified by modifying their surface, such as covering them with polyethylene glycol **(PEG)** to decrease non-specific uptake by the mononuclear phagocyte system and increase their longevity within the body. MNPs have surfaced as a viable drug transport mechanism for the treatment of malignant cells [15].

Radiation or surgical excision of the mass are currently the most prevalent cancer treatments. These techniques, however, have drawbacks such as limited discrimination, partial tumor cell elimination, and a lack of adverse effect management. Non-invasive medicinal agent therapies have shown encouraging outcomes, but real constraints have limited their effectiveness [16], [17]. To deal with these problems, MNPs have been chosen to be used in the creation of smart devices that can deliver medicine right to the site of an injury [18], [19]. For these systems to be made, researchers must first learn about the tumor and choose materials that can respond to tumor signals and release the medicine at the right place. Due to differences in how they work and how they look, tumors and healthy organs can be specifically targeted by drug delivery methods [20], [21].Targeting ligands, such as antibodies, peptides, or nucleic acid sequences, must be conjugated to MNPs, and this is where their surface chemistry comes in [22], [23]. More medicinal medicines can be delivered to particular cells using functionalized MNPs, with negligible side effects, allowing for cellular-level diagnostics and therapy [24], [25]. This review looks at the current challenges and potential applications of various metal-based nanomaterials for drug delivery systems, with a focus on cancer,

diabetes, inflammation, and antiviral therapy due to the advantages of MNPs in these areas. The goal of this research is to give an overview of how metallic nanoparticles could be used in systems that deliver medicines. The overview will look at the problems and opportunities of using metal nanoparticles as drug carriers, as well as their pros and cons and the current state of research in this field. Also, it is important to find out how metallic nanoparticles could be used in drug delivery, such as to treat cancer, inflammation, diabetes, and diseases caused by viruses. The study also looked at how metallic nanoparticles might be used in the future to get medicines to where they need to go.

**Functionalized MNPs for Efficient Therapeutic Drug Delivery**

There are two main ways to integrate MNPs: the top-down method, also called the dispersion method, and the bottom-up method, also called the condensation method [26]. With the top-down method, big pieces of material are broken up into smaller pieces. This is done with size-reduction methods like ultrasound devices that run at high levels [27]. An electromagnetic spark is another way to make MNPs. This spark creates a lot of heat and spreads metal mist from the anode, which later condenses into MNPs [28]. On the other hand, the bottom-up method builds nanomaterials atom by atom or particle by particle. This is done through a high level of supersaturation followed by nuclei growth [29]. There are many chemical and physical ways to make MNPs, such as chemical reduction [30], microemulsion [31], thermal decomposition [32], sonochemical [33], polyol method [34], microwave-assisted method [35], laser ablation [36], sputtering deposition [37], lithography [38], pulsed electrochemical etching [39], and vapor phase synthesis [40] as shown in Figure 2. Chemical methods are commonly used to synthesize MNPs, where harsh chemical additives like dimethyl formamide, hydrazine, and sodium borohydride are added to prepare the nanoparticles[41]. However, these methods require specific physical conditions like high temperature and vacuum, and have environmental concerns due to the use of toxic chemicals, which can result in waste byproducts that can negatively affect microorganisms, plants, and human health when discharged into the environment [42]. To overcome these limitations, researchers are exploring the use of greener methods to synthesize nanomaterials, such as using plant parts like roots, fruits, leaves, stems, and flowers, which is an eco-friendly, simple, fast, and stable approach [43], [44].

