Metallic Nanoparticles in Drug Delivery: Toxicity and Biodegradability Considerations

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ABSTRACT

Metal nanoparticles (MNPs) are becoming more and more interesting as possible drug delivery systems because they have special physical and chemical properties, such as a large surface area, low cost, and the ability to carry a lot of therapeutic agents. Because of these features, MNPs are very good at targeting particular tissues, making drugs more bioavailable, and making different treatments more efficient. But the growing use of MNPs in biomedical settings makes people worry about how toxic they might be and how long it will take for them to break down in the body. MNPs' toxicity depends on many things, such as their size, shape, surface charge, composition, and changes made to their surface. Even though MNPs can be very helpful in therapy, too much of them in living things can have bad effects, like oxidative stress, inflammation, and problems with how cells work. These nanoparticles can affect many systems, mainly the lungs, kidneys, and liver, based on how they are delivered and what kind of particles they are. Also, knowing how MNPs interact with immune systems and cell membranes is important for reducing their harmful effects and making sure that drug delivery applications are safe. Biodegradability is another important thing to think about when judging MNPs for drug delivery uses. Unlike other drug carriers, MNPs need to be made so that they break down into harmless byproducts once they've done their job. Most of the time, biodegradable MNPs are made from biodegradable plastics or metal alloys that can break down using chemical or biological processes. Biodegradation that works well lowers the chance that particles will build up in tissues for a long time and makes it easier for the body to get rid of them, so there is little damage to the environment

Keywords: Metallic nanoparticles, Drug delivery, Toxicity, Biodegradability, Biocompatibility

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INTRODUCTION

Metallic nanoparticles (MNPs) have gotten a lot of attention in the area of drug delivery because they have unique qualities that make them better than other drug carriers in many ways. The size of these nanoparticles is usually between 1 and 100 nanometres. They have special physical properties, like a high surface area-to-volume ratio, being easy to functionalize, and being able to hold and give different medicinal agents more effectively. MNPs can be made of different metals, like gold, silver, iron, and platinum. Depending on the purpose, each metal has its own benefits. Because they are so flexible, drug delivery systems can be made that can target particular tissues or cells. This makes treatments more effective and precise while reducing the side effects that are common with other drug delivery methods. Even though these things are good, using MNPs in biological settings, especially for drug delivery, causes a lot of worry because they might be harmful and not break down properly over time. Because MNPs are so small and have a very reactive surface, they can interact with living processes in a lot of different ways. Nanoparticles can be taken up by cells through a process called endocytosis.

Once inside the cell, they may build up and mess up how the cell works. The harm to cells that happens can cause inflammatory reactions, oxidative stress, and even organ poisoning, which makes it hard for them to be widely used in clinical settings. Figure 1 shows metals nanoparticles that are used to carry drugs, bringing up safety worries about their toxicity and ability to break down naturally

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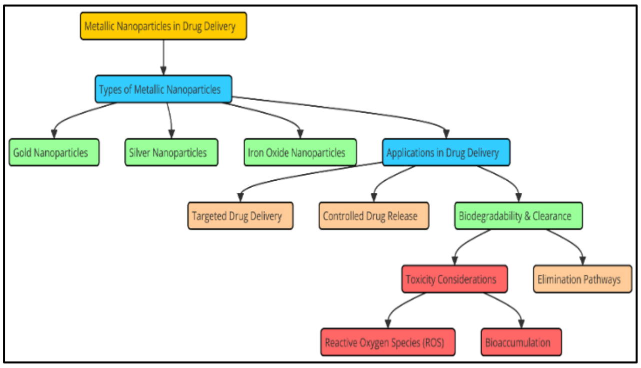

Figure 1: Metallic Nanoparticles in Drug Delivery: Toxicity and Biodegradability Considerations

The main reason for these toxicity worries is that MNPs can interact with cell walls, proteins, and nucleic acids, which can throw off the usual balance of cells. Many things, like their size, form, surface charge, and makeup, can change how harmful MNPs are. Because these nanoparticles' qualities can be changed to fit different uses, it is very important to know how these changes affect how they interact with living things to make sure they are safe [1]. Biodegradability is another important thing to think about when using MNPs to deliver drugs. For drug delivery systems to work and be safe, MNPs must not only do what they're supposed to do, but they must also break down naturally when their time is up. Nanoparticles that don't break down can build up in tissues over time, which could have harmful effects that last for a long time [5]. Biodegradable MNPs, on the other hand, are made to break down into harmless byproducts that the body can safely get rid of. Depending on what the nanoparticles are made of, the biodegradation process can happen through chemical, enzymatic, or hydrolytic routes.

