

APPLICATION OF NANOTECHNOLOGY IN VETERINARY SCIENCE

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Abstract

The term "nanotechnology" describes the processing of materials at the atomic or molecular level, particularly for the creation of minuscule devices capable of calculation, function, and organization. The size range of 1–100 nm is commonly referred to as the microscopic level. For this specific post, we choose to examine how nanotechnology is used in veterinary medicine and emphasize its contributions to bettering animal health and production. Through the creation of a system for the delivery of smart drugs, nanotechnology has a significant impact on the treatment of diseases in veterinary medicine and other facets of animal production. These days, nanotechnology has completely changed veterinary medicine and animal science fields by introducing novel, miniature tools, and materials that are advantageous to living things. Quantum dots, magnetic nanoparticles, nanopores, polymeric nanoparticles, nanoshells, fullerenes, liposomes, and dendrimers are a few examples of the nanoparticles utilized for illness detection, therapy, drug administration, animal breeding, and reproduction. Although nanotechnology is recognized as one of the most important technologies that have previously been used in a variety of fields, veterinary science is just beginning to use it. It is fair to assume that nanotechnology research will alter the science and technology of animal health in the following year and will aid in increasing livestock production. Since nanotechnology is still in its early stages of development and needs to be equipped to enable scientists, engineers, and biologists to work at the cellular and molecular levels for major improvements in healthcare and animal medicine, it won't have a large impact on the near future. However, it is realistic to assume that research in nanotechnology will change animal health and aid in increasing livestock production in the following year.

Keywords: Nanotechnology, Veterinary Science, Animal, SLN, Dendrimers

Introduction

The ability to calculate, function, and organize matter at the nanoscale is known as nanotechnology. The scale typically refers to particles with at least one dimension between 1 and 100 nm; however, it is frequently expanded to encompass particles smaller than 1 nm [1, 2]. It is not restricted to a single industry; rather, it is an enabling collection of technology that spans all industries and academic fields. The philosophy and methods of nanotechnology are used to comprehend and modify biosystems, which use biological ideas and components to develop new nanoscale systems and devices [3, 4].

Among the most impressive man-made materials, rationally designed nanostructures display unique chemical, physical, and/or biological properties [5]. The nanostructures can be used for a remarkable number of applications in a variety of industries, including electronics, agriculture, and

health care [6]. Closing the gap between macroscopy and microscopy, where nanoparticles are the ideal medium to communicate with biological systems, is one of the main advantages of nanotechnology [7]. Large active surfaces and easily adjustable surface chemistry that enables binding to small molecular medicines, imaging labels, and ligands including antibodies, peptides, and nucleic acids are just a few of the characteristics that set nanoparticles apart from bulk materials. Additionally, because of their small size, they can interact only intracellularly and extracellularly, allowing for enhanced permeability and retention in tumor tissues as well as extravasation via endothelial cells [8].

Since large NPs are typically avoided because they may cause embolisms, specific sizes of NPs may be used in medical domains. Additionally, they will be phagocytosed and removed from circulation quickly [8]. On the other hand, NPs will be quickly eliminated by the kidney if their size is exceedingly small. Aside from a certain increase in their biological and chemical reactivity, extremely small-sized materials may also become more hazardous and reactive when the surface area-to-volume ratio rises. Reactive oxygen species (ROS) and free radical generation are consequently increased [9]. ROS that has been released cause oxidative stress, inflammation, and severe cell damage. The NPs prefer to assemble in the mitochondria where they disrupt the cellular defense system against free radicals [9].

Materials have different physical, chemical, and biological properties at the nanoscale than they do at the macroscale. The molecules become more reactive (bio-active) and better soluble as a result of size reduction. Their potential rises, they are more stable, and oxidative inactivation has a smaller impact [10].

Based on this phenomenon, NPs are not only used as carriers but can also be used in the reformulation of conventional medications to increase their solubility, improve their pharmacokinetics, and decrease their side effects and immunotoxicity. For instance, the cancer therapy drug Paclitaxel (Cremophor-EL) may cause anaphylactic reactions in susceptible patients, which can be avoided by using the drug's nano-albumin formulation (Abraxane). Therefore, the development of a new science for nano-pharmacokinetics is necessary due to the novel properties that the same material acquires when it is nanosized [8-10].

In the twenty-first century, it is anticipated that nanotechnology will lead to a significant number of innovations that will advance the practice of clinical veterinary medicine and have the potential to modernize veterinary care, animal welfare, and other sectors of animal production [11]. Veterinary nanotechnology will improve the systems for diagnosing and treating patients, offer new tools for molecular and cellular breeding, record animal history from birth to consumer table, alter animal waste as discharged from livestock, identify pathogens, and much more [12].

We now have cutting-edge remedies for age-old veterinary issues because of nanotechnology. It has limitless potential for various areas of veterinary medicine and animal health. Numerous animal diseases, including those that cause severe chronic infections, intracellular pathogens, and blood parasites, can be eradicated with NPs [13]. The combination compounds can be employed for both diagnostic and therapeutic applications because of their strong antibody-binding affinity [14]. To create sophisticated nano-vaccines, NPs can also bind to a variety of antigens and proteins.

Nano-vaccines may take the place of the utilized adjuvant and extend the duration of immunization protection by the controlled release of the bound antigens [15].

Nanotechnology is being used in veterinary medicine in a variety of ways that go beyond just disease prevention and management, allowing farmers to raise animals in more profitable ways. Animal nutrition, reproduction, even animal welfare, and safety-derived products like pet care items like shampoo and body lotions are further used for nanotechnology [16]. The variety in the structure, characteristics, and nature of the created NPs is what enables such a wide range of nanotechnology applications.

In this work, we evaluate the use of nanotechnology in veterinary science and highlight its contributions to bettering animal health and productivity, as well as the many kinds of NPs and their uses in the veterinary field.

Historical perspectives

The particles are formed in this manner, precipitated in place, or somehow incorporated into the matrix when nano-composites are created in glassy or ceramic matrices. Some of these nanocomposites' synthesis and uses are not brand-new. One well-known old method is the creation and application of metallic nano-particles in a glassy phase. R. H. Brill and D. Whitehouse revealed that the Romans implanted fine gold particles to lend color to parts of their glass during the study of a Roman mosaic known as the "Thomas Panel" located at Faiyum, 100 km southwest of Cairo [16, 101]. Bright red to purple were among the hues obtained. The Lycurgus Cup (4th century AD), which stands 165mm tall and contains designs in an intense red color made possible by gold and silver nanoparticles present in the glassy phase, is the best specimen from this era [10, 101]. Copper and silver have been used to tint cathedral stained glass windows red and yellow, respectively, since the XIIth century. Depending on the required luminosity, these nanoparticles were either inserted in the glass's bulk or at its surface. Later, under the rule of K'angHsi, famous pink Chinese porcelain with embedded gold nanoparticles in enamel was created in China during the XVIIIth century. In Europe, these porcelains were widely utilized and enjoyed considerable success. Table 1 [101] provides a summary of the advancements in nanotechnology.