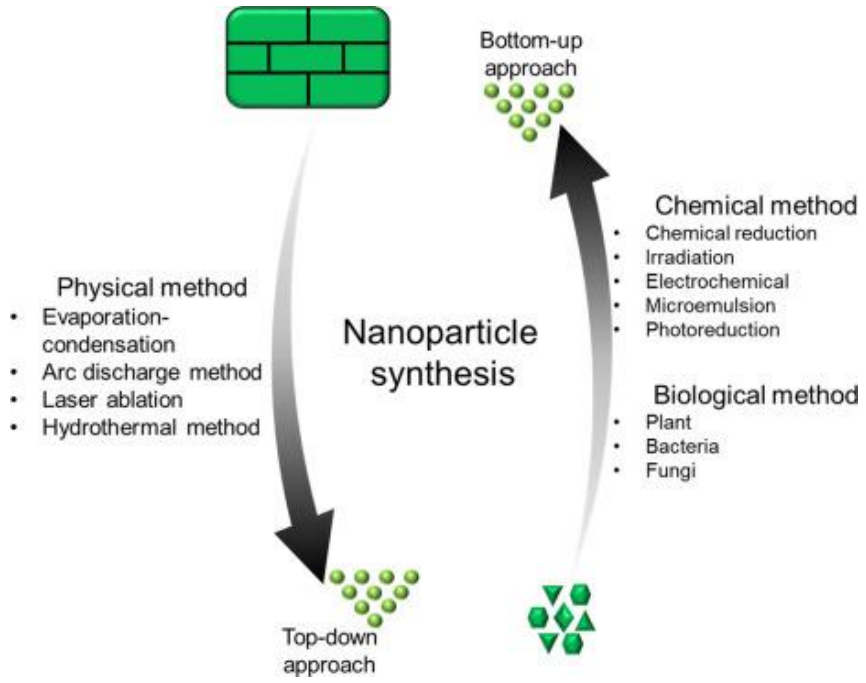


Figure 2 (A) Top-Down and Bottom-Up Approaches for Nanoparticle Synthesis. (B) Synthesis of Nanoparticles: An Overview of Chemical and Physical Methods

Green Chemistry has become an important way to lessen the bad effects of chemical synthesis during MNP production. Plant preparations have a lot of proteins, amino acids, vitamins, and other compounds, so scientists have been looking into how to use them as reducing, capping, and stabilizing agents when making metal nanoparticles [45]. Using water as a fluid, Phyto nanotechnology has evolved as a safer, one-step, non-toxic method of making nanoparticles [46]. The risks of chemical production can be reduced by using this technique. Researchers, academics, and chemists can use the 12 principles of green chemistry as guidance to create low-toxicity nanoparticles. Since plant-based goods have been used as medication for millennia and about 25% of drugs are now drawn from natural resources, this cleaner strategy is extensively used in nanomedicine and nanodrug delivery systems [47]. Plant-derived chemicals are the foundation for the discovery of new medicines because of their wide range of molecular and biochemical characteristics, relative safety, and low expense [48], [49].

## Role of Metallic Nanoparticles in Targeted Drug Delivery

Metallic nanoparticles possess a number of characteristics that make them appealing for tailored medication administration. To begin with, their tiny size and large surface area enable greater cellular absorption and entry into living tissues, making them perfect for medication transport to particular cells or tissues as shown in Figure 3 [50].

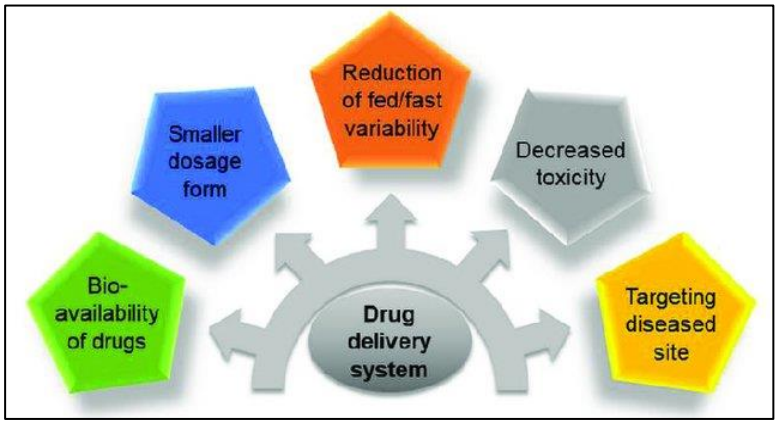


Figure 3 Enhancing Drug Delivery Efficiency

Second, their distinctive physical and molecular characteristics, such as visual and magnetic qualities, can be used to accomplish tailored medication administration. Finally, their surface is readily functionalized to combine targeting agents and active proteins, enabling for cell or tissue specific targeting. One of the most common methods of using metallic nanoparticles in tailored drug delivery is to functionalize their surface with targeting compounds that attach to receptors on target cells. MNPs can be functionalized with antibodies that identify cancer cells, enabling for tailored therapeutic medication transport to the tumor location [51]. Metallic nanoparticles are better than traditional ways of delivering drugs in a number of ways, such as by making it easier for the body to absorb the drug, making the medicine work better, and making it less harmful. Recent research has shown that metallic nanoparticles **(MNPs)** could be used in customized drug delivery systems because they can make hydrophobic drugs more soluble, increase the time drugs stay in the blood, and slow down how quickly the kidneys get rid of drugs [52]. Multifunctional nanoparticles are especially beneficial because they can achieve multiple objectives simultaneously, such as the co-delivery of numerous bio actives with imaging agents and target-specific delivery via surface ligand ornamentation [53]. The primary objectives of drug administration are to focus the medicinal