A lot of the time, biodegradable MNPs is made from metal alloys, biodegradable metal oxides, or biodegradable polymers. These materials let drugs break down and release in a controlled way. This method not only lowers the chance of long-term buildup, but it also makes sure that the particles don't hurt the environment [2]. It is very important to know both how poisonous MNPs are and how quickly they break down when they are used to deliver drugs.

II. Related Work

A lot of research has been done on using metallic nanoparticles (MNPs) in drug delivery systems over the last few decades because they might help treat a wide range of diseases better. A lot of research has gone into making MNPs better at delivering drugs to specific areas, looking at their physicochemical properties, biocompatibility, and therapeutic effectiveness [3]. But as the development of these nanoparticles for use in medicine moves forward, worries about their safety and ability to break down have become very important. To learn more about the harmful effects of MNPs on living things is an important area of study. Several studies have shown that MNPs' toxicity depends on their size, shape, surface charge, and the materials they are made of. For instance, gold nanoparticles, which are often used to carry drugs, have been shown to hurt cells and cause inflammation when they are present in higher amounts [4]. A study by Jain et al. showed that gold nanoparticles might cause oxidative stress in cells, which can damage DNA and kill cells. Furthermore, Bago et al. say that silver nanoparticles, which are known to kill microbes, have also been shown to kill cells, especially kidney and liver cells. The main way that MNPs are harmful is that they can make reactive oxygen species (ROS), which can mess up the way cells work, damage mitochondria, and set off defensive reactions. At the same time, biodegradability has been a big part of making MNPs for drug administration [6]. Nanoparticles that don't break down can build up in cells and cause long-term health problems. Because of this, a lot of research has been done on making biodegradable MNPs using materials like biodegradable polymers and biocompatible metals. For example, Liu et al. (2016) showed that iron oxide nanoparticles could break down into iron ions, which are naturally handled by the body [7]. This lowers the risk of buildup and poisoning. In the same way, polyvinyl alcohol (PVA) films have been used to make biodegradable gold nanoparticles that can slowly break down and release medicinal agents without building up in tissues. Recent research has focused on looking at both biodegradability and toxins at the same time. Scientists are looking into changing the surface of MNPs by adding safe molecules like polyethylene glycol (PEG) to make them less reactive to the immune system and more compatible with living things [8]. Also, scientists are looking into new ways to make sure that MNPs break down safely in the body. Table 1 summarizes related work, highlighting key findings, challenges, and the scope of various methods used. These include using biodegradable coatings, alloys, or hybrid materials that are less likely to make harmful byproducts

Table 1: Summary of Related Work

Method	**Key Finding**	**Challenges**	**Scope**
Chemical Reduction	Efficient and cost-effective for synthesizing MNPs with controlled size.	Difficult to achieve uniform size and surface characteristics.	Widely applicable to various metals, scalable for production.
Electrochemical Deposition	Allows precise shape and size control for nanostructures like rods and wires.	Requires sophisticated equipment and precise control over deposition.	Suitable for precise control, useful in diagnostics and therapy.

