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Application of Nanoparticles and Nano Technology for Treating Various Diseases Like Tumors and Carcinoma in Animals

[1]Rana Yousuf Rehman, Amir Zeeshan[2], Fahad Riaz[3*], Mohsin Farid Sulehri[4], Anam Saba[5], Umair Ahmed[6], Mohsin Saleem Ghouri[7], Sofia Safdar[8], Nafeesa Kainat[9], Hina Javed[10], Anum Sabir[11]

[1]Pathobiology And Biomedical Sciences, The Muhammad Nawaz Shareef University of Agriculture (MNSUAM), Multan, Punjab, Pakistan

[2]Department of Chemistry, Lahore Garrison University, Lahore, Punjab, Pakistan

[3]Department of Clinical Medicine and Surgery, University of Agriculture Faisalabad, Punjab, Pakistan*

[4]Department of General Surgery, Southern Medical University Guangzhou, China

[5]Department of Biotechnology, University of Agriculture, Faisalabad, Punjab, Pakistan

[6]Department of Surgery, University of Veterinary and Animal Sciences, Lahore, Punjab, Pakistan

[7]Department of Chemistry, Government Murray Graduate College, Sialkot, Punjab, Pakistan

[8]Department of Biological Sciences, Superior University, Lahore, Punjab, Pakistan

[9]Department of Zoology, Wildlife & Fisheries, PMAS Arid Agriculture University, Rawalpindi, Punjab, Pakistan

[10]Department of Biological Sciences, University of Veterinary and Animal Sciences, Lahore, Punjab, Pakistan

[11]Faculty of Veterinary Sciences, University of Veterinary and Animals Sciences Lahore Sub Campus, Jhang, Punjab, Pakistan

***Corresponding Author:** vetdr06ag@gmail.com*

Abstract

The application of nanoparticles and nanotechnology in treating diseases such as tumors and carcinoma in animals is revolutionizing veterinary care. This review synthesizes existing information regarding the utilization of nanoparticles in veterinary oncology, assesses their therapeutic and diagnostic uses, and investigates upcoming technologies such as nano vaccines and theranostics. This review critically analyzes recent advancements to identify key trends and innovations in nanoparticle formulations, targeted delivery systems, and multimodal imaging techniques while addressing notable gaps in the literature, such as the inconsistent efficacy of nanoparticle therapies across species and their toxicological and environmental implications. This review emphasizes the many categories of nanoparticles, including liposomes, dendrimers, and polymeric nanoparticles, and their distinct roles in veterinary cancer. It analyzes the difficulties presented by tumor biology, diversity, species-specific pharmacokinetics, and regulatory obstacles that hinder the broad implementation of nanoparticle-based therapeutics. This review examines the amalgamation of diagnostics and treatments via theranostic methodologies and the advancement of nano vaccines to boster immune responses against animal cancer. This underscores the necessity for species-specific formulations, environmentally sustainable processes, and thorough safety evaluations to guarantee the responsible implementation of nanotechnology in veterinary medicine. This review offers significant insights

for forthcoming research, clinical implementation, and policy formulation by examining these essential elements. This highlights the capacity of nanoparticles to transform veterinary oncology while promoting interdisciplinary cooperation to address current challenges. This synthesis seeks to enhance discipline, connect veterinary and human oncology, and foster innovation in cancer therapy.

Keywords: Nanoparticles, Veterinary Oncology, Nanotechnology, Targeted Drug Delivery, Diagnostic Imaging, Theranostics, Nanovaccines

1. Introduction

The use of nanoparticles and nanotechnology for treating diseases such as tumors and carcinoma in animals has emerged as a revolutionary field in veterinary medicine. Owing to their distinctive physicochemical features, nanoparticles facilitate precision-targeted drug delivery, enhance therapeutic efficacy, and diminish systemic toxicity, providing novel answers to enduring issues in cancer treatment (Din et al., 2017; Ramos et al., 2017). This domain is notably important, as veterinary oncology encounters distinct challenges, such as species-specific physiological differences, restricted diagnostic resources, and the necessity for minimally invasive treatment methods (Yang et al., 2021). This paper synthesizes recent developments, emphasizing the increasing significance of nanotechnology in tackling these issues and improving cancer therapy for animals, thus contributing to the broader domain of comparative oncology (Buhr et al., 2020).