Table 1: Evolution of Nanotechnology

Period	Development of Nanoscience and Technology
5000 years ago	The use of nanoparticles in medicine is described by the Ayurvedic medical system.
1857	Michel Faraday developed a gold colloidal solution synthetically.
1905	Einstein shares his research on the sugar molecule's size, which is about 1 nm.
1959	There is Plenty of Room at the Bottom, according to R. Feynman, who claims this in his talk at the American Association of Physical Sciences' annual meeting.
1974	The phrase "nanotechnology" was first used by Norio Taniguchi.
1981	E. Drexler develops molecular devices that resemble ribosomes and enzymes.
1984	1984 The definition of "dendrimer" as initially used by D.A. Tomalia and how PAMAM Dendrimers are made.
1991	Introduction of carbon nanotubes (CNTs)

1994	Drug delivery systems
1995	Doxil has FDA approval (liposomal doxorubicin)
1997	FDA-approved liposomal AmBisome (amphotericin B)
1998	DNA nanoparticles to distribute genes in a controlled manner
2000	The immunosuppressant sirolimus-solid Rapamune's dose formulation and the Liquid Crystals (Nano-Crystal Technology) technology were used in the first medical product to receive FDA clearance.
2005	The FDA has approved the nanotechnology-based paclitaxel compound Abraxane.
2008	In markets: PEG-Certolizumabpegol, often known as Cimzia, is an anti-TNF Fab used to treat Crohn's disease and rheumatoid arthritis.
2012	Systematic reviews of the literature on biomimetic drug delivery July 2015 Thermo Dox clinical trials were successful (lysothermosensitive liposomal doxorubicin)
October 2015	Irinotecan liposomal, Onivyde FDA-approved for advanced pancreatic cancer.

The goal of the area of nanoscience and nanotechnology has mostly been to emulate how nature produces and manipulates materials at comparable length scales. Scientists have been motivated to create innovative nanomaterials with precise control over their morphology and size by the intriguing characteristics and appealing architectures of biomaterials. These nanoscale materials have brand-new size- and shape-dependent characteristics that are beneficial for a wide range of applications in numerous scientific and engineering disciplines. As a result, recent technical advancements enable the creation of structures or devices that are fewer than 100 nanometers in size and have notable functional advantages over currently available technologies. It can completely alter the technological landscape as we know it. Indeed, the promises are so great that they even inspire the millennium goal of providing all people with inexpensive facilities. Nanotechnology is increasingly used in a variety of goods, including food, electronics, automobiles, clothes, and numerous biomedical applications [1-3, 17].

Based on their dimensionality, nanomaterials can be categorized. Let's look at a certain nanomaterial's three-dimensional space vectors. Nanomaterials can be classified as 0-dimensional particles or quantum dots if their sizes fall under the threshold range of 1-100 nm in all three dimension vectors, such as spherical nanoparticles of Au, Ag, CdS, or CdSe. Similar to the previous example, if the growth of nanomaterial is constrained within the critical range of 1-100 nm in two spatial dimensional vectors, allowing nanomaterial to grow only in the third direction, the resulting nanomaterial is known as a 1D nanostructure, such as quantum wires, nano-rods, nano-wires, single-walled carbon nanotubes, etc. Only one dimension in 2D nanostructures is constrained to that critical regime, allowing nanomaterial to develop in 2-dimensional vectors, such as quantum sheets. Nanomaterials, such as fullerene and silica NPs, are permitted to develop in all three dimensions in 3D nanostructures [17–19].

Another class of nanomaterials that have a chemical composition that differs on the surface from the core region is core-shell nanoparticles. The fascinating electrical behavior of non-metallic nanoparticles, which are made up of non-metal and organic molecules and can be adjusted to be conducting or insulating depending on size and composition, is another type of nanoparticle. The most well-known type of non-metallic nanoparticle is fullerene, which has uses in both technology and medicine. Another well-known type of nanomaterials is carbon nanotubes, which, depending on their diameter and chirality, can either be metallic or semiconducting. Table 2 shows a representation of the dimensionality in nanomaterials as follows:

Table 2: Dimensions of Materials at Nanoscale

Dimension	Properties	Examples
0-Dimensional	Substances whose dimensions are completely measured at the nanoscale (no dimension or 0-D is larger than 100nm)	Nanoparticles
1-Dimensional	Materials with a dimension larger than the nanoscale. This indicates that the nanoscale contains two dimensions.	Nanotubes, Nanorods, Nanowires
2-Dimensional	Substances with two dimensions outside of the nanoscale. This indicates that one dimension is located in the nanospace. Such nanomaterials display plate-like shapes.	Nanofilms, Nanocoating, Nanolayers,
3-Dimensional	Materials with three dimensions are larger than the nanoscale.	Nanoparticle dispersion, nanowire and nanotube bundles, and multilayers

Classifications of nanoparticles

Nanoparticles are minute particles that range in size from 1 nm to 100 nm [1, 2, and 17]. Over the past few decades, a wide range of newly created materials has been used to create particles such as nano-crystals, polymers, Dendrimers, silica oxides, carbon, metal oxides, lipids, and quantum dots [18]. Below are some of the often utilized nanoparticles.

