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Toxic Effects of Nanoparticles on The Major Organ Systems of Animals: A Review

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Abstract

Since the beginning of the industrial revolution, nanoparticles have been manufactured by many industries and incorporated into the development of various nanotechnologies. Our knowledge of the risks associated with them is limited, despite the fact that they are utilized in a wide variety of commercial applications. Even though a robust amount of studies have been carried out to gain a better understanding of the influence that nanoparticles have on animal health, there is still very little information available on the harmful impacts that they have. This article will provide an overview of the relevant information as well as the current knowledge of the harmful effects that nanoparticles have on important mammalian organ systems.

Keywords: Nanoparticles; animal health; oxidative stress; apoptosis; neurotoxicity; nanotechnology

Introduction

Nanotechnology

Nanotechnology is characterized by atomic, molecular, and macromolecular size research and development [1]. It includes the pattern, specification, manufacture, and application of objects in the nanometer range by influencing their shape and size [2]. A decade ago, as the "nano-epoch" was beginning, NP production and use throughout the world [3] grew owing to the potential of the technology [4]. Smaller nanoparticles in this size range have been used for thousands of years [5] by industries and individuals alike due to their unique properties. Nanotechnology has the potential to enhance the quality of the atmosphere, hydrosphere, and geosphere [6]. Nanoparticles are used in many different kinds of products, from cosmetics and food packaging to sensors for detecting and measuring pollutants. They have a broad variety of potential uses because of their compact size, wide range of dissemination, robustness, and versatile form [9, 10, 11].

Nanoparticles

Recently, the international scientific community has acknowledged that nanoparticles have a significant role and function in nanotechnology [12]. The basic blocks of nanotechnology are nanoparticles, which are particles with at least one dimension of 100 nanometers [13]. There is a wide range of uses for NPs in biomedicine because of their tiny size and the large surface-to-volume ratio [14]. Nanoparticles' tiny size has been linked to desired properties, such as mechanical, chemical and electrical for certain applications, despite the fact that the nanoparticles themselves are small. Since their numerous medicinal, consumer, industrial, and military applications, metallic nanoparticles have become increasingly popular [9]. All of these advantages might be the source of an unwanted biological or toxicological consequence. The use of nanoparticles in biological applications poses safety issues. Studies have shown that the size of Ag, Au, and Cu is associated with toxicity [15], even though the chemical is generally safe when it is in its natural condition. This highlights the need for more studies into metal nanoparticle safety. In addition, there is a paucity of knowledge on the safety and toxicity of metal nanoparticles [16].

Categories of Nanoparticles

The size, shape, origin, and intended use of nanoparticles all play a role in their classification. The most prevalent nanoparticles are inorganic, organic, and carbon-based (Figure **1**).