Synthesis of Biodegradable MNPs [9]	Reduces long-term toxicity through biodegradability.	Biodegradability is unpredictable; some nanoparticles degrade slowly or release toxic byproducts.	Helps minimize nanoparticle accumulation and improve safety.
MTT Assay	Provides reliable cell viability data for MNP toxicity screening.	Does not provide detailed information on organ-specific toxicity.	Quick and cost-effective screening of cytotoxicity in early stages.
LDH Assay	Effective for determining membrane damage due to MNP exposure.	LDH release may not correlate with in vivo toxicity in some organs.	Useful for assessing membrane integrity and quantifying damage.
In Vivo Toxicity Assessment	Demonstrates potential toxicity in liver, kidneys, and lungs.	Difficult to simulate human-specific toxicity and long-term effects in animal models.	Crucial for assessing systemic toxicity in animal models.
Nanoparticle Size Control [10]	Small nanoparticles influence toxicity, with smaller particles being more cytotoxic.	Small nanoparticles can cause unintended biological interactions and accumulation in organs.	Improves therapeutic efficacy by minimizing unwanted biological effects.
Surface Functionalization	Reduces immune response and improves biocompatibility.	Surface modifications may alter therapeutic potential or targeting ability.	Improves nanoparticle biocompatibility and reduces immune rejection.
Biodegradation Kinetics	Biodegradation rates can be controlled to match therapeutic timelines.	Impact of biodegradation products on the immune system is still under research.	Essential for safe use of biodegradable nanoparticles in therapy.
Organ-Specific Toxicity Studies [11]	Reveals that liver and kidneys are primarily affected by nanoparticle accumulation.	Not all biodegradable polymers are compatible with drug delivery applications.	Vital for determining the safety and long-term effects of MNPs in organs.
Incorporation of Biodegradable Polymers	Polymers like PLGA enhance biodegradability and reduce toxicity in vivo.	Achieving the right balance between biodegradability and nanoparticle stability is challenging.	Important for enhancing biocompatibility and biodegradability of MNPs in clinical settings.

TOXICITY OF METALLIC NANOPARTICLES

A. Cellular and molecular mechanisms of toxicity

Metallic nanoparticles (MNPs) are mostly harmful because they interact with molecular and cellular structures. MNPs can get into cells through endocytosis, a process in which cell walls take in the nanoparticles and store them inside the cell as vesicles. Once inside, the particles may stay in the cytoplasm or be sent to parts of the cell like the nucleus, mitochondria, or lysosomes, where they can stop the cell from working normally [12]. The most important way that nanoparticles are harmful is by making reactive oxygen species (ROS) when they interact with cell parts like DNA, lipids, and proteins. Oxidative stress can be caused by ROS. This can damage DNA, lipids, and proteins, all of which can make cells not work properly. MNPs can also mess up the function of mitochondria, which makes it harder for cells to make energy and can lead to apoptosis or death. Nanoparticles' toxicity is also affected by their surface properties, such as their size, charge, and any changes that have been made to the surface. For instance, nanoparticles that are smaller tend to have more surface area and more reaction, which can damage cells more severely [13]. In addition, MNPs' ability to link to proteins and change their shape can trigger immune reactions and inflammation pathways, making the toxins even stronger.

B. Acute vs. chronic toxicity

Metallic nanoparticles can be harmful in two ways: they can cause short-term or long-term effects, and each has different biological effects. Acute poisoning usually happens when MNPs are exposed in large amounts or for a short time. It shows up as serious, instant damage to the body. Acute toxicity to MNPs can cause ROS to be made quickly, which can cause inflammation, tissue damage, and organ dysfunction. For example, it has been shown that high amounts of silver nanoparticles can quickly damage the liver and kidneys because they can damage cells and cause reactive stress [14]. Chronic toxicity, on the other hand, happens when smaller amounts of MNPs are exposed for a long time and is usually linked to the buildup of nanoparticles in different organs. Because nanoparticles stay in the body and cause oxidative stress and inflammation all the time, long-term contact can hurt organs and cause them to fail. Besides that, long-term exposure to MNPs has been connected to the growth of fibrosis and cancer, since oxidative stress can cause genetic changes and abnormal cell growth. It can be hard to figure out how poisonous MNPs are over time because their harmful effects can happen slowly and in subtle ways. The effects may not be obvious at first, but they can build up over time and have very bad effects on health [15]. To make safer drug transport methods, we need to know how the short-term and long-term harmful effects of MNPs balance each other out.

C. Impact on different cell types (e.g., liver, kidney, immune cells)

Metallic nanoparticles are harmful to different types of cells in different ways, because each type of cell has its own duties and is sensitive to nanoparticles. Because it is one of the main organs that gets rid of unwanted chemicals, the liver is especially subject to MNP buildup. Researchers have found that nanoparticles, like gold and silver nanoparticles, can build up in the liver and damage it. This harm is usually caused by inflammation, oxidative stress, and changes in the way liver cells use energy, which can lead to liver damage, fibrosis, or failure [16]. In the same way, kidney cells are very vulnerable to the harmful effects of MNPs because they filter and get rid of waste. When MNPs build up in kidney tissues, they can damage glomeruli, cause inflammation in the kidneys, and make the kidneys less able to do their job.