Notwithstanding notable advancements, significant deficiencies persist in our comprehension and utilization of nanoparticles in veterinary oncology. Recent studies have shown that liposomes, dendrimers, and polymeric nanoparticles can enhance medication delivery and diagnostics; nevertheless, variable efficacy stemming from diversity in tumor biology and species-specific responses has impeded their general adoption (Chauhan, 2018; Palmerston Mendes et al., 2017). Moreover, the toxicological and environmental ramifications of nanoparticle utilization have been little investigated, presenting significant hazards to animal and ecosystem health (Graham et al., 2017; Naz et al., 2020). Addressing these gaps is essential for enhancing nanoparticle-based therapeutics' safety, efficacy, and sustainability. This review addresses existing knowledge gaps by thoroughly examining the present literature, highlighting new advances and their translational potential, and identifying further research and improvement areas (Brundo & Salvaggio, 2018; Mourdikoudis et al., 2018).

This review aims to thoroughly synthesize the present status of nanoparticle applications in veterinary oncology, emphasizing progress in cancer treatment, diagnostics, and emerging technologies, such as nano vaccines and theranostics (Wang et al., 2016). This review provides new insights into nanoparticles' design, implementation, and more enormous implications by overcoming the constraints of prior techniques, such as the absence of species-specific

formulations and standardized regulatory frameworks (Ismail et al., 2019). These contributions seek to influence future research and therapeutic practices and foster sustainable innovation in veterinary oncology (Yang et al., 2021).

2. Foundations of Nanotechnology in Veterinary Oncology

2.1 Principles of Nanotechnology in Cancer Therapy

Nanotechnology has changed the landscape of veterinary oncology, allowing the development of novel technologies for cancer treatment with a focus on targeted drug delivery (Fu & Xiang, 2020). The unique cellular properties of nanoparticles, which include small size, large surface area, and the ability for functionalization, allow better targeting of the therapeutic agent to the tumor site with minimal systemic toxicity (Ni et al., 2020). Smaller sizes allow them to penetrate deeper into tumors to provide localized drug delivery and therapeutic action (Navya et al., 2019). Moreover, conjugation with specific ligands improves the targeting of therapeutic agents, prevents cancer cells from healthy tissues, decreases side effects, and increases the effectiveness of cancer therapy (Lorkowski et al., 2021).

Nanoparticles employ passive and active targeting to increase the specificity and potency of cancer treatments as shown in **Figure 1.** Passive targeting utilizes the enhanced permeability and retention (EPR) effect, which describes the increased propensity of nanoparticles to localize in tumor tissues stemming from the leakiness of tumor vasculature in the tumor microenvironment (Mohapatra et al., 2021). The heterogeneity and variability of the EPR effect on which the application of nanoparticles relies, dependent on multiple factors, including tumor type, size, and vascular heterogeneity, limits their practical use in many clinical applications (Gao et al., 2021). On the other hand, active targeting relies on the functionalization of nanoparticles with ligands or antibodies that bind to tumor-specific markers, leading to higher precision in targeting and lower off-target interactions (Jia et al., 2021). In foundational studies, active targeting has been shown to drastically improve drug delivery efficiency and therapeutic outcomes in various animal cancer models. However, further development is required to enable scalability and specificity (Lee et al., 2017).

Despite nanotechnology's promise, conflicting arguments concerning its efficacy and limitations highlight the necessity for critical analysis. In some cases, discrepancies in the EPR effect across animal models have led to inconsistent nanoparticle accumulation in tumors. These differences highlight the importance of further exploring tumor biology-nanoparticle interplay for greater predictivity and efficacy (Gadag et al., 2020).

The problem with veterinary oncology provided an entryway to nanotechnology and the development of stimuli-responsive nanoparticles that release therapeutic agents on demand when exposed to a specific trigger generated by the tumor microenvironment, including a change in pH, temperature, or enzymatic activity. Such systems enable better targeting and low systemic

toxicity, acting in tumor-specific conditions (Liu et al., 2017). Nevertheless, clinical translation challenges still exist regarding long-term nanoparticle safety, cost-effectiveness, and veterinary regulation approval. Recent developments have sought to circumvent these problems by employing more biocompatible nanoparticles and assessing alternative, inexpensive production methods (Duan et al., 2016).