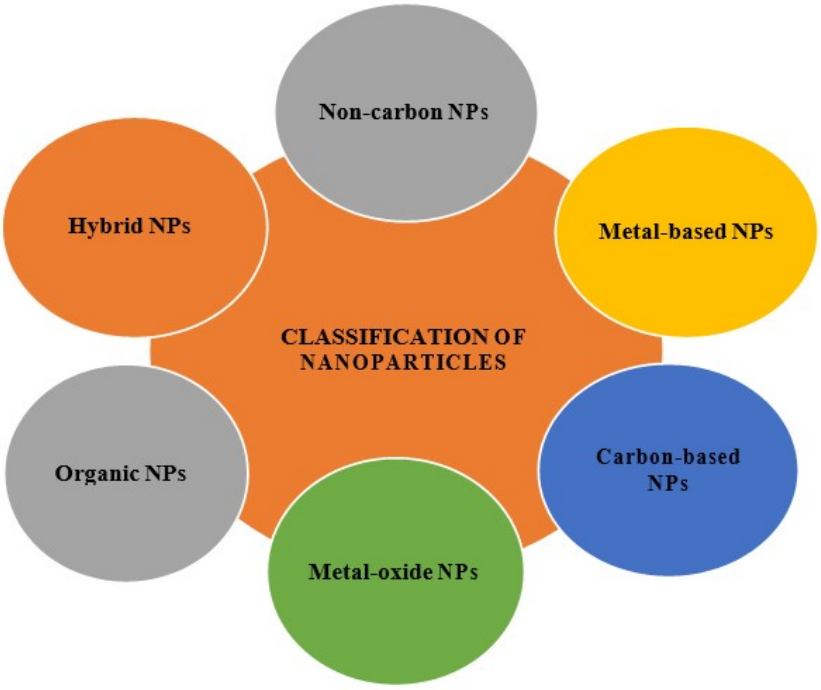

Figure 1: Classification of nanoparticles (NPs)

Non-Carbon NPs

Inorganic nanoparticles are the term for particles that are not carbon-based. These are made up of metal nanoparticles and metal oxide nanoparticles. These are biocompatible, cytotoxic-free chemicals having different optical and electrical characteristics that may be altered during assembly. Calcium phosphate, iron oxide, silver, and gold are just a few of the inorganic elements that fall into this group [17].

Metal-Based NPs

Nanoparticles derived from metals are known as metal-based nanoparticles and can be produced either destructively or constructively. Almost any metal may be reduced to nanoparticle size with this process. Metals often utilized in nanoparticle manufacturing include zinc (Zn), silver (Ag), cadmium, aluminum, iron, lead, gold, copper, and cobalt (Au) (Zn). Size ranges from 10 to 100nm; high surface area to volume ratio; high density; color; and environmental sensitivities (e.g. sunlight; heat) are all characteristics of these nanoparticles [18].

Metal-Oxide NPs

Fe2O3 (Fe2O3) nanoparticles, for example, rapidly oxidize to iron oxide (Fe2O3) in the presence of oxygen (ambient) temperature in the presence of (Fe) nanoparticles. Metal oxide nanoparticles are developed because of their improved reactivity and efficiency. Magnetic (Fe3O4, Cerium oxide (CeO2), Fe2O3, Zinc oxide (ZnO), Al2O3, Al2SiO3, SiO2, and Titanium oxide (TiO2) are the most regularly produced materials in the field of metallurgy today (TiO2). Comparing these NPs to metal equivalents, they show extraordinary characteristics [19].

Organic NPs

Ferritin, dendrimers, micelles, liposomes, and other organic polymers make up organic nanoparticles (NPs). In certain cases, nanoparticles have a hollow core and are very receptive to both heat and light. Biomedical sectors such as medicine delivery

systems typically use organic nanoparticles because they are efficacious and may be targeted to specific bodily locations, a procedure known as "targeted drug delivery" [20].

Carbon-Based NPs

Carbon-based nanoparticles are those that are entirely comprised of carbon. Carbon-based NPs include graphene, fullerenes, carbon black as well as CNT fibres [21].

Hybrid NPs

A polymer-lipid hybrid system, for example, is comprised of polymeric NPs and liposomes, two different forms of hybrid nanoparticles. A biodegradable hydrophobic polymer-based final product contains hydrophilic drugs for quick release that have been put into biodegradable polymers. The quantity of water that enters nanoparticles and even the amount of medicine that is released from them is both controlled by the lipid layer [22].

Sources of Nanoparticles

Nanoparticles can come from a variety of places. Nanoparticles can be emitted directly from both fixed and mobile sources during combustion processes. They can originate in the atmosphere as a result of vapor precursor reaction and/or nucleation, or as a result of radioactive decay [23]. Nanoparticles are also routinely manufactured in industrial settings. The existence and possible emissions of manufactured nanoparticles have become a significant issue with the recent growth of nanotechnology. The disappearance of nanoparticles (those smaller than 100 nm) when substantial quantities of larger particles are present is an interesting phenomenon found in several sorts of sources (stationary mobile, atmospheric conversion, and occupational settings) [24].