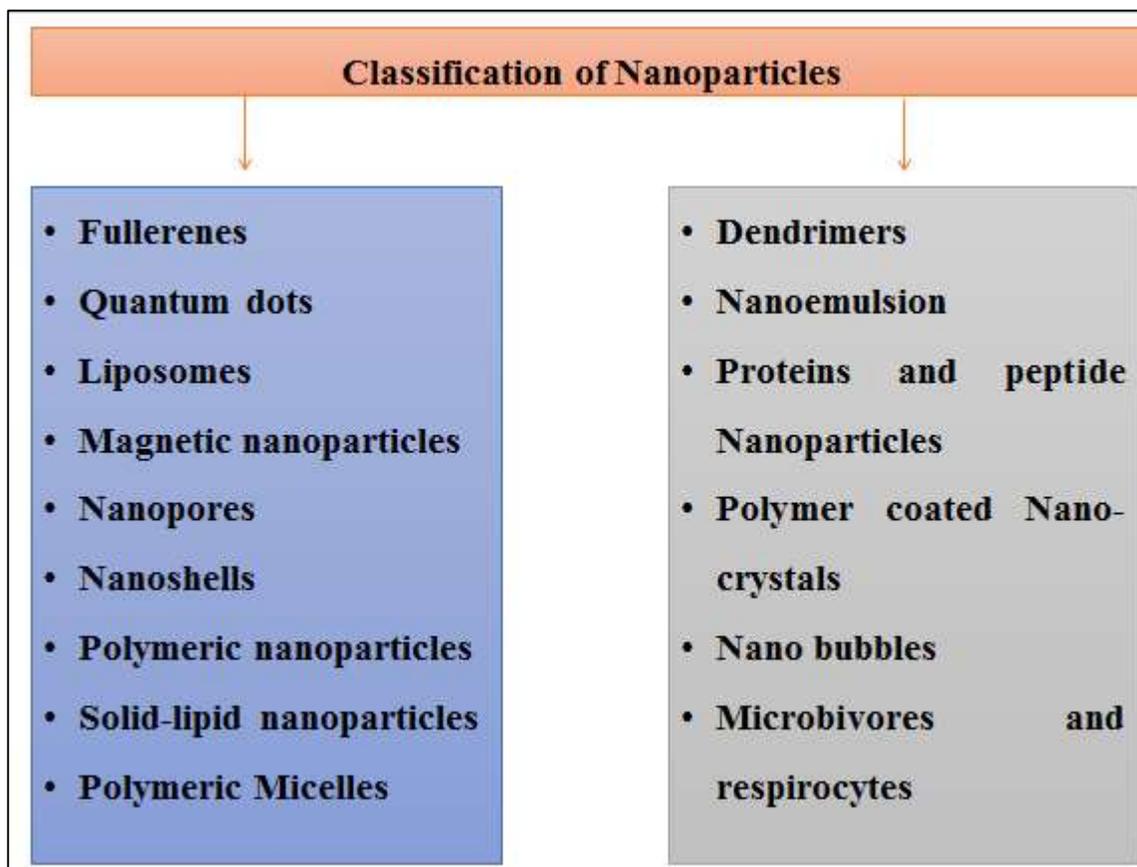


Fig.1: Classification of Nanoparticles

Fullerenes

The nanoparticles known as fullerenes are made completely of carbon-based compounds. Their potential for use in nanomedicine has been thoroughly investigated, and their application in the manufacturing industry is already well-established [19]. High aspect ratio and thermal, electrical, and mechanical properties are only a few of the qualities that carbon nanoparticles possess that make them effective in therapy and regenerative medicine. Carbon Nanotubes (CNTs), which can have a single or many walls, are one of the fullerenes utilized in nanotechnology that are most frequently used (SW, MW). Due to their "needle-like" ability to penetrate cells [20] and their ability to obtain nuclear exposure by shortening their length, SWCNTs offer a novel method for drug administration. This phenomenon is very beneficial since CNTs can be charged or conjugated with medications to increase therapeutic efficiency. [21, 22].

Quantum dots

When stimulated by light, quantum dots, which are nanocrystals that range in size from 2 to 10 nm, can illuminate [23]. They are made up of an inorganic center, whose size determines the hue of the inorganic shell that is emitted, and an aqueous organic coating that is mixed with biomolecules. It can be utilized for both clinical and diagnostic biological applications, and it can be used to image sentinel nodes in cancer patients to stage tumors and plan therapy [24].

Liposomes

Liposomes are manufactured nanoscale-sized spheres made of cholesterol and phospholipids from nature [25]. The first drug delivery system to be tested used liposomes. They are colloidal or micro-particular carriers, typically ranging in size from 80 to 300 nm [26]. These can be utilized as efficient drug administration methods. When administered as liposomal medications as opposed to conventional formulations, toxic and cancer-treating medications such as amphotericin and hamycin exhibit higher efficacy and protection [27].

Magnetic nanoparticles

Because antibodies may bind to the surfaces of magnetic nanoparticles like iron oxide paramagnetic compounds and because they can be targeted with an external magnetic field, they are promising candidates for the therapy of illness [13]. Superparamagnetic iron oxide nanoparticles with a diameter of less than 10 nm and outstanding magnetic characteristics are typically the most effective materials. They are tiny, thermally agitating magnets in liquids known as "ferromagnetic fluids" or "Ferrofluids." Superparamagnetism is only possible in the presence of a magnetic field; if this field is taken away, the magnetization will disappear, the particles will stop interacting, and potential vascular embolization can be prevented [13,28].

Nanopores

Desai and Ferrari first proposed the idea of nanopores in 1997 [29] consists of wafers with a high porosity density and a diameter of up to 20 nm. The pores let the movement of insulin, glucose, oxygen, and other substances. However, moving through immunoglobulin and cells is not necessary for this. Utilizing nanopores can help shield transplanted tissues from the host's defensive mechanism. The recipient's body may be filled with β -pancreatic cells that have been folded inside the nanopore system. This tissue sample avoids rejection because it takes up nutrients from the neighboring tissues while evading detection by the immune system. For people with insulin-dependent diabetes mellitus, it may be a more recent therapy option [30].

Nanoshells

West and Halas had both made nanoshells [31]. A thin metal layer covers the silica nucleus nanoparticles that makeup nanoshells. This can be applied utilizing immunological techniques to the right tissue. Tumor therapy is being investigated using this method. The used nanoshells display the nanoshell's thermoablative properties by absorbing infrared radiation when exposed from an external source [31].

Microbivores and respirocytes

Respirocytes independently mimic the components of both white blood cells and red blood cells. Microbivores catch infections while profitably supplying the tissues with O₂ and avoiding the accumulated CO₂ by employing extraordinary management sensors. The removed microorganisms transform due to an enzymatic process in which they are initially transformed into building blocks made up of unsaturated fatty acids, amino acids, and nucleotides [32].

Solid lipid nanoparticles (SLN)

Lipids that are in a fluid configuration and are in balance. They contain a lipophilic center, which enables their application in the treatment of cancer. It is possible to conjugate various hydrophilic

drugs or antibodies to their hydrophilic outer shell. The capacity of the medication's bio-profit is also enhanced by the outer shell. Furthermore, cationic solid lipid nanoparticles can legally join nucleic acid components through electrostatic linkage, enabling their application for high-quality treatment [34]. This kind of nanoparticles can be administered in many routes, including topical, oral, and subcutaneous injections. They can effectively deliver drugs into the central nervous system because they can pass the blood-brain barrier. In addition to using strong lipid nanoparticles, using fluid lipid nanoparticles is now being evaluated [33, 34].