MNPs can interact with immune cells including dendritic cells, macrophages, and neutrophils in the immune system, therefore generating inflammation. When these cells absorb nanoparticles, they can spew chemokines and pro-inflammatory cytokines. Problems with the immune system and continuous inflammation might result from this. Furthermore influencing the body's capacity to fight off diseases and cancers might be MNPs' changes in the communication between immune cells. The fact that MNPs affect different kinds of cells indicates the need of considering tissue-specific toxicity while designing nanoparticle-based medication delivery systems.

BIODEGRADABILITY OF METALLIC NANOPARTICLES

A. Biodegradation mechanisms

Natural breakdown of metallic nanoparticles (MNPs) either by chemical or biological means results in smaller, non-harmful fragments. We term this process biodegradation. Maintaining nanoparticles from accumulating in tissues over time—which can lead to long-term damage—is mostly dependent on this mechanism. MNP biodegradation largely proceeds by oxidation, hydrolysis, and enzyme breakdown. For metals like iron and silver, oxidation is quite crucial as it generates metal ions when they come into touch with oxygen or ROS in the body. These ions are usually less harmful than the nanoparticles themselves most of the time. Iron oxide nanoparticles, for example, can oxidise and become iron ions the body can more readily utilise.

Hydrolysis is another common way that things break down, especially metal oxide nanoparticles. This is when water molecules break the bond between the metal and oxide, letting metal ions escape. Enzymatic decay is a biological process in which enzymes, which can be found naturally in the body or added by changing nanoparticles, help break down nanoparticles [17]. Esterases and proteases, for instance, can break down the compostable polymeric coats on nanoparticles, which eventually causes them to break down. It is very important that these biodegradation processes work well so that MNPs don't stay in the body for too long and are safely removed after they've done their job.

B. Materials and pathways for nanoparticle degradation

Biodegradable metals nanoparticles have been made from a number of different materials, with the goal of speeding up their breakdown and lowering their toxicity. When choosing materials for MNPs, biocompatibility, biodegradability, and the ability to break down into harmless byproducts are usually the main things that are looked at. Alloys and hybrid materials that mix metals with compostable plastics or metal oxides are often used. Examples include gold-silver alloys, iron oxide, and zinc oxide nanoparticles. People choose these materials because they break down easily and don't tend to build up in the body. Zinc oxide nanoparticles, for example, are known to break down into zinc ions.

Zinc ions are important micronutrients for the body and don't cause major harm when present in small amounts. Biodegradable polymeric coatings are another option. These coats let the drug break down and release slowly. Metal nanoparticles are often mixed with materials like poly(lactic-co-glycolic acid) (PLGA) and polycaprolactone (PCL) to make them more biodegradable. The main way these materials break down is through hydrolysis, which is when water molecules break down the polymer backbone over time. This lets the medicinal nanoparticles out slowly. These plastic coats can also make MNPs more biocompatible by keeping them from interacting directly with living cells and making them less harmful. So, the materials used to make nanoparticles need to be carefully chosen to make sure that they break down effectively and that the body can safely get rid of the breakdown products.

C. Effects of degradation products on biological systems

Figuring out how safe and efficient the drug transport mechanism is overall depends on the breaking down of metallic nanoparticles (MNPs). Ideally, the effects of deterioration should not be negative and should be readily eliminated by living entities. Iron oxide nanoparticles, for instance, break down into iron ions—which are required for numerous biological functions. Little levels of these ions may be safely handled by the body by regular processes including cells absorbing them and the kidneys and liver eliminating them. On the other hand, too many metal ions could finally turn harmful. For instance, it has been shown that when large amounts of silver nanoparticles are released, they cause oxidative stress and cell damage, especially to immune cells and kidney organs.

In the same way, zinc oxide nanoparticles can release zinc ions that, in large amounts, can damage cells and make them poisonous, especially in the liver and kidneys. Reactive oxygen species (ROS) can be made when these metal ions are released. ROS can damage cellular parts like lipids, proteins, and DNA, which can cause inflammation, death, and possibly long-term damage to tissues. Some breakdown products may also have molecular effects that were not meant to happen, like changing how cells talk to each other or how the defence system responds. Because of this, it is very important to carefully look at the breakdown products of MNPs to make sure they don't pose a big health risk. The main goal of this field of study is to create nanoparticles that break down slowly and produce safe byproducts so that they are less likely to be harmful and still work well as medicines.