Larger particles can act as a sink for ultrafine particles and their vapor precursors, allowing them to be scavenged. This phenomenon creates a significant and difficult dilemma regarding the establishment of regulatory standards, particularly if ultrafine particle concentrations are to be limited on a numerical basis. Controlling condensable species and/or vapor precursors at the source, with the end goal of reducing ultrafine or nanoparticle concentrations, is an essential aspect that has not received much attention [25].

Mechanism of Action of Nanoparticles

NPs are naturally occurring particles in the earth's atmosphere as a result of biological activities and volcanic eruptions [26]. NPs enter the bodies of living beings after intake, where they build up before being eliminated. Because of their unusual physical and chemical features, NPs are seen as foreign invaders by living systems. Exposure to NPs can occur in a variety of ways, but the most common are cutaneous, inhalation, and ingestive. NPs have been shown to pass the blood-testis as well as a blood-brain barrier in several investigations [27].

NPs can attach to both cells and macromolecules such as proteins and DNA [28]. NPs are taken up in several ways when they come into contact with cells. Because of their tiny size, NPs may readily pass through the plasma membrane and other biological barriers to enter the cell and reach organelles like mitochondria. These nanoparticles can affect general composition by interacting with biomolecules [16], resulting in severe repercussions at several levels such as cell metabolic processes being disrupted and cell death being promoted (Figure. **2**).

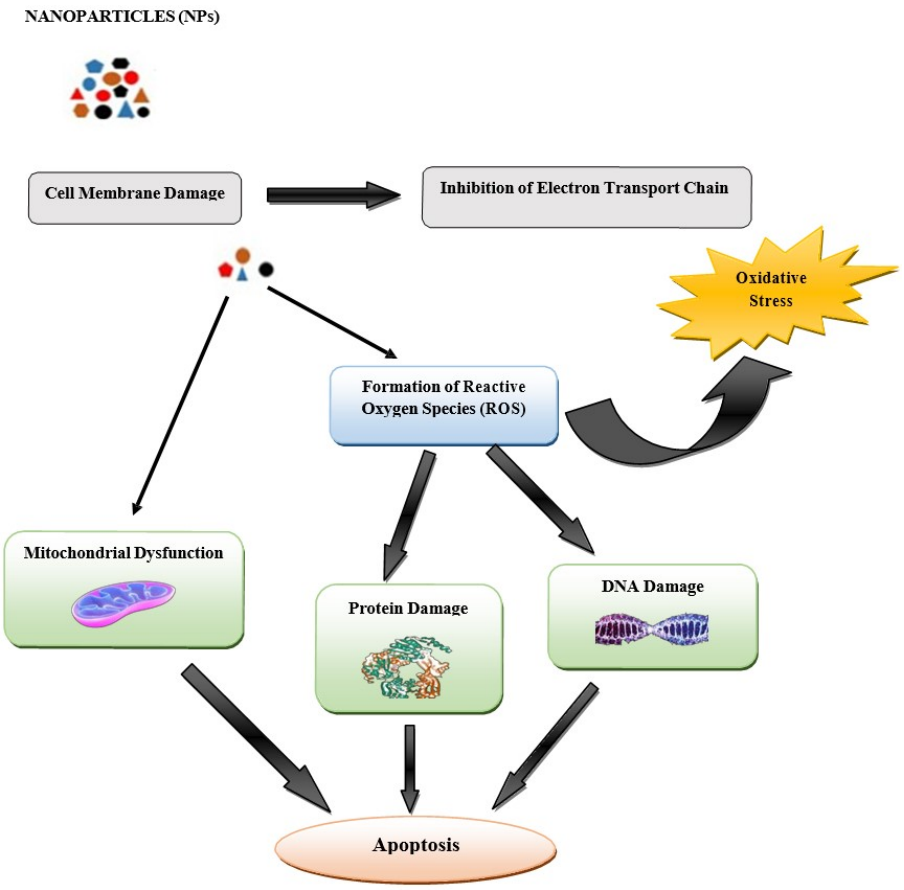

Figure 2: Mechanism of action of nanoparticles

NPs can interact with the plasma membrane and influence processes such as ion transport and signal transduction because of their size and shape. These particles may disrupt normal physiochemical and physiological processes in developing embryos and growing adults. This can cause problems in embryo development, which can be deadly [29]. Because of the nanoparticles' small size and high surface area, there may be some justification for health concerns. Because of their physical and chemical characteristics, NPs are cytotoxic. NPs with positive charges have the potential to damage the lipid bilayers that make up the membrane. It is also possible that other molecules, such as pollutants, could interfere with the structure of cells, altering the effects of nanoparticles. Additionally, NPs can remove hazardous substances from the environment [30].