Polymer coated Nano crystals Polymeric Nanospheres

They enable the development of a potent nanosuspension Macrophage dependent transport to areas of HIV infection and sequestration and inhibit aggregation [13]. Using polymers that are either biodegradable or not, uniform spherical frameworks much smaller than a micron in size are generated. It might be utilized to study type-2 human epidermal growth factor receptor and in-vitro integrin cancer cell proliferation, which is groundbreaking for transdermal drug delivery [35].

Dendrimers

They are exceedingly rare hyper-branched nanomaterials that are dissolved in water and were produced from tiny, smaller-than-body polymers [36–38]. When infused into the flow, their diminutive size and composition arrangement keep any unwanted resistant reactions from being strategically stimulated [38]. They resemble a tree made of expanding 3D atoms. Medication connections or potential conjugation inside the circle are present on the surface of the dendrimer [13]. Dendrimers can be stacked with numerous water-soluble and water-insoluble restorative drugs through physical and chemical coupling. These drugs can also be put inside the empty centers by nonbonding stacking. Covalent conjugation between dendrimers and layered drugs may occur, increasing solidity and enhancing therapeutic efficacy. They are fundamentally used in the treatment of cancer [39].

Dendrimers are recognized by their enormous, intricately branching structure. Dendrimers may be added to medications that are used for imaging. Numerous investigations have demonstrated the superior antibacterial efficacy of dendrimer-loaded nanocomposites against *Pseudomonas aeruginosa*, *E. coli*, and *Staphylococcus aureus*. The dumping of their drug or radioactive compound stock into the tumor causes movement. Finally, signals are delivered with the execution of dangerous cells if the treatment is successful. In a study, a research team led by Landers designed dendritic polymers conjugated with sialic acid to fight flu infection. The preparation was able to catch infections with inactivation and disposal, according to the authors [39].

Nanoemulsion

As bactericidal and virucidal drugs, nanoemulsions have positive potential for recovery. Oil drops adhere to the envelope or layer in the animal body when they come into contact with bacterial or viral coats due to a surface tension feature. This combination causes the treatment to enter the microbial cells. Additionally, nanoemulsions can act as delivery systems for antigens. Different antigens can be mixed in a single nanoparticle [40]. They are tiny, lubricous drops in water that have a thin surfactant film covering them to allow for physical modification. The two main varieties of nanoemulsion are oil in water and water in oil emulsion. For nanoemulsions delivered

using low-essence techniques, the best storage temperature is 4°C, room temperature, and the capacity time is over 2 months [36]. Since the water/oil nanoparticle emulsions can regularly release the antigens, they serve as adjuvants to enhance the development of high-titer antibodies [37]. A few analysts warn of the effects of fat drops on RBCs and sperm cells when they are administered systemically [38]. Numerous audits concluded that nanoemulsions may be used on eukaryotic cells without causing any problems [41–44].

Nanobubbles

They remain stable at ambient temperature, but when they are slightly warmed when exposed to ultrasonic waves, they group to produce microbubbles. They are mostly utilized for drug delivery, particularly drug administration into cancer tissues. Gene therapy also makes use of liposomal nanobubbles [41].

Polymeric Nanoparticles

In addition to synthetic polymers like polyethylene glycol (PGE), there are also two types of natural polymers based on polysaccharides like inulin and chitosan. The active molecules are adsorbed onto the surface of NP polymers to large and varied spherical structures of tree-shaped hyper-branched polymers, which is how they are made [13]. Except the various numbers of branching points on the branches emanating from the core, this structure resembles the dendrimer. They stand out for having a large loading/conjugating capacity. The polymers may also be applied to generate hydrogel nanoparticles (NPs), which have high water content and a sizable surface area [13].

Proteins and peptide Nanoparticles

Due to their low toxicity, low production costs, high biodegradability, and biocompatibility, they are primarily used in gene delivery tests (e.g., gelatin). The fact that they are amphiphilic allows them to interact with a variety of payloads. The iso-electric points of the two varieties of utilized gelatin, type A (extracted from tissues by acids) and type B (extracted by bases), differ [13, 45]. Gelatin B has the benefit of having an isoelectric point between 4.8 and 5.2, which enables it to interact with molecules that are positively charged at physiological pH. Gelatin B initially has a negative charge, but when it comes into contact with an endosome, it converts to a positive charge, allowing the positively charged load to be gently released inside the cells. The gelatin molecule needs to be conjugated to a highly positive compound (like protonated sulfate) to trap the DNA within the molecular complex [46]. When the genetic material and therapeutic agents are co-loaded in core-shell NPs with albumin as the core protein, the genetic material, and therapeutic agents can be delivered simultaneously [47]. Other proteins used for the same purpose include silk fibroin (from silkworm or specific spider species) and maize protein (Zein) [13, 48, and 49].

Different methods for the preparation of nanoparticles

The different methods for the preparation of nanoparticles are explained in given Table 3.

Table 3: Method of Preparation of Nanoparticles

Method	Description
Emulsion Solvent Evaporation Method	It involves two steps. This procedure is modified to include solvent evaporation and high-pressure emulsification [50].
Twofold Emulsion and Dissipation Method	This technique involves forming water/oil emulsions by vigorously swirling organic polymer solutions with hydrophilic drug solutions to encapsulate water-soluble medicines [51].
Salting out Technique	Essentially rely on separating a solvent with water miscibility from a watery solution via the salting out effect [52].
Emulsion Diffusion Method	It depends on partially dissolving the polymer in a water-miscible solvent and fully submerging it in water. In the long run, a watery arrangement that contains a stabilizer was formed into an emulsion, encouraging the formation of nanospheres or nanocapsules and dissolvable dissemination to the outer stage. Large amounts of water that must be disposed of negatively affect exemplification performance [53].
Solvent Displacement Method/ Precipitation Method	Included are the dispersion of typical soluble in a fluid medium in the presence or absence of surfactant, as well as the precipitation of a preformed polymer from a typical arrangement. In semi-polar water-soluble, such as $(\text{CH}_3)_2\text{CO}_2$ or ethanol, medication disintegrates. This approach is suitable for poorly soluble medicines [54].

Different methods for nanoparticles characterization

Molecule size of nanoparticles

The dosage release is influenced by particle size. Greater surface area is provided by smaller particles. As a result, the molecular surface can be made aware of the maximum amount of medication that can be stacked onto them to hasten drug release [54].

There are various methods for measuring nanoparticle size, including:

Scanning Electron Microscope (SEM)

Direct perception of morphology is provided by scanning electron microscopy. They provide precise information on the size distribution and the average of the actual population. This method is time-consuming, expensive, and frequently demands mutual insights into determining dispersion [55].