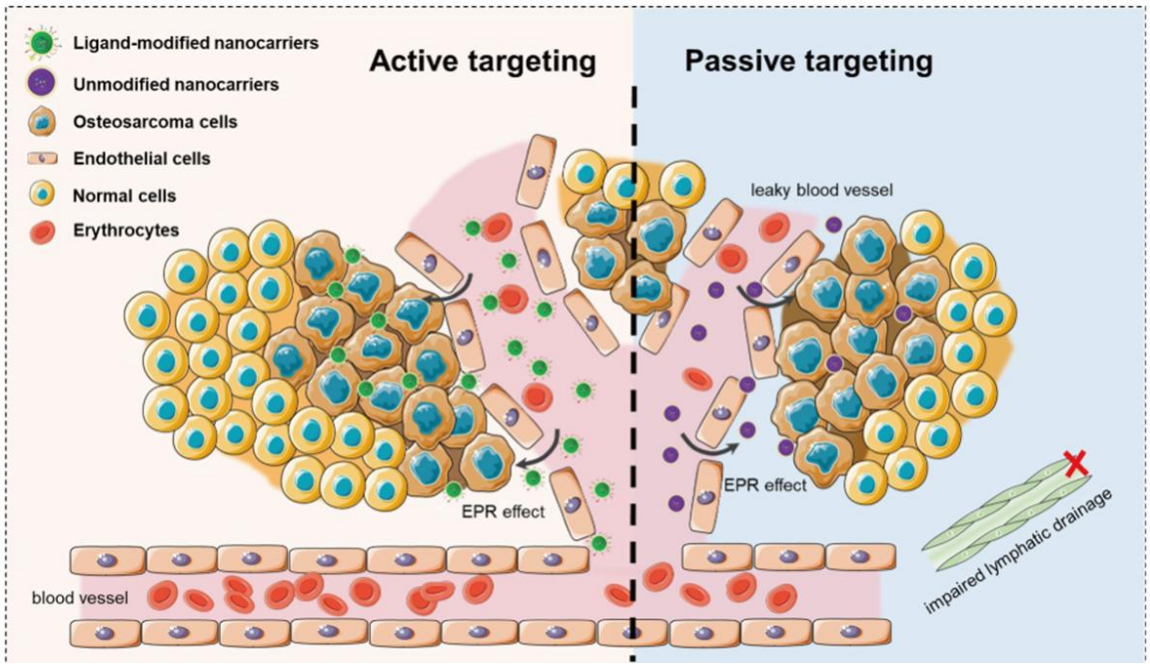

Figure 1: This diagram presents a comparative depiction of active and passive targeting techniques utilized in nanoparticle-based cancer therapy. Passive targeting utilizes the Enhanced Permeability and Retention (EPR) effect, wherein nanoparticles aggregate in tumor tissues owing to the tumor microenvironment's compromised vascular and deficient lymphatic outflow. Conversely, active targeting employs ligand-modified nanocarriers that specifically attach to overexpressed receptors on tumor cells, enabling receptor-mediated endocytosis for accurate drug delivery. The figure also emphasizes the functions of other cell types, including endothelial cells, osteosarcoma cells, and erythrocytes, in these systems. The graphic contrasts the two techniques, highlighting their complementary roles in enhancing the localization and efficacy of anticancer medicines while minimizing off-target consequences.

2.2 Types and Characteristics of Nanoparticles in Veterinary Applications

Nano particles (NPs) with specific therapeutic properties have been used in veterinary oncology as shown in **Table 1**. Liposomes, phospholipid bilayer structures, have been used extensively for many years as chsemotherapeutic carriers due to their ability to solubilize, increase drug bioavailability, and increase systemic safety (Crintea et al., 2021). These branched structures enable precise control over the loading of drug molecules and their subsequent release

in a therapeutically active form, offering the possibility of targeted drug therapy with reduced side effects (Din et al., 2017). Widely characterized polymeric nanoparticles, with the advantages of biodegradation, can encapsulate a spectrum of therapeutic agents and achieve enhanced therapeutic efficacy with sustained drug release at the tumor site (Bai et al., 2018).