Toxicity of Nanoparticles

The toxicity of any given nanoparticle is a function of the organism's genetic makeup, which provides the metabolic toolbox to adapt to and battle hazardous substances. Oxidative stress, alteration of calcium homeostasis, gene expression, pro-inflammatory responses, and cellular signaling are the primary mechanisms that cause toxicity from NPs [31]. Instead of relying primarily on Vitro/cytotoxicological approaches, in vivo toxicity diagnostics is an important element of laboratory diagnostics that has to be addressed. Acute toxicity in organs such as the kidneys, spleen, and liver was observed in mice given copper nanoparticles by oral gavage in vivo [32, 33].

The Effects of NPS on Major Organ Systems

NPs that can enter the body via inhalation are a common hazard for mammals, including humans, and various researchers have examined the potential medical effects of NPs in humans. The penetration of NPs through the skin is also conceivable. When the

size of nanoparticles allows endocytosis and transcytosis to reach several cells simultaneously, this is the case [13]. When breathed in, NPs can travel up the olfactory epithelium's axons and into the brain's olfactory bulbs, where they affect neurons. Researchers used a different approach in which NPs began with the lungs before moving on to serum, and ultimately to the blood-brain barrier itself. Bone marrow, lymph nodes and spleen are also possible destinations for the disease. There have been numerous studies that show that NPs can cause inflammation, oxidative stress, mitochondrial distribution modification, and mitochondrial depletion. They were dose- and NP-type dependent effects [34].

Additionally, these findings are based on studies into the distinct hazardous effects of NPs in diverse mammalian organs or organ systems, for instance, the lungs, digestive tract, carcinogenicity, and skin toxicity [35].

Effect of Nanoparticles on The Respiratory System

Animal studies have indicated that exposure to NPs through the lungs can result in mild to severe damage to the respiratory system. After exposure to NPs, animal lung tissue infiltrates with inflammatory cells and fibrosis [36]. Asthma exacerbation, metal fume fever, fibrosis, chronic inflammatory pulmonary diseases, and carcinogenesis have all been linked to nanoparticle inhalation toxicities. It could be possible that persons who are exposed to these dangers would suffer health consequences as a result. The biggest risk of exposure to nanoparticles is posed by those now engaged in nanoparticle research and manufacturing. Public exposure to nanomaterial-related dangers will likely increase, however, as more commercial products are created and marketed [37].

Experiments on animals using the airway to study the pulmonary effects of nanoparticles have yielded some interesting results. Although the inflammation and fibrosis in the lungs have been the primary outcomes of concern in this research. Some important factors must be considered when evaluating research that purports to show direct nanoparticle transportation from the lungs to the circulatory system and secondary organs. Solubility, probable radiolabel leaching, inflammation, or injury produced by the nanoparticle, while others are among the factors to be taken into account. Some of these properties can be seen in rats that consume solid iridium and metallic nanoparticles, as well as aqueous cadmium oxide nanoparticles [38].

Human lung tissue was used to test the cytotoxicity of silica nanoparticles. SiO2 NPs exposure increased reactive oxygen species (ROS) levels and decreased glutathione levels. To sum up, human bronchial carcinoma-derived cells in culture show dose-dependent cytotoxicity after being exposed to SiO2 nanoparticles, and this toxicity is directly correlated with elevated oxidative stress [39].