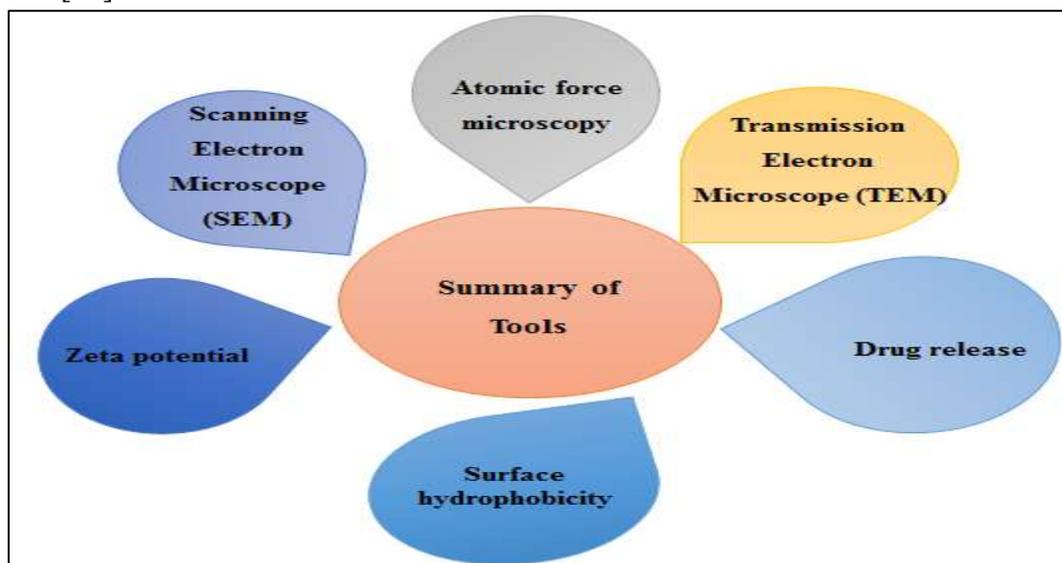


Fig.2: Summary of tools for determining nanoparticle size

Transmission Electron Microscope (TEM)

The main purpose of a transmission electron microscope is to provide verifiable evidence of the manufactured nanoparticles' morphology.

Atomic force microscopy

Nanoparticle surface topography and roughness profiles are determined using 2D and 3D AFM images.

Zeta potential

It is used to calculate the surface charge, zeta potential value, and nanoparticle size [56].

Surface hydrophobicity

Determined using a variety of methods, including hydrophobic interaction chromatography, biphasic partitioning, and probe adsorption [57].

Drug release

Like drug loading assays, which are used to study the drug release mechanism, drug release assays do the same [58].

Applications of nanotechnology in veterinary science

For the development of nanoscale pharmaceuticals, controlled delivery systems, contamination detection, and the creation of molecular and cellular biology nanodevices, nanotechnology is used [59]. In addition to playing a crucial role in disease prevention through the installation of a smart drug delivery system, it will play a significant role in animal welfare, veterinary medicine, and other fields related to animal production. One currently the under-development application of nanotechnology in medicine is the use of nanoparticles to deliver medications or other ingredients

to particular cell types. Particles are designed to gravitate toward sick cells, causing some cells to be handled directly [60].

Nanotechnology is currently being used in similar ways in the food and medical sectors. By utilizing the huge surface area and small volume of nanoparticles, lab-on-a-chip technologies are improving medical diagnostics and food safety testing. These molecular technologies don't require huge benchtop machines, require less samples, have shorter run times, and are simpler to use [61]. Collecting real-time data in the field is one of the main benefits of lab-on-a-chip technology. Similar to the food business, where nanoparticles are being researched as delivery methods for nutraceuticals and as biocides to better preserve food products, therapeutic nanoparticles, and nanoparticles as therapy delivery systems are both generating considerable attention in the medical area. While naturally occurring and nanostructured materials can entrap and safeguard nutrients for distribution, bactericidal metal and polymeric nanoparticles assault the strength of microbial cell walls [59–61].

The animal industry, where livestock health is closely related to food safety, serves as the best illustration of how the medical and food industries complement one another. To enhance profitability, livestock producers need their herds and flocks to quickly attain appropriate slaughter weights. Antibiotics are currently added to feed as a prophylactic measure to avoid disease and speed up growth, shortening the length of the animal production cycle. Although beneficial for production, this global practice has fueled the spread of antibiotic-resistant bacteria that can infect cattle and contaminate the meat. The bulk of antibiotics is used in agriculture and fewer in humans, according to global trends in antibiotic use. Due to this, legislation limiting the use of antibiotics in animal production has been passed in several nations [62].

Nanoparticles can potentially close the gap left by these limitations while simultaneously preventing the development of antibiotic resistance in microorganisms. Additionally, the animal production industry could benefit from nanotechnology in the fields of nanovaccines, nutrient delivery, biocides, veterinary treatment, and reproduction. An overview of some of the most important nano-technological methods used in veterinary research is provided here [61–63].

Nanovaccines

A novel approach to immunization is emerging: the nanovaccine. Compared to conventional immunizations, nanovaccines can activate the immune system's humoral and cell-mediated responses. They claim to direct the immune system of the body to fight pathogens and stop the spread of infections and disorders [61, 62]. The tradition of using live, dead creatures for immunization has been replaced with a far safer candidate: synthetics and recombinants. Such novel vaccine candidates require a designed adjuvant that improves immunogenicity because they are frequently weakly immunogenic and susceptible to degradation [63].

The development of nanotechnology has led to several innovative antigen-carrying techniques because conventional adjuvants are not adaptable. Such adjuvants based on nanoparticles can be created for a comfortable route of administration and a lower dose frequency to produce a specific target immune response, such as the intranasal route to enhance the target mucosal immunity. This makes them especially well-suited for veterinary medicine, where handling numerous animals at

once is necessary, or where traditional immunization methods are impracticable because of extensive management systems or a lack of accessibility [64].

A. Recombinant B. anthracis spore-based vaccines and influenza vaccines are two examples of nano-emulsion vaccines. B. Vaccines loaded on PLGA nanoparticles produce Immunoglobulin type G and Immunoglobulin type A immunological reactions after being administered orally. Examples of these vaccines are the tetanus toxoid, bordetella pertussis, and bovine para influenza type III vaccines. C. The recombinant Leishmania SOD vaccine is an example of a vaccine loaded with chitosan nanoparticles and administered via subcutaneous injection. Additionally, the pneumococcal antigen A vaccine and the Streptococci equi vaccine are loaded with chitosan and administered via the intranasal method. A vaccine made of gold nanoparticles is administered to prevent foot and mouth disease. D. Vaccines against the virus known as African horse illness that affects horses and has an empty capsid and particle-like center [65–76].