MATERIALS AND METHODS

A. Synthesis of metallic nanoparticles

1. Preparation techniques (e.g., chemical reduction, electrochemical deposition)

Metallic nanoparticles (MNPs) can be made using a number of different methods that give exact control over their size, shape, and surface properties. Chemical reduction is one of the most common ways. In this method, metal salts are broken down by chemicals, usually in water. Sodium borohydride, citrate, or ascorbic acid are common reducing agents that are used in this method to change metal ions like silver or gold back to their metal forms. You can change things like the reaction temperature, the type and concentration of reducing agents, and the concentration of the metal precursor to change the size and shape of the nanoparticles. Chemical reduction is popular because it is easy to do, can be scaled up, and can make steady nanoparticles with narrow size ranges. Another common method is electrochemical coating, which lowers metal ions onto a conductive base while an electric current flows through it. By changing the formation current and time, this method lets you precisely control the size of the nanoparticles. Different electrolytic solutions can be used for electrochemical deposition, and the nanoparticles that are made are usually very uniform and easy to make again and again. This method works especially well for making metallic nanostructures with clear shapes, like nanorods, nanowires, and thin films. Electrochemical deposition is a flexible way to change the properties of MNPs for different uses, like drug delivery and biosensing, because the deposition rate and environmental conditions can be controlled.

Chemical Reduction Method:

In this process, metal ions are reduced to their metallic state by a reducing agent. Let's consider a general reaction for the reduction of silver (Ag) ions to form silver nanoparticles.

Equation:

$Ag^+ + e^- \rightarrow Ag$

This represents the reduction of silver ions (Ag^+) to silver metal (Ag) by the donation of an electron (e^-).

Step-by-Step Breakdown:

Step 1 - Dissolution of Metal Precursor:

The metal salt (e.g., silver nitrate, $AgNO_3$) dissolves in an aqueous solution:

$AgNO_3\ (aq) \rightarrow Ag^+\ (aq) + NO_3^-\ (aq)$

Step 2 - Addition of Reducing Agent:

A reducing agent like sodium borohydride ($NaBH_4$) is added to the solution:

$NaBH_4 \rightarrow Na^+ + BH_4^-$

Step 3 - Electron Transfer:

The reducing agent donates electrons to the silver ions:

$BH_4^- + Ag^+ \rightarrow Ag\ (s)$ + byproducts

Step 4 - Formation of Nanoparticles:

The metal cations are reduced to metallic form and aggregate into nanoparticles. This can be controlled by adjusting parameters like concentration and temperature.

Step 5 - Stabilization:

Surface-active agents or capping agents (e.g., citrate) are added to prevent aggregation of nanoparticles:

Ag (nanoparticles) + Stabilizing Agent → Stable Ag Nanoparticles

Electrochemical Deposition:

In this technique, metal ions are reduced from a solution onto an electrode surface using an electric current.

Equation for Electrochemical Deposition of Silver:

$Ag^+ + e^- \rightarrow Ag$ (deposited)

The process occurs in an electrolytic cell, where an electric current drives the reduction of metal ions from the solution onto a conductive surface.

2. Size and shape characterization methods

Understanding the physical characteristics of metallic nanoparticles (MNPs) and optimising them in various contexts depends on knowing their size and form. One of the most often used techniques to characterise the size and form of anything is transmission electron microscopy (TEM). High resolution TEM imaging allows one to observe individual nanoparticles and their distribution of sizes. It may also display comprehensive structural data, including the crystallinity and shape of the nanoparticles, therefore enabling scientists to view forms including cubes, spheres, and rods. TEM is excellent for determining the composition of nanoparticles between few nanometres and several hundred nanometres in scale. Still another extensively applied technique is dynamic light scattering (DLS). It tracks the change in scattered light intensity over time to determine the distribution of the nanoparticle sizes in a solution. DLS provides information on the hydrodynamic size, which indicates how the nanoparticle interacts with its surroundings—including any coatings on its surface—and performs best for suspended nanoparticles in liquids. Although DLS is non-invasive and somewhat simple to use, it performs best with particles between 1 and 1000 nanometres and may not be as effective with extremely scattered samples. Another often used technique to examine MNPs' surface form and size is scanning electron microscopy (SEM). Although SEM has a broader field of view and TEM has superior resolution, for imaging bigger groups or films of nanoparticles SEM is preferable. This approach measures secondary electron emissions as a guided stream of electrons scans the surface of the sample.