However, these nanoparticle systems also have unique challenges that must be overcome. Liposomes, for example, suffer from instability in vivo, whereas dendrimers have a complex synthesis and may exert cytotoxicity (Sherje et al., 2018). Polymeric nanoparticles provide an opportunity for more rapid infusion but less predictability in drug release rates, complicating therapeutic windows. These limitations can be solved with more advanced formulations, and we need to work on them to make them more efficient and better for veterinary medicine (Chibuk et al., 2021).

In addition, biocompatibility and pharmacokinetics are essential for expanding the utility of this promising method in animal models. Given these immune reactions against some metals used in various nanoparticles, biocompatible polymers (such as PLGA and chitosan) are required for their small nanocarriers to possess negligible side effects (Youssef et al., 2019). In addition, PEGylated nanoparticles have been shown to have long-circulating properties and enhanced drug bioavailability. Despite these developments, significant challenges remain, including tissue heterogeneity and differential drug release, highlighting the need to optimize nanoparticle formulations (Kischkel et al., 2020).

Table 1: Summary of Nanoparticle Types and Their Characteristics

Nanoparticle Type	Key Properties	Advantages	Challenges	Applications	Reference
Liposomes	Phospholipid bilayer	Biocompatibility	Stability in vivo	Chemotherapy delivery	(Zabielska-Koczywąs & Lechowski, 2017)
Dendrimers	Branched structure	Precise drug loading	Synthesis complexity	Targeted drug delivery	(Wang et al., 2022)
Polymeric NPs	Biodegradable polymers	Sustained drug release	Variable release rates	Veterinary oncology	(Cerbu et al., 2021)
Gold NPs	Strong optical properties	Imaging contrast	Cost, toxicity	Tumor imaging	(Alkilany & Murphy, 2010)
Iron Oxide NPs	Superparamagnetic	MRI contrast	Long-term safety concerns	Lymph node metastasis imaging	(Yan et al., 2023)

2.3 Advances in Nanoparticle Formulations

Nanoparticle formulations have recently been developed to maximize efficacy and reduce toxicity in veterinary cancer patients. On the one hand, as related to the classical drug delivery aspects, chitosan nanoparticles, for instance, enhance the bioavailability and specificity of drugs, thus decreasing the pharmacological intrinsic toxicity of anticancer agents (Qin & Li, 2020). Liposomes are also effective for encapsulating chemotherapeutics, protecting the drug from degradation, and allowing targeted drug delivery to the tumor site. Silver nano particles (AgNPs) are dual anticancer and antimicrobial agents that simultaneously overcome oncological and secondary infections in veterinary patients (Dakal et al., 2016).

This is coupled with improvements in controlled-release strategies that have driven the success of nanoparticle-based drug delivery to the next level. Aliphatic polycarbonate nanoparticles are an example of stimuli-responsive nanocarriers, which release their cargo in response to an environmental external stimulus such as pH or temperature for more targeted delivery (Qin & Li, 2020). Localized and sustained drug release achieved by hybrid systems of nanoparticles and hydrogels improves drug therapeutic performance. Polymer drug conjugates provide degradation protection, bioavailability, and a basis for targetedness (Nicolas, 2016).

To overcome interspecies differences in pharmacokinetics, species-specific nanoparticle formulations have been developed. By incorporating differences in drug metabolism, distribution, and clearance rates between species, these innovations allow for safer and more effective treatments (Wustefeld-Janssens et al., 2021). For example, nanoparticles with idiosyncratic ligands can maximize target specificity and minimize systemic toxicity in dogs and cats. These personalized therapies are essential for discovering reproducible and potent anticancer treatments for various veterinary populations (Bai et al., 2018).

3. Nanoparticle-Based Cancer Therapies in Veterinary Medicine

3.1 Targeted Drug Delivery Systems

Nanoparticles have also been considered effective drug delivery systems in veterinary oncology, with distinct advantages over conventional chemotherapy. Of these, liposomal formulations have been widely researched and used as they can load anticancer agents in the lipid bilayers, effectively increasing the solubility and structural stability of the drug and allowing drug localization at tumor sites (He et al., 2019). Through the enhanced permeability and retention (EPR) effect, whereby nanoparticles preferentially accumulate in tumor tissues owing to leaky vasculature, liposomes enhance therapeutic efficacy and reduce off-target effects (Riaz et al., 2018). Because of this targeted delivery, systemic toxicity is decreased, with studies reporting significantly fewer adverse events with liposomal formulations than complimentary drug therapies (Lila & Ishida, 2017).