Effect of Nanoparticles on The Reproductive System

In the context of human reproduction, the term "reproductive toxicity" refers to substances that have an adverse effect on any stage of reproduction or pregnancy, including the development of healthy embryos in women of childbearing age. At any age, parents' exposure to harmful chemicals can have a negative impact on their children's health. The adverse consequences on human and animal development and reproduction of a wide range of natural pollutants, such as pollution [40]. When looking into whether or not NPs are hazardous to female reproductive systems, researchers look at how they affect fertility, teratogenic effects during embryonic development, and impacts on offspring in the postnatal period [41]. Few NPs were shown to be absorbed by cells known as granulosa, resulting in changes in hormone production and ovum dysplasia when tested in vitro. Studies have shown that NPs can enter cells like thecal and granules, disrupting their normal functioning, especially when hormone release is involved. Androgens and androstenedione, which are produced by thecal cells and diffuse into granular cells before ovulation, are transformed into steroid hormones in the granular cells. Sex hormone secretion can be altered by destroying secretory cells in the ovaries, which is something that NPs are capable of doing [42].

Titanium dioxide nanoparticles were shown to alter the expression of ovarian genes, increase oxidative stress, and reduce fertility in female mice after being exposed to them for 90 days in an in vivo investigation [43].

Nucleic acid particles, or NPs, can reach the testis, epididymis, and seminiferous tubule in male mice via a variety of routes, including via the testis and the epididymis, according to studies. One study found that nanosized TiO2 had a devastating effect on male rats' reproductive systems. Over time, a considerable shift in body weight and testicular and accessory male sex organs' relative weight was seen following the injection of nanosized TiO2. Numerous studies have demonstrated the reproductive toxicity of NPs [41].

Effect of Nanoparticles on The Urinary System

Since the kidneys filter blood and remove waste, they play a significant role in nanoparticle transport and clearance in living systems [44]. The size, shape, and surface chemistry of nanoparticles may be precisely altered to influence their interactions with specific kidney compartments. Quantitative knowledge of the molecular interactions between nanoparticle kidneys is essential for more accurate and efficient drug delivery and clearance, as well as a reduction in nanomedicine-related health hazards [45]. As far as titanium dioxide nanoparticles' effects on the kidney go, it is assumed that they have been deposited in the cells [46].

However, the kidney is frequently disregarded as a secondary organ. The mechanism of nanoparticle-induced cytotoxicity was studied by exposing human embryonic kidney cells to silica nanoparticles of 20 and 50 nm [47]. Aerosol inhalation harms the lungs, but nano-SiO2 may be absorbed into the bloodstream and deposited in some organs, where it can have harmful effects on cells and organs. Recent studies [48] focused on the cytotoxicity of nano-SiO2 of varying sizes on two renal proximal tubular cell lines (human HK-2 and swine LLC-PK1). Exposure to SiO2 nanoparticles was associated with a dose-dependent increase in cytotoxicity and oxidative stress [47].

Effect of Nanoparticles on The Central Nervous System

Because of their unique CNS qualities, nurse practitioners (NPs) are increasingly being used to diagnose, monitor, and treat disorders of the central nervous system [49]. For example, nanoparticles are used in the treatment of central nervous system illnesses as a drug carrier to help drugs cross the blood-brain barrier, as nano scaffolds for axon regeneration, and in molecular and CNS imaging [50]. As nanotechnology's applications in biological systems have expanded, so has the danger of human exposure to NMs. When it comes to neurotoxicity, the biological safety of NMs is more valuable. When it comes to taking in NPs, the body has many options, including through the digestive tract, olfactory nerves, and sensory nerves. The brain is a secondary target organ for NPs, and harm to the central nervous system is possible after acceptance. In animals, recent studies have found that nanoparticles (NPs) can induce severe neurotoxicity [51] as depicted in (Figure.3).