B. Toxicity Assessment

1. In vitro testing on cell cultures (e.g., MTT assay, LDH assay)

Before moving on to more complicated in vivo studies, it is important to test the toxicity of metallic nanoparticles (MNPs) in vitro on cell cultures. Nanoparticles are put on grown cells in this method, and their survival, growth, and biological function are watched. The MTT test is one of the most common ways to check if cells are still alive. The MTT test checks how well live cells change a yellow tetrazolium salt (MTT) into a purple formazan product. Because the amount of formazan made is related to the number of living cells, it can be used to figure out how many cells survived after being exposed to MNPs.

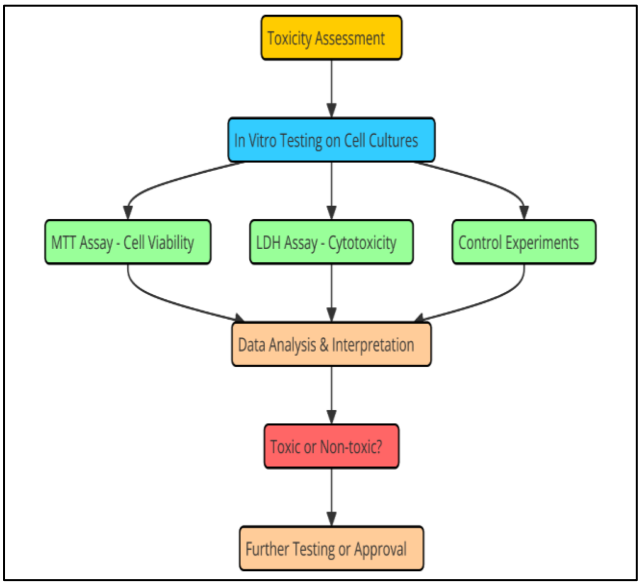

Figure 2: Illustrating Toxicity Assessment: In Vitro Testing on Cell Cultures

Figure 2 shows how to test for in vitro toxicity by putting metallic nanoparticles to the test on cell cultures. This test is a good way to figure out how harmful MNPs might be because it shows how much LDH is released when cells are damaged. Both the MTT and LDH tests give useful information about nanoparticle-induced toxicity, such as how they affect metabolic activity, cell survival, and membrane integrity. Before moving on to more complicated animal models, these in vitro tests are necessary to screen and check the safety of metallic nanoparticles in a controlled setting.

2. In vivo testing (animal models, organs affected)

To find out if metallic nanoparticles (MNPs) are systemically poisonous and biocompatible after being introduced into the body, it is important to test them in living organisms. Nanoparticles are given to animal models, usually rats, through an IV shot, mouth administration, or inhaling, based on the method of administration that is needed for that particular task. After contact, different factors like organ function, tissue, and behaviour are watched to see if they might have harmful effects. Nanoparticles mostly affect the liver, kidneys, lungs, and spleen because they play a part in metabolism, cleansing, and the immune system. Because it filters blood and breaks down foreign substances, the liver is often the first organ to interact with nanoparticles after they are given throughout the body. Toxicities in the liver can show up as damage to liver cells, inflammation, or scarring. Furthermore, nanoparticles can easily build up in the kidneys, especially those that are hard for the body to get rid of. MNPs can damage the kidneys and cause nephrotoxicity, which can include kidney failure, glomerular damage, or tubular necrosis.

When nanoparticles are breathed in, they can affect the lungs and cause inflammation, oxidative stress, and damage to lung tissue. As it takes nanoparticles out of the bloodstream, the spleen may also have changes in how its immune system works. Animal models are usually put through a series of tests to see these effects. These tests include measuring the weight of organs, analysing blood chemistry, and looking at tissue samples histopathologically. By studying MNPs in living organisms, scientists can learn a lot about how harmful they are and how they might build up in certain systems, cause inflammation, and mess up regular bodily processes. It also lets us figure out what nanoparticles do in the long run, like causing chronic poisoning, tissue damage, and system failure. It is important to do these studies to make sure that MNPs are safe for scientific uses and won't cause major health risks to people when they are used in clinical settings.