However, the variability of the EPR effect poses significant hurdles to consistently providing therapeutic benefits. The accumulation and distribution of nanoparticles are also significantly affected by parameters related to the tumor, such as the tumor size, tumor type, and tumor microenvironment. EPR-mediated delivery efficiencies are still relatively low (1-5%), which makes translating preclinical data to clinics very challenging (Anselmo & Mitragotri, 2019). Moreover, the unequal distribution of drugs, which worsens due to the heterogeneity of tumor vasculature, emphasizes the need to optimize nanoparticle design and delivery approaches to improve specificity. While these factors are critical for nanoparticle-based cancer therapies in veterinary oncology, addressing these challenges is an equally significant hurdle for veterinary oncologists who wish to translate nanoparticle-based cancer therapy to the clinic (Hong et al., 2019).

Nanoparticle-based drug delivery systems have endeavored with tremendous efforts through attempts and analysis, and a few case studies are highlighted to understand the circumstances where some limitations exist. For instance, both animal models have shown enhanced local drug delivery and therapeutic effects (Allahou et al., 2021). Unfortunately, they still have some drawbacks, such as inconsistency in drug release rates and formulation difficulties. For example, nanoparticles have been shown to improve the EPR-mediated tumor accumulation of chemotherapeutics by as much as 100-fold (Bardania et al., 2017). However, the clinical translation of nanoparticles is also limited in part by poor consistency in EPR effects between tumor types. Stability issues and the necessity of a target-specific delivery strategy further hamper the clinical utility of liposomal formulations (Signorell et al., 2018). Success in addressing these hurdles is essential to implement profitable nanoparticle-assisted therapies in the veterinary field (Skakic et al., 2022).

3.2 Comparative Efficacy Across Species

Improving their application as a veterinary oncologic therapy requires a basic understanding of species-specific nanoparticle metabolism and efficiency differences as given in detailed in **Table 2**. This phenomenon is more pronounced in smaller animals, such as rodents, where quicker energy expenditures and more rapid clearance mechanisms result in rapid nanoparticle clearance from circulation (Cerbu et al., 2021). However, larger animals, such as dogs, ponies, rabbits, or rats, have slower metabolisms and thus may keep the nanoparticles longer, allowing improved therapeutic performance. These differences suggest that nanoparticle formulations must be species-stratified to achieve optimal drug delivery with reduced toxicity (Patel & Patel, 2023).

Interspecies studies on nanoparticle retention, biodistribution, and therapeutic effects reveal important differences affecting their use in veterinary oncology. Mobility nan establishing the neoplasia differ due to the diversities of the vascular structures and metabolic rates in nonpractitioners, such as nanoparticle uptake at the tumors. For example, small animals

such as mice demonstrate rapid clearance by nanoparticles that are followed by minimal tumor retention (Zhu et al., 2017). In contrast, relatively larger animals, such as dogs, have deep tissue harboring slow circulation times conducive to therapeutic gain (Fawzy et al., 2021). Such physiological differences further highlight the imperative to develop species-specific formulations of nanoparticles to maximize therapeutic efficacy by establishing appropriate pharmacokinetics and biodistribution, enabling practical applications across the veterinary continuum (Bai et al., 2018).

Comparative oncologists gain insights from both veterinary and human medicine to identify opportunities for advancing human medicine. Common therapeutic targets can be identified through molecular homology and genetic similarities between human cancers and spontaneous tumors that develop in animals, such as canine melanomas. These similarities enable translational research, with fewer drug development steps, taking less time, and being less expensive than identical trials in humans (Gerosa et al., 2020). However, tumor biology discrepancies and species' modality responses limit their direct clinical utility (Hua et al., 2018). While these observations have important implications for improving the efficacy of nanoparticle-based cancer therapies for both veterinary and human indications, they highlight the need to address such disparities to maximize the translational potential of nanomedicine (Hua et al., 2018). The use of nanoparticle-based cancer therapeutics to improve therapeutic clinical efficacy across species has garnered significant attention, which is a transformative application as these are equally applicable to diagnostic and therapeutic monitoring (Patel & Patel, 2023).