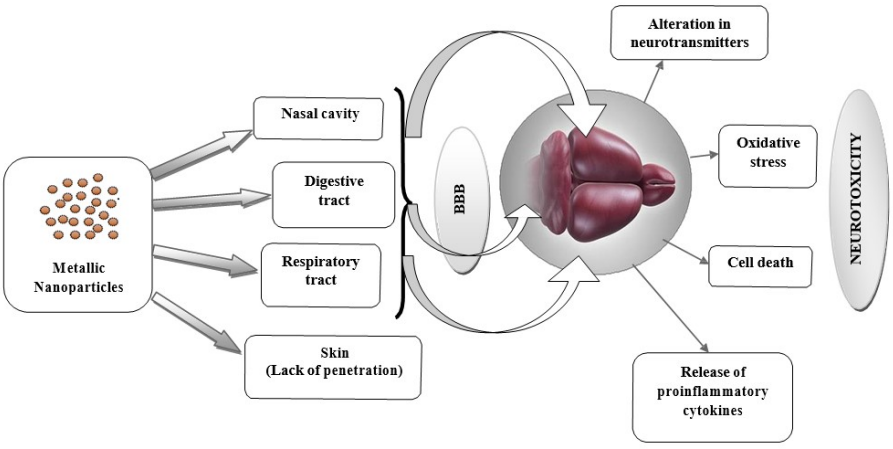

Figure 3: Effect of nanoparticles on the nervous system of rat

NPs have been shown to have deleterious effects on the brain in animal studies. Rats were administered low dosages of Cu-NPs (40 and 60 nm diameter) (about 1.5 g/mL) and the endothelial cells in their brain capillaries grew. At larger dosages (about 50 g/mL), prostaglandin E2 levels rose. Blood-brain barrier damage was finally caused by an increase in extracellular TNF/IL concentrations [52]. Ag-NPs with diameters of 25, 40, or 80 nm were shown to disrupt the blood-brain barrier in rats over 24 hours, creating a proinflammatory response that may lead to brain inflammation and neurotoxic effects. Cytotoxicity was shown to be greater in the smaller NPs (25 and 40 nm) than in the larger ones (80 nm) [53]. Ag-NPs with a diameter of 7.5 nm were responsible for the rat's weight loss and decreased locomotor activity [54]. There have been other studies done on rats or mice that show that NPs impair the blood-brain barrier's permeability, leading to reduced blood flow to the brain and the development of cerebral edoema. Neurons may be damaged, glial cell activity may be changed, and myelin fibre loss may occur as a result of morphological changes caused by HSP activation (hotshock proteins).

Copper and Ag-NPs with 50 to 60 nm diameters had more of an impact than Al-NPs with 50 to 60 nm diameters. It was also shown that the effects were more pronounced in rats as compared to mice [55].

It was observed in a study that ZnO NPs reduced the learning and memory capacities of rats. Following intragastric injection, TiO2 nanoparticles were found in the animal hippocampus, and this accumulation led to cell death and memory impairment [56]. The bulk of the NPs studied so far have neurotoxic effects, however other NPs have protective qualities for the central nervous system (CNS). Fullerenol, for instance, was shown to reduce the damage induced by hydrogen peroxide and cumene hydroperoxide in rat hippocampal slices [51].

Animals exposed to AgNPs may have changes in the hippocampus, cerebellum, and hypothalamus. In the rat hippocampus, 502 genes were upregulated and 703 genes were downregulated following 24 hours of exposure to AgNPs [57]. These were shown to be linked to interactions among ligands and receptors, cytokines and receptors, and so forth. These findings show that silver nanoparticles generated by them can pass through the blood-brain barrier (BBB) and alter brain activities [58].

Effect of Nanoparticles on The Circulatory System

Numerous routes of administration exist for NPs to enter the bloodstream, including inhalation, olfaction, intratracheal instillation, or pulmonary administration, as well as gastrointestinal absorption by gavage, inhalation, or direct contact. Long-term exposure to air particle matter has been associated with several cardiovascular issues in recent research [35]. It's generally agreed that nanoparticles provide a serious threat to the cardiovascular system. Respiratory delivery of NPs to mammals and in vitro assays all resulted in vascular damage [59]. In vivo studies found that exposure to NP affected blood pressure and heart rate, while in vitro studies found that NP caused alterations in vascular tone and dysfunction. To study the effects that NPs have on the vascular system, a model system called the Langendorff heart was utilized. Both the dosage of NPs and the rate of arrhythmia increased in tandem with one another, and both were observed in the same animals [60].