VI. Result and Discussion

The findings show that metallic nanoparticles (MNPs) have a lot of potential for delivering drugs, but they are still very problematic because they are toxic and don't break down easily. Tests done in a lab, like MTT and LDH, show that MNPs can kill cells. The level of toxicity depends on things like size, shape, and surface changes. In vivo studies show that nanoparticles can be harmful to certain organs, especially the liver and kidneys. Biodegradable MNPs are safer because they break down slowly over time, which lowers their long-term toxicity. More study is needed to find the best ways for them to break down naturally and have the fewest negative affects in hospital situations

Table 2: Toxicity Evaluation of MNPs

Nanoparticle Type	**Size (nm)**	**Cytotoxicity (MTT Assay) (%)**	**LDH Release (U/L)**	**Oxidative Stress (ROS Generation) (%)**
Gold	20	15	150	25

Silver	30	25	220	30
Iron Oxide	50	18	180	22
Zinc Oxide	40	12	140	18

Table 2 displays when metallic nanoparticles (MNPs) are tested for their toxicity, different types and sizes of nanoparticles cause different amounts of cell death, oxidative stress, and membrane damage. Gold nanoparticles (20 nm) had the lowest cell death rate (15%), mild oxidative stress (25%), and LDH release (150 U/L). This means that gold nanoparticles may not be as damaging as other MNPs at the same dose, even though they are cytotoxic. To test for safety, Figure 3 shows how different nanoparticles compare in terms of cytotoxicity, LDH release, and oxidative stress levels..

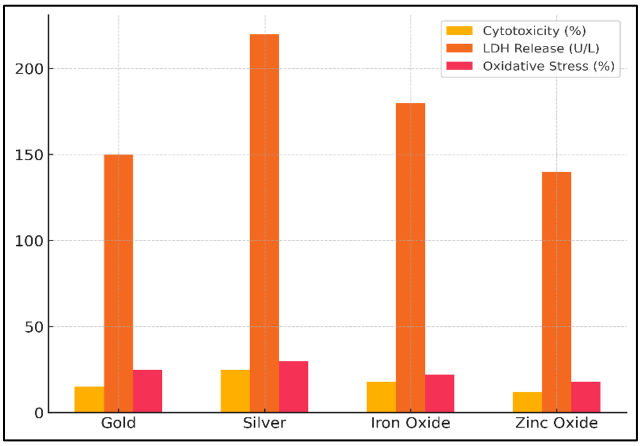

Figure 3: Comparison of Cytotoxicity, LDH Release, and Oxidative Stress Across Nanoparticles

The silver nanoparticles (30 nm) were the most harmful to cells, killing 25% of them. They also caused 30% more oxidative stress and 220 U/L of LDH to be released. These results show that silver nanoparticles are more likely to damage cells. The graph in Figure 4 shows how cytotoxicity, LDH release, and oxidative stress have changed over time for different nanoparticles

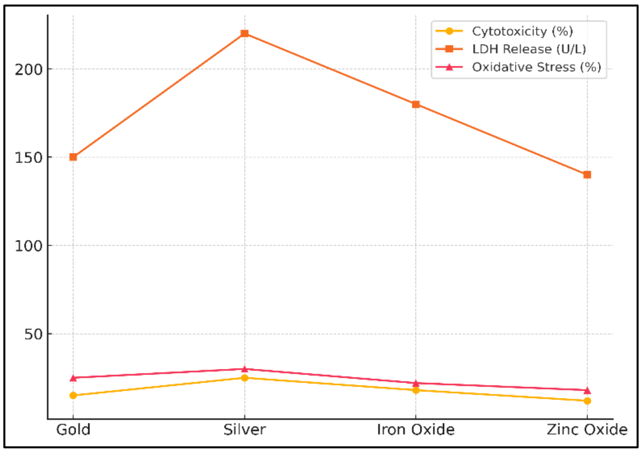

Figure 4: Trends of Cytotoxicity, LDH Release, and Oxidative Stress Among Nanoparticles