Table 2: Comparative Efficacy of Nanoparticle Applications Across Species

Species	Nanoparticle Type	Key Findings	Challenges	References
Rodents	Liposomes	High clearance rates	Short circulation times	(Gabizon et al., 1993)
Dogs	Gold NPs	Prolonged retention, enhanced imaging	Interspecies biodistribution	(Axiak-Bechtel et al., 2014)
Cats	Polymeric NPs	Improved tumor targeting	Immune variability	(Zabielska-Koczywąs & Lechowski, 2017)
Horses	Iron Oxide NPs	Effective MRI imaging	High dose requirements	(Labens et al., 2017)

4. Diagnostics and Imaging Using Nanoparticles

4.1 Applications of Gold and Iron Oxide Nanoparticles

Gold nanoparticles (AuNPs) and iron oxide nanoparticles (IONPs) have shown great promise for supporting advanced imaging in veterinary oncology. AuNPs have unique optical properties and have been used in various optical imaging modalities (e.g., optical coherence tomography [OCT] and photoacoustic imaging) to enhance tumor imaging by altering tumor vasculature and margins (Bouché et al., 2019). A study of gold nano particles found a 54% increase in melanoma microvasculature visibility, thus showing their ability to enhance diagnostic precision (Bai et al., 2020). Due to their good biocompatibility and enhanced permeability and retention (EPR) effect, AuNPs are also important for accurately differentiating tumor tissue from healthy tissue to improve imaging (Zhang et al., 2020).

Superparamagnetic iron oxide nanoparticles (IONPs) are high-performance contrast agents for magnetic resonance imaging (MRI) with optimal properties for detecting lymph node metastases in veterinary oncology. They double MRI sensitivity, enabling imaging of small metastatic lymph nodes that standard imaging approaches can lack (Vallabani & Singh, 2018). Ultra-a minuscule superparamagnetic iron oxide (USPIO) nanoparticles have achieved more than 90% diagnostic accuracy in diagnosing lymph node involvement in dogs with cancers. This highlights the importance of IONPs in the early detection and treatment of metastatic diseases in pets (Mulens-Arias et al., 2020).

Diagnostically efficient AuNPs and IONPs, with their unique advantages suited for specific diagnoses, are known, but their performance varies with imaging modality and tumor. Gold nanoparticles (AuNPs) have proven to be efficient imaging agents in computed tomography and photoacoustic imaging, owing to their intense optical properties and versatile surface functionalization (Riley & Day, 2017). On the other hand, IONPs display superior imaging properties for deep tissue imaging using MRI that allows tumor expansion to be observed in real-time. These nanoparticles have the potential to be combined for multimodal imaging, allowing their possible integration into multimodal diagnostic modalities, which would significantly improve veterinary diagnostics (Chouhan et al., 2021).

4.2 Multimodal Imaging Techniques

Multimodal imaging modalities with nanoparticles have evolved into useful diagnostic and/or therapeutic tools to overcome some tumor detection and treatment challenges in veterinary oncology. Combining complementary imaging modalities such as magnetic resonance imaging (MRI) and computed tomography (CT) enables simultaneous assessment of tumor morphology and function and potential enhancement of diagnosis as given in **Table 3.** For instance, gadolinium chelate-coated gold nanoparticles are high-relativity contrast agents that combine imaging modalities to overcome the limitations of single-modality techniques (i.e., low

sensitivity or lack of specificity). This allows for a comprehensive perspective of tumor traits, assisting in more precise diagnosis and improved treatment (Klein et al., 2021).

AuNPs and IONPs are significant modalities in multimodal imaging frameworks for imaging contrast and sensitivity (Upputuri & Pramanik, 2020). For example, photoacoustic imaging benefits from AuNPs as the imaging contrast provides the optimal resolution, while IONPs improve imaging of deep tissue in MRI. As a result, multimodal imaging enables comprehensive characterization of tumor microenvironments and metastatic disease, supplying critical information to inform surgical planning and therapeutic targeting. Integrating nanoparticles with imaging modalities reflects their game-changing capability in veterinary oncology (Arms et al., 2018).