Based on data from experimental and epidemiological research, three broad pathways of pulmonary exposure to man-made nanoparticles have been theorized for detrimental effects on the cardiovascular system: (1) nanoparticles can easily enter the circulatory system and cause obsessive changes in cardiac tissue directly, (2) these can induce oxidative stress or inflammatory response and alter the circulatory system, or (3) with the assistance of neurogenic pathway, nanoparticles can change the cardiovascular system. Because nanoparticles are so intricate, however, they may employ any or all of the mechanisms outlined above to modify the circulatory system. Direct exposure of the circulatory system to generated nanoparticles has been shown to cause tissue injury or functional abnormalities in vitro experiments [59].

Effect of Nanoparticles on The Digestive System

One of the most prevalent routes for micro- and nanoparticles to reach the gastrointestinal tract is through food. It is now possible to deliver specific medicines via the GI system using nanotechnology [61]. A wide range of nanoparticles can reach the digestive system. It is possible to swallow them through food, water, medication, and cosmetics, and via the air, we breathe. It is easier for smaller particles to pass through Intestinal secretions, enter the circulation, and move to other parts of the body [33].

Jeong *et al.* claim that the intestinal secretagogue silver nanoparticles affect the composition of mucins in rats' intestinal mucosa [62].

ZnO nanoparticles can exist at high enough concentrations to have harmful effects on cells, including oxidative stress and mitochondrial malfunction. This feature permits the targeting of the liver, lungs, and kidneys for particle accumulation and detrimental repercussions, which appear unaffected by particle size or gender [63]. ZnO nanoparticles may be readily taken up by the gastrointestinal tract into circulation when given as a single oral dosage. Zn2+ is the most toxic chemical in the human body when it is released into the body by oral admi nistration of ZnO nanoparticles. In a study, ZnO nanoparticles were shown to target the liver as the primary and most important organ [64]. It was expected that an experimental dosage of Zinc oxide nanoparticles would generate adverse effects due to Zn accruing in the liver and decreasing the eradication rate of various medications, resulting in hazardous health consequences and drug accumulation [65].

Effect of Nanoparticles on The Endocrine System of Animals

The International Organization for Standardization (ISO) states a nanoparticle is a nano-object with a diameter of 1 to 100 nanometers and three exterior dimensions [23]. When an animal's reproductive as well as some other systems are formed, hormones play a critical role in regulating their functions. Since silver nanoparticles are anti-microbial [66], they are the most often employed nanoparticles. Nanoparticle size allows it to pass bio-membranes and restrict at any organ location, including the liver, thyroid, brain, kidney and gonads to cause toxicity [67, 68]. Neuronal development, heart functions, bone remodelling, and metabolic processes are all controlled by the thyroid gland [69, 70].

About 10% of the population tolerates thyroid gland abnormalities, for example, and it is noticed as a critical health issue [71] because the endocrine system is very sensitive to environmental toxins. Often, a negative feedback system includes the hypothalamus and pituitary gland exchanging signals to support thyroid function (TRH release) [72]. Thyroid hormones are used to regulate this process. In animals, the tiny size of NPs, such as AgNPs, which penetrate deep tissue, disrupts the thyroid gland's form and composition [73]. Inflammation, DNA damage, and cell death can result from the free oxygen radical generation of AgNPs [74, 75].

Effect of Nanoparticles on The Muscular System of Animals

The majority of issues have been dragged into muscle accumulations [76]. During 15 days of exposure to silver nanoparticles, muscle sections lose interstitial fibres between muscle fibres, and necrosis and clement inflammatory cell infiltration are seen. A thickening and fracturing of myofibrils develop as the AgNP concentration increases. [77].