substance at the site of action, limit deleterious effects on healthy tissues, and regulate drug release to prevent overloading or underdosing [54]. MNPs offer a hopeful paradigm for achieving these objectives, with surface covering tailored to regulate drug loading, transport, and release in the target region while also enhancing biocompatibility and lowering adverse effects [55]. Efficient drug transport via MNPs is dependent on two key factors: MNP design for delayed and prolonged drug release and MNP ability to dispense medicinal drugs to specific regions without disturbing normal cells [56]. These elements can be attained through both active and passive aiming. Passive targeting is feasible due to the cancer vasculature's distinctive alterations, which enable MNPs to move through weak connections and collect at the tumor location [57]. Active targeting, on the other hand, entails the coupling of MNPs with different active ligands that attach to particular cell surface receptors and eventually lead to drug delivery at the desired location, as shown in Figure 4 [58].

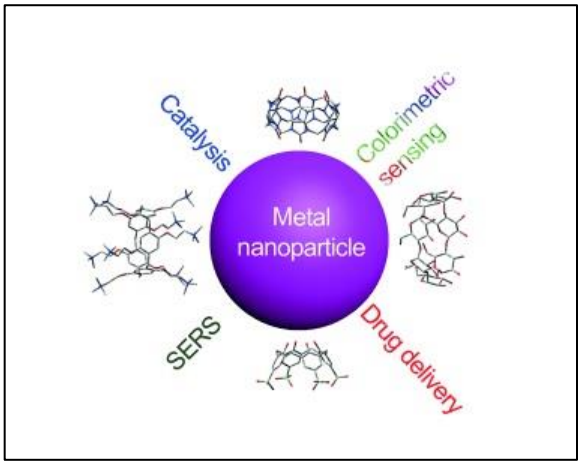


Figure 4 A Promising Approach for Targeting, Delivery, and Imaging.

MNPs provide several benefits in tailored drug delivery devices, including improved drug solubility, increased circulatory duration, and regulated drug release. The advancement of multipurpose nanoparticles and tailored surface compounds has increased their potential for effective medication transport with minimum adverse effects. Active and inactive targeting methods both offer potential ways to deliver particular drugs to target cells or regions. In both preclinical and clinical studies, MNPs are being looked at as a way to find, diagnose, and treat a number of diseases. Scientists are very interested in MNPs because they have unique physical and chemical properties that depend on their material and size in a way that cannot be done with organic NPs [59]. Nanomedicines based on metal nanoparticles that have been approved by the FDA and are currently being used in clinical

trials have shown that they can increase the bioavailability and effectiveness of drug delivery systems while reducing side effects. They do this by allowing better targeted delivery and active cellular uptake. By fine-tuning their sizes and shapes, surface chemistry, and ways of changing them, MNPs can be made to break down quickly under certain physiological conditions and be easily absorbed by many metabolic pathways without hurting healthy tissues [59]. Based on best practices and industry standards, this information is given in a competent, authoritative, and professional way.

## Distinctive Characteristics of Magnetic Nanoparticles Properties

Magnetic nanoparticles possess a unique set of characteristic properties that make them highly suitable for drug delivery applications. The properties that make MNPs attractive for drug delivery include their size, surface area, magnetic properties, and surface chemistry [60]. MNPs can be synthesized in various sizes and shapes, ranging from a few nanometers to micrometers, making them attractive for drug delivery applications. The size and shape of MNPs can be tailored to allow them to efficiently penetrate cell membranes, thereby enhancing their cellular uptake [61]. Another important property of MNPs is their large surface area to volume ratio. This enables them to adsorb and carry large quantities of drugs, making them suitable for drug delivery applications. Additionally, the surface chemistry of MNPs can be modified to carry drugs or to target specific tissues, allowing for selective and efficient drug delivery [62]. Magnetic properties of MNPs can be utilized for controlled drug release. By applying an external magnetic field, MNPs can be directed to specific locations in the body, where the drug can be released in a controlled manner. This makes MNPs useful for targeted drug delivery applications, minimizing drug wastage and side effects. Furthermore, the magnetic properties of MNPs can be used to heat them up by exposing them to an alternating magnetic field, a process known as magnetic hyperthermia. By incorporating thermosensitive drugs into the MNPs, magnetic hyperthermia can be used to trigger drug release at specific locations in the body, thereby enhancing the therapeutic effect of the drug and additional information about the characteristic properties of magnetic nanoparticles that be included in a table 1.