Delivery of Nutrients

Since casein phosphoproteins account for around 80% of the protein composition in cow's milk, casein micelles are naturally occurring nanoparticles in milk [77, 78]. To facilitate transmission from mother to child, some casein isoforms group together with calcium, proteins, and other nutrients. Choice hydrophobic nutrients have been included by manipulating these micelles [79]. These casein nanoparticles were used to deliver vitamin D to human volunteers, boosting the vitamin's bioavailability in vivo as a result of the casein particles' proteolytic cleavage in the stomach, which releases the vitamins they are encapsulated with [80].

As young children's immunological and digestive systems are still developing, weaning is a delicate time for them and might be assisted by manufacturers using a similar method. Weanlings must adjust to a complex carbohydrate diet and less immunological protection without the mother's milk. This is a crucial stage for productivity, as well as animal welfare concerns since weanlings that maintain their growth rates through the weaning process, are healthier and heavier at the time of slaughter [81]. Bottle-fed animals and poultry may benefit from the growth-promoting effects of dietary supplements as well [82]. This supplementing might be facilitated by nutrient-delivery nanoparticles, which would also boost animal growth rates by improving the bioavailability of their nutrient payload.

According to research by Akbari and Wu [83], cruciferin, a protein found in canola, can be used to make nanoparticles. These researchers showed that these particles could encapsulate both hydrophobic and hydrophilic bioactive compounds, shield them from a simulated stomach environment, and release them in a simulated intestinal environment. By examining the bone mineral densities of mice, Huang et al. [84] tested the bioavailability of calcium carbonate and calcium citrate at the nano- and microscales. Compared to mice given microcalcium and controls, mice given calcium compounds at the nanoscale exhibited denser bones. Given that body bulk is significantly selected for over-leg strength, which makes it challenging for turkeys to support themselves, it would be interesting to look into whether calcium delivery in nanoform may aid to strengthen the bones of production animals like turkeys [85].

Acting as Biocides

Nanoparticles might be a workable substitute for antibiotics and might prevent diseases from getting into places where animals are produced [86]. Because current animal production facilities are so densely populated, which encourages and hastens the spread of disease, limiting the use of antibiotics calls for the development of alternatives [87]. Negatively charged bacterial membranes are pulled to metal nanoparticles with net positive charges, causing leakage and bacterial lysis [88]. Kim et al. [89] discovered that silver nanoparticles could stop the development of yeast isolated from a case of bovine mastitis and hemorrhagic enteritis-instigating *E. coli* O157:H7 with an estimated MIC of 3.3-6.6 nmol/L and 6.6-13.2 nmol/L, respectively.

By increasing the activity of lipase and phospholipase A in the small intestine, Gonzales-Eguia et al. [90] showed that nanoform copper might enhance piglet energy and crude fat digestion more effectively than a basic meal supplemented with CuSO₄. The daily weight gain, metabolic rates, and immunological function of these pigs all increased. Despite hematological differences between experimental groups, total globulin and superoxide dismutase concentrations in blood serum were considerably higher after analysis of the effects of nanocopper on the immune system. These findings imply that the nutritious content of feed can be increased by using nanoscale antibacterial metal additions.

Improve meat and egg quality

It has also been looked into whether utilizing nanoparticles could improve the quality of meat and eggs. For instance, Wang and Xu [91] showed that finishing pigs intended for market were 14.06% slimmer at slaughter than control pigs fed a basic diet of corn-soybean meal when they were given chromium nanoparticles (200µg/kg) in feed. An increase in skeletal muscle mass and enhanced pork quality were attained, with comparable results found when finishing pigs were offered chitosan nanoparticle supplements enriched with chromium [92, 93]. These chromium-loaded chitosan nanoparticles increased the hormone-sensitive lipase activity in adipose tissue while lowering the activity of fatty acid synthase and enhancing immunological components in blood serum [92, 93].

Nanomaterials can improve the quality of the final product and the production process when added to animal feed or water. The addition of chromium nanoparticles to chicken feed increased the average daily growth and feed efficiency of the broilers in the experimental group fed 500µg/kg Cr³⁺ while also having a positive impact on the protein composition of the breast and thigh muscles and decreasing cholesterol [94]. These findings mean that less feed will be needed to get broilers to market weight, which will result in shorter production cycles and better-quality meat. In a study where silver nanoparticles in water were used in place of an antibiotic to treat coccidiosis, bioaccumulation of nanoparticles in the liver was observed in the experimental group. This finding was confirmed by Chauke and Siebrits [95] (0.083mg/kg of silver equated to 0.001mg/kg in the control). Regardless of particle size, adding nutrient supplements to livestock feed will benefit the producer as long as there is still a market for the finished product. Consumers are likely to still favor meat and eggs made from animals fed supplements containing nanoparticles if they are enhanced or unrecognizably different from the original product.

Application in milk and related ailments

A typical condition affecting dairy cows is mastitis, which can be brought on by several different sources, many of which are bacterial and can be treated with medicines. If administered at a concentration that is too high, the medication tilmicosin, which is used to treat mastitis, might have adverse side effects. Han et al. attempted to use hydrogenated castor oil-solid lipid nanoparticle carriers to regulate the release of tilmicosin in light of this. Given that tilmicosin was available in mouse blood serum for 5 h without nanocarrier delivery and 8 d with nanocarrier delivery, one worry was what the therapeutic's prolonged half-life would indicate for milk disposal timings [96]. A 40-minute colorimetric test for the presence of *S. aureus* in milk was created by Sung et al. [97] using nanocomposites made of anti-*S. aureus* antibodies, gold nanoparticles, and magnetic nanoparticles. The antibody, whose specificity and selectivity might be altered to target a range of diseases [97], is an intriguing component of these nanocomposites. By using polyclonal antibodies and gold nanoparticle immune chromatographic strips, Wang et al. [98] established a comparable method for detecting toxins contained in milk within 10 minutes, using the carcinogenic aflatoxin M1 as an example.

Veterinary Medicine

The interesting field of nanomedicine is making advancements in both diagnostics and therapies. In biomedical research, metallic and nanostructured particles are helpful diagnostic instruments that can be utilized to see how a cell is doing or where medicine is being distributed in the body. Magnetic resonance imaging (MRI) can be used to image magnetic nanoform metals, such as iron oxide, in vivo at high concentrations. Through fluorescent nano-carriers, drug delivery can be observed. For instance, it is possible to track the distribution of bound chemotherapies using light-activated fluorescent nanostructured glucose and sucrose-derived nanoparticles [100]. Ajmal et al. [100] have proven the biocompatibility of carbohydrate-derived nanoparticles in a human lung cancer cell line.