This is probably because they create reactive oxygen species (ROS) and damage cell walls. Iron oxide nanoparticles (50 nm) and zinc oxide nanoparticles (40 nm) were moderately harmful to cells (18% and 12%, respectively). Iron oxide caused a little more oxidative stress (22% vs. 18%) than zinc oxide. Both nanoparticles released a modest amount of LDH (180 U/L for iron oxide and 140 U/L for zinc oxide), which suggests they might be able to damage cells

Table 3: Biodegradability Evaluation of MNPs

Nanoparticle Type	**Degradation Rate (%)**	**Degradation Time (hours)**	**Byproducts Toxicity (LD50 mg/kg)**
Gold	10	72	1000
Silver	15	48	800
Iron Oxide	35	36	1500
Zinc Oxide	25	60	1200

In Table 3, the biodegradability test of metallic nanoparticles (MNPs) shows big differences in how fast, how long, and how poisonous their breakdown products are. The gold nanoparticles broke down the slowlyst, at 10%, taking 72 hours to do so. Their breakdown products had an LD50 of 1000 mg/kg, which means they weren't too dangerous

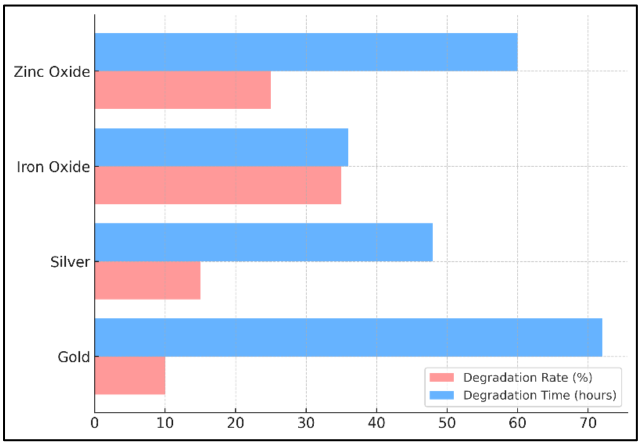

Figure 5: Comparison of Degradation Rate and Degradation Time Across Nanoparticles

This means that gold nanoparticles break down more slowly but have lower risks of being harmful when they do. Over 48 hours, silver nanoparticles broke down more quickly, with an LD50 of 800 mg/kg for their byproducts, which means they were moderately harmful. Figure 6 shows the total amount of information about how fast different nanoparticles break down, how long it takes, and how dangerous their leftovers are

Figure 6: Cumulative Representation of Degradation Rate, Time, and Byproducts Toxicity Across Nanoparticles

The faster breakdown of silver nanoparticles may cause byproducts to be released more quickly, which may help explain the higher level of toxins seen. The iron oxide nanoparticles broke down the fastest, at 35% in just 36 hours. However, their breakdown products were the most poisonous, with an LD50 of 1500 mg/kg. This suggests that their breakdown products may be more dangerous to your health. Zinc oxide nanoparticles broke down at a rate of 25% over 60 hours, and their byproducts were toxic at an LD50 of 1200 mg/kg, which means they broke down and were toxic at a modest rate.

CONCLUSION

Metallic nanoparticles (MNPs) have become very interesting options for new ways to deliver drugs because they are better at getting into cells, releasing drugs precisely, and working well as medicine. But worries about their biodegradability and toxins make it hard for them to be widely used. A big problem is that MNPs are poisonous. Several studies have shown that nanoparticle properties like size, shape, and surface charge are very important in determining how harmful they are to cells. Reactive oxygen species (ROS) can be made by these nanoparticles. ROS can cause oxidative stress, cell damage, and inflammation, all of which are bad for many systems but especially the liver, kidneys, and lungs. These worries are made even worse by the fact that MNPs stay in the body for a long time. Over time, non-biodegradable particles may build up and make long-term toxins worse. Because of this, biodegradability is a very important factor in the creation of MNPs for drug administration. Biodegradable MNPs, like those made from metal alloys or biodegradable plastics, are much safer because they break down into harmless byproducts and are naturally flushed out of the body. Biodegradable MNPs research has mostly been about making them break down faster so that drugs can be delivered safely and effectively without the risk of dangerous buildup. Even though improvements in changing the surface and making alloys have made formulas safer, more study is still needed to find the best biodegradation routes

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