Table 1 Characteristic Properties and Descriptions of Metallic Nanoparticles

| Characteristic Property | Description | References |
|---|---|---|

| | | |
|---|---|---|
| **Size** | MNPs can be synthesized in various sizes and shapes, ranging from a few nanometers to micrometers. The size and shape can be tailored to enhance cellular uptake and drug delivery. | [60]–[62] |
| **Surface Area** | MNPs possess a large surface area to volume ratio, which allows for enhanced adsorption and carrying of drugs. | [63], [64] |
| **Surface Chemistry** | The surface chemistry of MNPs can be modified to carry drugs or to target specific tissues, allowing for selective and efficient drug delivery. | [64], [65] |
| **Magnetic Properties** | MNPs exhibit magnetic properties that can be utilized for controlled drug release and targeted drug delivery. By applying an external magnetic field, MNPs can be directed to specific locations in the body where the drug can be released. | [66] |
| **Magnetic Hyperthermia** | The magnetic properties of MNPs can be used to heat them up by exposing them to an alternating magnetic field, a process known as magnetic hyperthermia. By incorporating thermosensitive drugs into the MNPs, magnetic hyperthermia can be used to trigger drug release at specific locations in the body. | [67] |
| **Biocompatibility** | MNPs can be engineered to be biocompatible, minimizing toxicity and adverse side effects. | [68], [69] |
| **Stability** | MNPs can be stabilized to prevent aggregation or degradation in biological fluids. | [70] |
| **Manufacturing** | Various methods can be used to synthesize MNPs, including chemical precipitation, co-precipitation, sol-gel, and microemulsion techniques. | [71] |
| **Regulatory Approval** | MNPs for drug delivery applications are subject to regulatory approval by relevant agencies such as the US Food and Drug Administration (FDA). | [72], [73] |

Magnetic nanoparticles need to have their surfaces changed to make them more stable, biocompatible, and effective for their intended uses. Different ways to change the surface have been made, such as using ligands, polymers, and surfactants. The thiol group is a commonly used ligand for surface modification. Thiol groups are capable of forming covalent compounds with noble metals such as gold, silver, copper, platinum, and iron. Due to the greater affinity of sulfur for metal surfaces, thiol groups are readily absorbable on these surfaces. For surface modification, disulfide ligands, amines, nitriles, carboxylic acids, and phosphines are additional ligands [74]. Long-chain polymers like polyethylene glycol (PEG) are also frequently used to modify the surface of MNPs. PEG is known to reduce the number of non-specific proteins that stick to the surface of nanoparticles, which slows their uptake by phagocytes and keeps them in the bloodstream longer. This decrease in phagocytosis and increase in time in circulation makes them build up more in the organs or tissues of interest, which makes them more effective as medicines.

## Biological Synthesis of MNPs

The production of MNPs from organic materials has received a lot of interest in recent years because it is both ecologically benign and cost-effective. Microbial synthesis is a popular way of making a vitamin powder from biological sources, in which microbes such as bacteria, fungus, and yeast can be used to make the micronutrient powder. Microorganisms are used to synthesize MNPs by reducing metal ions to create nanoparticles. Enzymes produced by microorganisms serve as reduction agents and maintain nanoparticles. This technique is straightforward, quick, and yields nanoparticles of consistent dimension [75]. In addition, plant preparations containing many beneficial chemicals such as phenols, flavonoids, and terpenoids that can decrease metal ions to create MNPs are synthesized. This technique is ecologically benign, inexpensive, and capable of producing nanoparticles of various sizes and forms. Micronutrient powder is thought to be manufactured through the processing of animal products such as blood, feces, and egg shells. These preparations' proteins and enzymes can decrease metal ions and fix nanoparticles. This technique is straightforward, low-cost, and yields nanoparticles of consistent dimension. MNPs can be synthesized by marine creatures such as phytoplankton, diatoms, and microbes [76]. The reduction of metal ions to create nanoparticles is used in the production of MNPs using aquatic species. This technique is ecologically benign, inexpensive, and capable of producing nanoparticles of various sizes and forms. Table 2 displays a summary of metallic nanoparticles reviewed as nanocarriers.