Animal Production

Animals intended for slaughter are the core of animal production. Finishing animals are the descendants of individuals with superior genotypes and phenotypes who are meant for breeding. Breeders are highly valued because of their characteristics and capacity for reproduction. Through the functional groups they carry, certain nanoparticles have been shown to improve fertility and safeguard spermatozoa. A better understanding of Lives-tock gamete biology and reproductive barriers to fertilization is required to maximize the effectiveness of artificial insemination. To better comprehend the mobility of mammalian spermatozoons and oocytes as well as their interactions in a physiological setting, quantum dots have recently been investigated as a study methodology. These self-illuminating, inorganic nanoparticles are of interest to the study of oenology because they are biocompatible, photo-stable, and have a stronger signal than organic fluorescent molecules, which have previously been utilized to imaging gametes and other cell types in vivo [101-103].

In-vitro, *in-situ*, and *ex-vivo* monitoring of bioluminescent resonance energy transfer-conjugated quantum dot (BRET-QD) nanoparticles were achieved by Feugang et al. utilizing pig male gametes

(*Sus scrofa domesticus*). As a result of their size, emission wavelengths, and conjugation options, quantum dots can offer either targeted or non-targeted imaging [101, 104]. Similar to fluorescent proteins but operating at deeper tissue levels, this designed nanoparticle offers a new method for visualizing the molecular and cellular activities occurring during conception [104, 105].

To distinguish unhealthy, unharmed sperm from damaged sperm, semen can be nanopurified. For a protein-based elimination strategy, one technique is to coat magnetic nanoparticles with antibodies against ubiquitin, a surface marker of faulty sperm [106]. The glycan exposed at the surface of the sperm due to acrosomal destruction is bound by magnetic nanoparticles coated with lectins in a lectin-based method [107]. By using nano-protectant compounds in extenders, sperm cryopreservation can be improved. Extenders are buffering chemicals that are used to dilute sperm and provide it with the nutrients it needs for long-term storage. To stop bacterial development from lowering sperm quality and infecting artificially inseminated females, they preserve and contain antibiotics [108]. Since some antibiotics have been found to reduce sperm motility and viability in a dose-dependent manner [109], antimicrobial nanoparticles may eventually replace extender drugs.

Nanoparticles have the potential to be very important in animal reproduction with more research and development. It is important to keep in mind that some nanoparticles are spermatotoxic, which could have major repercussions if breeder reproduction is harmed. Examples of nanoparticles that weaken membranes and break DNA to impair *in vitro* sperm viability include zinc oxide and titanium oxide [110, 111] nanoparticles. After incubating human sperm with zinc oxide nanoparticles for 45 min, Barkhordari et al. [110] discovered that a concentration of 500 µg/mL would considerably increase cell death, while a concentration of 100 µg/mL would greatly increase cell death after 180 min.

The viability of buffalo sperm (*Bubalus bubalis*) cultured with 100 µg/mL of titanium oxide nanoparticles was reported to be decreased by Pawar and Kaul [111]. The final necessary stage of sperm maturation for egg penetration and fertilization, known as sperm capacitation, was discovered to be prematurely increased by titanium oxide at a concentration of 10 µg/mL. While using nanoparticles to boost reproduction may be a step in the right direction for the animal production business, care should also be taken.

Diagnosis and treatment of diseases

A novel class of optically controllable nanoparticles called a "nanoshell" is made up of a core made of a dielectric material, like silica, and a very thin covering of a metallic material, like gold. Targeted drugs can be added to nanoshells to make them seek out and cling to the surface receptors of cancer cells before being injected into an animal's bloodstream. According to Hirsch et al. [112], infrared light illumination of the body increases the cell temperature to roughly 55°C, which "burns" and destroys the tumor. Others are exploring "smart" superparamagnetic nanoparticles that, when injected into the circulation, target cells that have tumor receptors. These nanoparticles are formed of iron oxides, which, when exposed to a magnetic field, improve their capacity to find tumor cells. The nanoparticles release an associated drug at the tumor site, killing the cancer cells.

Quantum dots, which are nanometer-scale crystals initially developed for optoelectronic uses, are another type of nanomaterial. Chen and Scott, [113] studied animals' bloodstreams that can be injected with quantum dots, which can identify dysfunctional cells. It may be able to illuminate the body with light and trigger the quantum dot to heat up sufficiently to destroy the malignant cell because quantum dots react to light. Powerful new approaches to providing therapeutic or preventative treatment for specific diseases are provided by nucleic acid engineering-based probes and procedures developed by Luo et al. [114]. These numerous nanotechnology techniques might be used as therapeutic assistance to lessen the health issues that animals face.

Animal Breeding

For dairy and swine farmers, managing breeding is an expensive and time-consuming issue. A nanotube implanted beneath the skin to offer a real-time assessment of changes in the level of estradiol in the blood is one approach that is currently being researched. Because the nanotubes O'Connell et al., [115] can bind and detect the estradiol antibody at the time of oestrus via near-infrared fluorescence, they are employed as a method of tracking oestrus in animals. A central monitoring and control system will use the input from this sensor to activate breeding. Today, traditional in vitro fertilization methods used in animal breeding is greatly simplified by the use of microfluidics. Sperm and eggs are physically separated during cattle breeding.

Implications of nanostructures

The development and safe application of nanostructured substances depends on a careful evaluation of the effects of their use on people, animals, and the environment. Because of this, multiple elements, such as the chemical composition, electrical charge, size, and form of the material used to generate nanostructures, among others, may have an impact on the toxicity of nanostructures due to the variety in their biological and physicochemical properties.

A combination of in vitro and in vivo research is necessary for the assessment of nanostructure formulation security. Using cell culture models and analyses of gene expression in cells, one first step is to assess in vitro cytotoxicity, genotoxicity, the impact of nanostructures on cell signaling, and other cellular activities. Nanomaterials can produce reactive oxygen species when they are internalized in cells, surpassing the antioxidant enzymes' capacity to maintain the balance of intracellular oxidation-reduction reactions, leading to oxidative stress, one of the primary causes of the cytotoxicity these nanoparticles cause. Therefore, pharmacokinetic, pharmacodynamics and toxic kinetic investigations should be used to determine how each nanostructure formulation is absorbed, distributed, metabolized, and excreted.