Customizing nanoparticle-based imaging protocols for particular animal species is crucial for achieving optimal diagnostic performance. Due to differences in anatomy, physiology, and tumor biology, the doses of nanoparticles and imaging parameters must be optimized and adjusted accordingly. For example, smaller animals may require lower dosages of nanoparticles to avoid saturating the signal (Lin et al., 2020). Changes in how imaging is performed (e.g., improving the specificity of photoacoustic imaging in certain species) predict that diagnostic techniques will be available for broader veterinary populations. This functionality allows clinicians to personalize the treatment for individual patients (Mavridi-Printezi et al., 2020).

Multimodal nanoparticle imaging enables better therapeutic planning and follow-up assessment of therapeutic responses. The application of MRI provides a means of simultaneous evaluation of tumor microenvironments and assessment of treatment efficacy by close monitoring with positron emission tomography (PET), allowing for dynamic alteration of therapeutic strategies by clinical care teams (Moore et al., 2019). Combining such modalities further increases diagnostic accuracy and provides a histopathological framework for precision medicine in veterinary oncology while facilitating prognostic stratification and improved patient care (DiStasio et al., 2018).

Table 3: Applications of Multimodal Imaging Using Nanoparticles

Imaging Modality	Nanoparticle Type	Diagnostic Capabilities	Veterinary Applications	References
MRI	SPIONs	High-resolution deep tissue imaging	Lymph node metastasis detection	(Madru et al., 2012)
CT	Gold NPs	Enhanced tumor contrast	Tumor visualization	(Luo et al., 2021)
Photoacoustic Imaging	Gold NPs	Tumor margin identification	Surgical planning	(Guan et al., 2017)

5. Toxicological and Environmental Implications of Nanoparticles

5.1 Nanotoxicology in Veterinary Applications

Toxicity in Veterinary Oncology Nanoparticle action in toxicology occurs mainly through oxidative stress and DNA damage. Nanoparticles produce ROS upon entry into biological systems, resulting in unbalanced cellular homeostasis, leading to lipid peroxidation, protein denaturation, and DNA damage (El-Kenawy et al., 2017). However, after being subjected to specific stressors, eventual disruptions either promote existing tumors or lead to carcinogenesis. Physicochemical characteristics, such as size, shape, and surface charge, are crucial in determining NP interactions with biological systems that ultimately dictate their toxicity profiles (Jeevanandam et al., 2018). Finally, a clear understanding of these processes' interactions is fundamental to guide the design of NP formulations that ensure safety and efficacy when applied in veterinary medicine (Entzian & Aigner, 2021).

Recent research has pinpointed particular side effects of nanoparticle carriers, such as reproductive and organ-specific toxicity as given in **Table 4**. For example, silver nanoparticles have been shown to induce oxidative stress and inflammatory responses, leading to their concern for chronic toxicity in veterinary medicine (Mathur et al., 2018). Likewise, iron oxide nanoparticles have been utilized in clinical diagnostics; however, irreparable DNA damage, cytotoxic effects found in important organs, and other damages appear to limit the usage of these promising products. Such results emphasize the need for thorough safety evaluations to reduce the potential dangers of nanoparticle therapies (Raies & Bajic, 2016).

This outlines the significance of mitigation strategies to address such toxicological challenges. Properly optimizing nanoparticle characteristics for lower surface reactivity and higher biocompatibility through surface coating, such as polyethylene glycol, can reduce undesirable effects (Raies & Bajic, 2016). Additionally, in silico modeling and employing alternative organisms, such as zebrafish, provide ethical and efficient tools for early toxicity testing to complement and reduce animal models (Patlewicz & Fitzpatrick, 2016). Monitoring the biodistribution and bioaccumulation of NPs in animal tissues over prolonged periods is crucial for the safety of clinical applications (Aragao-Santiago et al., 2016).

The next step is to link the consequences of nanoparticle use to their more contextual implications, specifically to highlight the principle that the management of toxicological risks in veterinary medicine is an important part of mitigating environmental consequences. This overlap between animal health and ecological safety illustrates the intermingling of this species.

Table 4: Toxicological Effects and Mitigation Strategies

Nanoparticle Type	Observed Toxicity	Mechanisms	Mitigation Strategies	References
Silver NPs	Reproductive toxicity	Oxidative stress, inflammation	Surface coating, PEGylation	(Skóra et al., 2024)
Iron Oxide NPs	Organ-specific cytotoxicity	DNA damage	Biocompatible coatings	(Chrishtop et al., 2021)
Polymeric NPs	Variable biodistribution	Immune responses	PLGA, chitosan use	(Jia et al.)