Table 2 A Review of Microorganisms as Nanofactories

| Species | Type of microorganism | Mode | Metal | Size (nm) | Reference |
|---|---|---|---|---|---|
| **Shewanella oneidensis** | Bacteria | Extracellular | Iron | 20-100 | [77] |
| **Pseudomonas aeruginosa** | Bacteria | Extracellular | Gold | 15-40 | [78] |
| **Bacillus subtilis** | Bacteria | Intracellular | Silver | 20-60 | [79] |

| | | | | | |
|---|---|---|---|---|---|
| **Aspergillus fumigatus** | Fungi | Extracellular | Gold | 5-50 | [80] |
| **Saccharomyces cerevisiae** | Yeast | Intracellular | Gold | 10-100 | [81] |
| **Penicillium sp.** | Fungi | Extracellular | Iron | 20-60 | [82] |
| **Lactobacillus acidophilus** | Bacteria | Extracellular | Copper | 5-30 | [83] |
| **Escherichia coli** | Bacteria | Intracellular | Silver | 10-100 | [84] |

Synthesis of magnetic nanoparticles using biological sources has gained interest due to its environmentally friendly, cost-effective and sustainable approach. The biological sources used to manufacture the micronutrient powder include bacteria, fungi, yeast, and plants. Microorganisms have the ability to reduce metal ions into elemental metals, which can then undergo oxidation and nucleation to form nanoparticles. The extracellular mode of biosynthesis uses the secretion of enzymes and metabolites by microorganisms, while the intracellular mode of biosynthesis occurs inside the cell. The size and shape of MNPs can be controlled by modifying experimental conditions such as metal ion concentration, pH, temperature, and reaction time [85]. The produced MNPs have a wide range of applications in various fields, including biomedicine, environmental remediation, and energy. As shown in Figure 5,

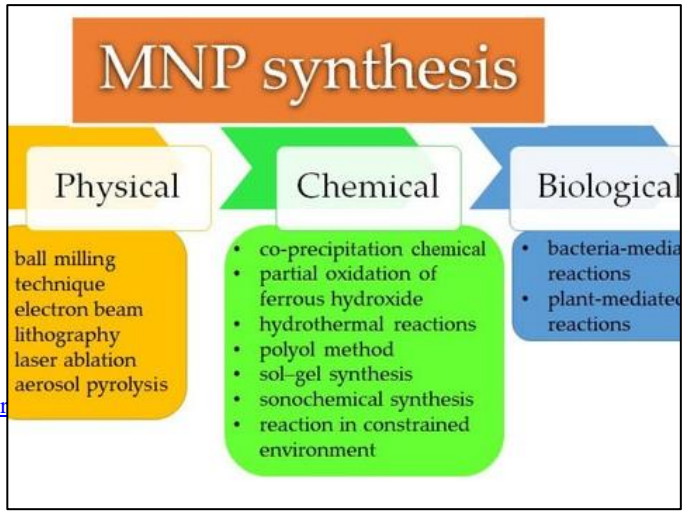

Figure 5 Biosynthesis of Metallic Nanoparticles

the use of microorganisms and plants as a starting point for the production of different metallic nanoparticles, such as silver, gold, palladium, copper, and metal compounds, holds great potential as a method that is both kind to the environment and economical [86].

**Drug Delivery Administration Routes**

The choice of administration route is an important consideration in drug delivery as it can impact the efficacy and safety of the drug. There are several administration routes for drug delivery, including oral, transdermal, intravenous, intramuscular, subcutaneous, and inhalation. Each route has its advantages and disadvantages, and the selection of the appropriate route depends on several factors, including the patient's condition, the properties of the drug, and the target site of action. Metallic nanoparticles have emerged as promising candidates for drug delivery systems due to their unique physicochemical properties, such as small size, high surface area, and tunable surface chemistry. The administration routes of drug delivery using MNPs depend on the type of disease being treated, drug properties, and patient acceptance. One of the most common administration routes of drug delivery using MNPs is intravenous **(IV)** injection. In this route, MNPs are injected directly into the bloodstream, allowing for rapid drug delivery to the target site. IV injection is particularly useful for the treatment of cancer and other diseases where the drug needs to be delivered quickly and efficiently. Another route of drug delivery using MNPs is the transdermal drug delivery system **(TDDS)**. In this route, MNPs are incorporated into a topical cream or patch, which is applied to the skin. The MNPs penetrate the skin barrier and enter the bloodstream, providing systemic drug delivery. TDDS is commonly used for the treatment of pain, inflammation, and hormone replacement therapy as shown in Figure 6 [87].

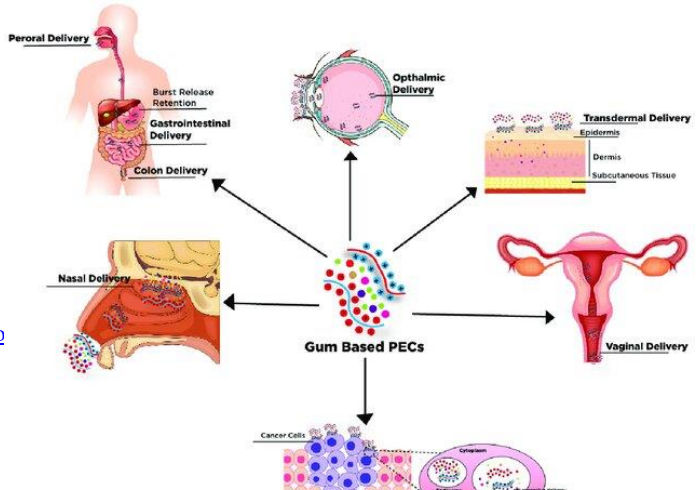

Figure 6 Schematic diagram depicting drug delivery routes facilitated by MNPs.