Nanostructures that are not biodegradable, especially inorganic ones may have negative impacts. Furthermore, compared to biodegradable nanostructures, they have a higher potential for tissue accumulation. However, as a result of the product's or its metabolite's biodegradation, biodegradable nanostructures could show hazardous properties. As a result, further research must be done to determine the toxicity of nanostructured chemicals, specifically how they may affect the environment. Ecotoxicity is viewed as one of the primary issues that must be dealt with in an interdisciplinary manner to comprehend how nanomaterials behave in the environment [116].

Safety

Although most NPs are safe to use, some could have harmful effects on (1) pharmaceutical company employees (for example, prolonged pulmonary exposure to carbon nanotubes may cause reproductive disorders [117], and (2) patients (e.g., the accumulation of magnetic iron oxide NPs inside the body, or through damages caused due to unstable binding between the therapeutic agent and the particles which may release the drug in healthy tissues instead of the target tissues) [118]. In addition to causing healthy tissue toxicity, the preparation's partial release outside of its target will also send sub-therapeutic levels to the target part. Their capacity to traverse numerous biological barriers within the body, including the BBB, makes any error have serious repercussions [13], or even (3) on the environment (for example, the rising demand for radionuclides or carbon nanofibers are also implicated in the ozone layer in the atmosphere's depletion [13, 118]).

Future prospects

The range of uses for nanotechnology in the animal production sector will grow as it advances and attracts more attention. It is likely possible soon to regularly add nano-supplements to livestock feed to improve it; however, it will take more time before nanoparticles completely replace antibiotics in feed because many biocidal candidates still need to be tested *in vivo* before going through clinical trials and food safety tests following government regulations. Nanoparticles have previously been used outside of animal products, such as in antiseptic wound dressings, and more will come [119, 120].

It is crucial to look into nanoparticle cytotoxicity in both cancer cell lines and normal, healthy cell lines for studies interested in nanoparticles with anti-cancer potential. Claiming the nanoparticle under examination only has anti-cancer characteristics and only utilizes cancer cells may be misleading because the nanoparticle may be harmful to all cell types. The functionalities of nanoparticles discovered *in vitro* research must be confirmed in *in vivo* studies. Table 4 lists nanoparticle studies important to the animal agriculture sector as well as knowledge gaps that will call for additional study.

Table 4: Summary of Nanoparticle studies relevant to veterinary science

Nanoparticle	Type	Experiment	In-vitro/ In-vivo	Application	
Mesoporous Silica	Nanostructured	Release of the drug spatial imaging throughout the body	In-vitro	Veterinary Medicine	[121]
Poly(L-lactide)- and Poly(D-lactide)-b- poly(acrylic acid)	Nanostructured	Research into novel controlled delivery for pharmaceuticals	In-vitro	Veterinary Medicine	

Albumin-dextran	Nanostructured	To make watery solutions, engage hydrophobic drugs.	In-vitro	Veterinary Medicine	[121]
Zinc oxide	Metal	Implications of toxins on animal sperm	In-vitro	Reproduction	
Titanium oxide	Metal	Implications of toxins on animal sperm	In-vitro	Reproduction	
Antibody-coated or Lectin-coated Fe ₂ O ₃	Metal	Semen Nano-purification	In-vitro	Reproduction	
Mesoporous Silica	Nanostructured	Protein/nucleic acid cargo transfer mediator for sperm	In-vitro	Reproduction	
Silver	Metal	Silver nanoparticles bonded to cellulose fibers with alkali lignin were tested for antimicrobial activity.	In-vitro E-coli	Biocide and veterinary medicine	
Biocellulose	Natural	Designing a disinfectant, and treatment for wounds that stimulates collagen	In-vitro infectious bacteria	Biocide and veterinary medicine	
Copper and gold	Metal	Biological water treatment agents	In-vitro	Biocide	
Casein Micelles	Natural	Estimating the bioavailability of encapsulated bioactive substances and their capacity for preservation and stability	In-vivo	Nutrient delivery	
Lipid Nanoparticle	Nanostructured	Test of the bioavailability of loaded chemicals via simulated digestion	In-vitro	Nutrient delivery	
Gold	Metal	Amoxicillin should be functionalized to combat bacterial resistance	In-vitro/ In-vivo Mice	Biocide	

Chitosan	Polymer	The effectiveness of drug loading and release being evaluated	In-vitro	Biocide	
Iron Oxide	Metal	Applications of imaging in in-vitro functional investigations	In-vitro	Veterinary Medicine	[121]
Carbon (Glucose-sucrose-derived)	Nanostructured	Demonstrating the bioactivity of loaded drugs against cancer	In-vitro	Veterinary Medicine	

Conclusion

The ability to interact at the nuclear and molecular levels to study, manage and apply nanometer-dimensionality is what makes nanotechnology such an exciting and rapidly developing field of engineering. It has made new potential uses in molecular biology and biotechnology possible. By delivering in-depth information and revealing what is happening inside an organism's inner body, nanotechnology has changed practically all of the veterinary and animal science fields, particularly in industrialized nations. Quantum dots, magnetic nanoparticles, nanopores, polymeric nanoparticles, nanoshells, fullerenes, liposomes, and dendrimers are a few examples of nanoparticles that are utilized for illness detection, therapy, medication administration, animal breeding, and reproduction.

Comparative to other sister disciplines, nanotechnology is regarded as one of the major advancements now employed in a variety of fields, but it is still in the early phases of application to veterinary science. In addition, the technology's complexity and expensive cost made it difficult for underdeveloped nations, in particular, to utilize it in the field of animal science. Numerous different types of nanoparticles have been created thanks to the quick progress in developing and manipulating nanomaterials. Personalization of the medical interferences is then made possible by this. All areas of veterinary medicine, including diagnosis, treatment, immunization, animal production and reproduction, feeding, and hygiene, have seen dramatic advancements because of nanotechnology.

Numerous advantages of nanotechnology exist in several branches of business and science, including those about people, animals, and the environment. The application of nanostructures in the pharmacological and immunological fields of veterinary care appears promising. Although still in its infancy, the use of nanotechnology in veterinary medicine has shown a wide range of potential for basic and applied research, as well as numerous improvements in animal health and production. In particular, pharmacological therapies have offered promising treatments for illnesses with poor prognoses. We underlined that nanotechnology is a young and exciting field of study that has been challenging many preconceptions and that further research is necessary to confirm its safe application in veterinary care. Therefore, to ensure the safety of nanostructured

compounds, aspects relating to ecotoxicity as well as bioaccumulation of nanoparticles in animal and plant tissues must be examined. Regarding thoughts for the future, we thought that increased spending on science and technology could help to advance and strengthen nanotechnology globally.

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