Studies showed that Ag-NPs with sizes of 25, 40, and 80 nm, as well as Cu-NPs with sizes of 40 and 60 nm, had pathogenic effects on the blood-brain barrier in the pig, but Au-NPs with sizes of 3 and 5 nm had a diminished effect [78]. Ag-NPs with a diameter of 45 nm affected the action of acetylcholine in rats, which led to the generation of NO (nitric oxide) as well as hyperactivity of the tracheal smooth muscle. Injections of 100 or 500 mg/kg of 25 nm Ag-NPs were administered to mice, and this led to oxidative stress in the animals [79].

All of the red pulp of the spleen, the lung, and the renal kidneys were found to contain NP aggregates, with no structural changes

except for the nasal airway [80]. The consequences of Au-NPs (5 and 15 nm diameter) were studied on a culture of mouse fibroblasts. Once within the fibroblasts, the nanoparticles stayed put. Actin filaments were disrupted in the cells, narrowing and constricting them. Only the smallest NPs (5nm) influenced cell shape. Cells treated with Au-NPs over 72 hours destroyed the heavy chain of clathrin, a cytoskeleton protein [81].

Effect of Nanoparticles on An Integumentary System of Animals

Sykes and his colleagues reported in 2014 that mice treated with a high amount of gold nanoparticles intravenously exhibit blue skin, but mice treated with quantum dots produce green, yellow, or red fluorescence after actinic irradiation. Furthermore, the administered dosage and accumulation of nanoparticles in the spleen and liver are directly connected by elemental skin analysis. A further route of nanoparticle toxicity might be dermal accumulation, which could be used to cause tachycardia in response to UV and visible light [82].

Contradictory, Se-NPs (80 to 200 nm), which are commonly employed to protect the endotracheal tube against bacterial infection in particular medical situations, exhibited no cytotoxic influence on rat dermis fibroblasts [83].

Nanoparticles	Organ System	Animal Model	Toxic Effects	References
SiO2 NPs	Respiratory	Humans	Oxidative stress	[39]
TiO2 NPs	Reproductive	Female mice	Created an imbalance of sexhormones	[43]
TiO2 NPs	Reproductive	Male rats	Changes in body weight andthe relative weights of the testis and accessory male sex organs	[41]
SiO2 NPs	Urinary	Humans	Oxidative stress	[47]
ZnO NPs	CNS	Rats	Reduced learning andmemory abilities	[51]
TiO2 NPs	CNS	Mouse	Caused apoptosis ofhippocampus and memory impairment	[51]
AgNPs	CNS	-	Altered brain activities	[58]
Cu-NPs	CNS	Rats	Growth of endothelial cellsin brain capillaries	[52]
Ag-NPs	CNS	Rats	caused a proinflammatoryresponse that might lead to brain inflammation	[53]
AgNPs	Digestive	Rats	Caused an aberrant mucincomposition in the intestinal mucosa	[62]
AgNPs	Muscular	-	Loss of interstitial fibres,focal degeneration, and necrosis	[71]
AgNPs	Endocrine	-	Deep tissue penetration,disturb the thyroid gland's structure and function	[73]
AuNPs	Integumentary	Mice	Blue skin	[82]
Se-NPs	Integumentary	Rats	No cytotoxic impact on rat dermis fibroblasts	[83]

Table 1: Effect of nanoparticles on major organ systems of animals.

Conclusion

NPs may be found in both aquatic and terrestrial environments, where they are consumed by living organisms before being expelled from the bodies. Because of their tiny size, NPs are considered foreign materials in organisms with their physicochemical characteristics. A direct influence on the living organism is crucial to understand how nanoparticles may interfere with the proper functioning of embryos and growing animals as well as adults. More study and characterization of severely dangerous NPs is needed, even though the detrimental consequences of NPs are beginning to be understood. So far, many studies on nanoparticles have focused on the impact of nanoparticles on animal organ systems.

Conflict of Interest

The authors declare no conflict of interest.

Acknowledgments

Declared none.

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