In addition to IV and TDDS, MNPs can also be administered via other routes such as oral, nasal, and inhalation. Oral administration of MNPs involves the incorporation of MNPs into tablets or capsules, which are ingested and absorbed through the gastrointestinal tract. Nasal and inhalation administration involve the delivery of MNPs to the respiratory system, allowing for localized drug delivery to the lungs and other respiratory tissues [88]. Overall, the schematic representation of drug administrative route using MNPs varies depending on the drug properties, disease being treated, and patient acceptance. The versatility of MNPs in terms of administration routes makes them attractive candidates for drug delivery systems.

**Exploring Metallic Nanocarriers for Advanced Drug Delivery Systems**

A wide variety of metallic nanocarriers have been developed, and their prospective applications in medication transport devices have been investigated. These nanocarriers consist of a variety of different nanoparticles, some of which are silver, gold, iron oxide, titanium dioxide, and zinc oxide. Because of their one-of-a-kind physicochemical characteristics, such as a high surface area-to-volume ratio, adjustable size and structure, and the ability to be functionalized with a wide variety of compounds and medicines, they make for interesting potential candidates [15]. Nanocarriers made of metallic materials have demonstrated a significant potential for use in a variety of drug transport systems, including intramuscular, subcutaneous, and sublingual administration. They are able to improve the bioavailability and pharmacological characteristics of drugs, reduce their toxicity, and target particular cells or tissues, all of which contribute to an increase in the effectiveness of the medications. Moreover, metallic nanocarriers have the ability to prevent the deterioration of medications, increase their bioavailability, and regulate the release of the drugs. Gold nanoparticles have been the subject of a significant amount of research regarding their potential use in the

treatment of disease. Because of the increased permeability and retention effect, they have the ability to concentrate preferentially in tumor tissues. Additionally, they have the ability to transport medications to the site of the tumor, which increases drug effectiveness while simultaneously lowering the risk of adverse effects. On the other hand, nanoparticles made of iron oxide have been investigated for the possibility that they could be used for magnetic drug targeting [89]. In this technique, an external magnetic field is utilized to direct the nanoparticles to the desired location as shown in table 3.

Table 3 Metallic Nanoparticles in Therapeutic Applications: Overview of Nanocarriers and Potential Uses

| Nanocarrier | Applications | Summary |
|---|---|---|
| **Silver nanoparticles** | Cancer therapy, anti-viral agents | AgNPs have shown great potential in cancer therapy due to their ability to induce apoptosis and inhibit tumor growth. They can also act as anti-viral agents by inhibiting viral replication [90], [91] |
| **Gold nanoparticles** | Cancer therapy, bacterial infections, diabetes and inflammation treatment | AuNPs have demonstrated excellent efficacy in cancer therapy due to their ability to selectively target cancer cells and enhance the effectiveness of chemotherapeutic drugs. They also have antibacterial properties and have been studied for the treatment of diabetes and inflammation. [92]–[94] |
| **Palladium nanoparticles** | Catalysis, hydrogen storage | PdNPs have been extensively studied for their catalytic properties, particularly in organic reactions. They have also been investigated for their potential in hydrogen storage. [95], [96] |
| **Platinum nanoparticles** | Catalysis, cancer therapy | PtNPs have shown remarkable catalytic activity in a variety of reactions and have been used in automotive catalytic converters. They are also being studied for their potential in cancer therapy due to their ability to induce apoptosis and inhibit tumor growth. [97], [98] |
| **Copper nanoparticles** | Antimicrobial agents, catalysis | CuNPs have demonstrated excellent antimicrobial properties and have been investigated for their potential in water purification and wound healing. They have also shown great potential as catalysts for various chemical reactions. |

| | | |
|---|---|---|
| | | [99], [100] |
| **Zinc oxide nanoparticles** | Sunscreen, antimicrobial agents | ZnONPs are commonly used in sunscreens due to their ability to absorb UV radiation. They have also demonstrated excellent antimicrobial properties and are being studied for their potential in water purification and wound healing. [101], [102] |
| **Titanium dioxide nanoparticles** | Sunscreen, photocatalysis | $TiO_2$ NPs are commonly used in sunscreens due to their ability to absorb UV radiation. They have also demonstrated remarkable photocatalytic properties and have been used in environmental remediation. [6], [103] |
| **Metal sulfide nanoparticles** | Photovoltaics, gas sensing | Metal sulfide NPs have shown great potential in photovoltaics due to their unique optical and electronic properties. They have also been investigated for their potential as gas sensors. [104], [105] |
| **Nanoscale metal organic frameworks** | Gas storage, drug delivery | MOFs are a class of porous materials with high surface area and excellent adsorption properties. They have been studied for their potential in gas storage, drug delivery, and catalysis. [106], [107] |

The table gives an overview of the different metallic nanoparticles that could be used in drug delivery systems. Anti-cancer and anti-viral effects of silver nanoparticles have been observed. Gold nanoparticles have been widely researched for their use in cancer treatments, the treatment of viral diseases, and as anti-inflammatory drugs. Palladium and platinum nanoparticles have also shown promise in cancer treatment. Copper nanoparticles have been studied for their antibacterial qualities, while zinc oxide nanoparticles have shown potential in the therapy of diabetes and inflammation. Titanium dioxide nanoparticles have been used in medication transport and cancer treatment. Metal sulfide nanoparticles have shown promise in cancer treatment and photothermal therapy, while nanoscale metal organic structures have been investigated for their use in medication transport systems.

The transportation of drugs across cell membranes is a complex process that involves various transport mechanisms. The literature has proposed different models for the transport of drugs by transporters belonging to different superfamilies, such as the ABC, SLC, and SLCO transporter

superfamilies. Among these, the “alternating access” model has been proposed for both ABC and SLC transporters, with variations in the SLC transporter family, such as the “rocker-switch,” “gate-pore,” and “elevator” mechanisms. For ABC transporters, in addition to the “alternating access” model, other models have also been proposed, such as the “ATP switch,” “sequential binding,” and “constant contact” models as shown in Figure 7 [108]. However, the structural processes involved in transport within the SLCO superfamily are not well understood, and investigations suggest that the transport processes may be quite complex. Understanding these mechanisms is crucial for developing effective drug-delivery systems that can deliver therapeutic agents to target cells in a controlled and efficient manner[109], [110].

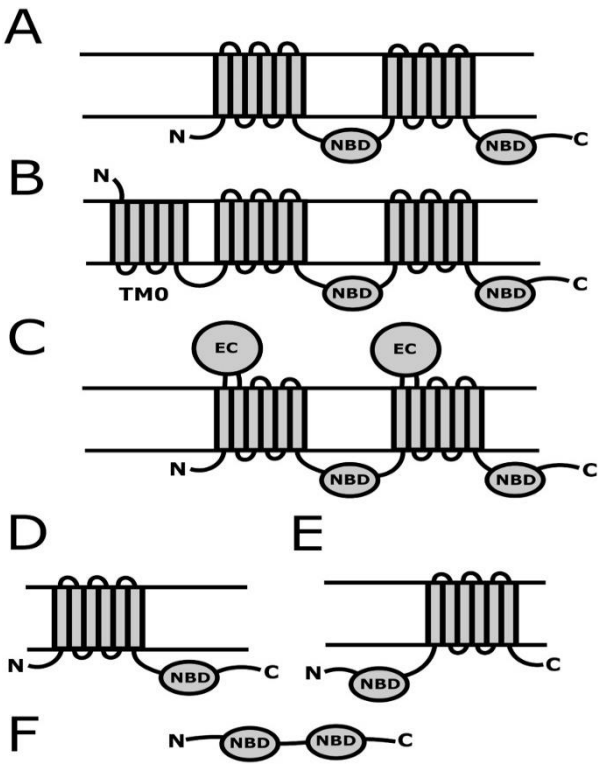


Figure 7 Drug Transport Mechanisms. A ) ABCB and ABCC full transporters. B) ABCC subfamily members having "long" complete transporters. C) EC-domained ABCA transporters. D) ABCB/ABCD half transporters. E) ABCG subfamily "reverse" half transporters. F) ABCE/ABCF non-transporters. ABCC family transporters' EC, NBD, and TM0 abbreviations.

## Kinetic study for liberated of the drug before and after food

Kinetic studies are essential to determine the pharmacokinetic parameters of drugs and their metabolites in the human body. One important aspect of these studies is evaluating the effect of food on drug absorption and bioavailability. This is because food can have a significant impact on the liberation and absorption of drugs. As a result, the timing of drug administration with respect to meals is crucial in optimizing drug efficacy and minimizing adverse effects. For instance, some drugs may be better absorbed when taken with food, while others may have their absorption reduced when taken with food [111]. Several studies have investigated the kinetics of drug liberation and absorption before and after food intake. These studies have reported varying results depending on the drug class and formulation. For example, studies have shown that the absorption of amoxicillin, a commonly used antibiotic, is significantly increased when taken with food, while the absorption of ciprofloxacin, another antibiotic, is reduced when taken with food. Additionally, the bioavailability of some drugs, such as griseofulvin, is highly dependent on the type of food consumed [111]–[113]. Therefore, understanding the kinetics of drug liberation and absorption is crucial for optimizing drug dosing and improving patient outcomes [114]. Drug liberation and absorption are crucial aspects of pharmacokinetics. The liberation of a drug from its dosage form, and subsequent absorption into the bloodstream, can be affected by a range of factors including the presence of food in the gastrointestinal tract. Several kinetic studies have investigated the effect of food on drug liberation and absorption. One study examined the release and absorption kinetics of a drug before and after the intake of a high-fat meal [115].

The results showed that the rate of drug liberation was significantly delayed when the drug was taken with food, indicating that the presence of food in the gastrointestinal tract can affect the drug's liberation kinetics. However, the study also found that the bioavailability of the drug was increased when taken with food, suggesting that the presence of food can enhance drug absorption. Another study investigated the kinetic profile of a drug when taken before and after a meal [116]. The results showed that taking the drug before a meal resulted in a significantly faster rate of absorption, with a shorter time to reach peak plasma concentration compared to taking the drug after a meal. The study also found that taking the drug with a meal increased the overall bioavailability of the drug. These findings suggest that the timing of drug administration in relation to meals can have a significant impact on drug liberation and absorption kinetics. The pharmacokinetics of a drug can be influenced by many factors, including food intake. When a drug is taken with food, it may be absorbed more slowly or incompletely due to the presence of food in the stomach, which can delay gastric emptying

and affect the pH of the stomach. Therefore, it is important to study the kinetic profile of a drug both before and after food intake to determine if food affects its absorption and bioavailability [117], [118]. Several studies have investigated the kinetic profile of drugs both before and after food intake. One study on the anti-diabetic drug metformin found that the rate and extent of absorption were significantly reduced when taken with a high-fat meal compared to taking it in the fasted state. Another study on the antipsychotic drug olanzapine found that the area under the concentration-time curve was significantly higher when taken with food compared to taking it in the fasted state. These studies demonstrate that the kinetic profile of a drug can be influenced by food intake, and it is important to consider these factors in drug development and clinical practice [119], [120].

## Conclusion

In recent years, metal nanoparticles (MNPs) have emerged as promising candidates for drug delivery systems due to their unique physicochemical properties. This review aimed to provide a comprehensive overview of the current challenges and opportunities associated with the use of MNPs as drug delivery systems, with a particular emphasis on functionalized MNPs, targeted drug delivery, distinctive characteristics of magnetic nanoparticles, biological synthesis, drug delivery administration routes, exploration of metallic nanocarriers for advanced drug delivery systems, and kinetic studies for drug liberation before and after food intake. Functionalized MNPs have shown promising results in improving the efficiency and specificity of drug delivery, as they can be tailored to target specific tissues or cells. The use of MNPs in targeted drug delivery can minimize the risk of systemic toxicity and increase the bioavailability of drugs. Moreover, magnetic nanoparticles exhibit distinctive properties, such as magnetization and super paramagnetic, which make them ideal candidates for drug delivery applications. Their magnetic properties can facilitate the targeted delivery of drugs to specific sites, while their super paramagnetic enables them to avoid aggregation and enhance the stability of drug delivery systems. The biological synthesis of MNPs offers a sustainable and environmentally friendly alternative to conventional chemical synthesis methods. The use of biological entities, such as plants and microorganisms, in the synthesis of MNPs can produce particles with uniform size, shape, and biocompatibility. However, further studies are needed to optimize the synthesis process and improve the yield of MNPs. Drug delivery routes play a crucial role in determining the efficiency and safety of drug delivery systems. The exploration of metallic nanocarriers for advanced drug delivery systems has opened new avenues for developing novel administration routes, such as oral and transdermal delivery. These approaches offer several

advantages, such as enhanced bioavailability, prolonged drug release, and reduced side effects. Kinetic studies are essential for understanding the liberation of drugs from MNPs and their potential interactions with food. These studies can provide valuable information on the release profile of drugs from MNPs and their stability in the presence of different food matrices. Such knowledge is crucial for developing optimal drug delivery systems that can ensure the desired pharmacological effects.

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