5.2 Environmental Impact of Veterinary Nanomedicine

Nanoparticles may remain persistent in an ecosystem and have the potential for bioaccumulation, which can play a significant role in the impact of veterinary nanoparticles on ecosystems. They enter through injection, ingestion, or inhalation and then bioaccumulate in organs such as the liver, spleen, and kidneys (Cerbu et al., 2021). Their resilience is not limited to biological systems; nanoparticle exposure leads to developmental and behavioral toxicity in zebrafish. This environmental persistence highlights the importance of thorough assessments to prevent the ecological dangers of veterinary nanomedicine (Cerbu et al., 2021).

This One Health perspective invites consideration of the interconnectedness of animal, human, and environmental health and urges more comprehensive approaches to nanoparticle safety. For example, some studies found that nanoparticulate iron oxide used in veterinary diagnostic tests leached into the soil, affecting both the water systems and the organisms in them, thus posing a threat to both aquatic and terrestrial ecosystems (Cerbu et al., 2021). The integration of green chemistry approaches for developing biodegradable NPs is fundamental to mitigate these risks without hindering the progress of veterinary nanomedicine (Su & Kang, 2020).

Environmental concerns also stem from the use and disposal of nanoparticle-based veterinary medicines. Widespread scientific usage of these reagents and compounds could lead to nanoparticle persistence in soil and water ecosystems, impacting the physiology and reproduction of wildlife. In addition, the nanoparticles, being very infamous, are still in circulation, raising the alarm about bioaccumulation and long-term ecological effects. To avoid these environmental concerns, combining effective waste management strategies and biodegradable nanoparticle formulations should be prioritized when applying nanotechnology in veterinary medicine (Su & Kang, 2020).

The connection between addressing toxicological risks in veterinary medicine and mitigating environmental impacts underscores the broader responsibility of nanoparticle use. A cohesive strategy is required to ensure that advancements in veterinary nanomedicine do not compromise ecological balance (Cerbu et al., 2021).

5.3 Safety and Regulation

However, there is a need for strict safety measures guaranteed by pharmacists trained responsibly in the trend of using nanoparticles in veterinary oncological applications. Safety assessments are mainly focused on the uptake of nanoparticles and their acute toxicity by evaluating nanoparticle physicochemical properties and biodistribution (Zhang et al., 2016). However, the reader also points out important missing parts for testing long-term safety and environmental impacts, such as assessing nanoparticle accumulation in tissues and ecosystems. Some gaps in the data need to be filled, such as the effects of composite chronic exposure and sustainable disposal practices in vivo, which need to be a high priority (Mohammadpour et al., 2019).

Challenges of the legislative background in veterinary nanoparticle therapies Specific guidelines for veterinary use are currently lacking, which leads to inconsistencies in the assessment of safety and efficacy. Because animal species exhibit variable biological responses, developing dose or treatment protocols based on human studies that can be extrapolated to all other animals is challenging (Mochel et al., 2019). Establishing regulatory frameworks incorporating species-specific data and aligning standards across veterinary and human medicine will be essential for tackling these issues (Mochel et al., 2019).

Addressing regulatory compliance through blanket safety evaluation frameworks will be necessary in future strategies. Long-term toxicity studies and environmental impact assessments should be conducted to ensure comprehensive safety (Bai et al., 2018). Guidelines that directly consider species-specific responses to nanoparticles will come from collaboration between regulatory bodies, researchers, and practitioners (Mochel et al., 2019). On a One Health basis, ongoing assessment of biodistribution and degradation of nanoparticles will provide further assurance of responsible nanoparticle use for animal and environmental health (Mohammadpour et al., 2019).

6. Future Directions and Translational Applications

6.1 Nanovaccine Development

Self-assembled protein nanoparticles (SAPNs) have been introduced as a promising new front for developing nano vaccines in veterinary oncology as shown in **Figure 2**. These nanoparticles were successfully loaded with antigens but could improve immunogenicity and reduce immunotoxicity (López-Sagaseta et al., 2016). SAPNs have unique features such as better

stability, targeted delivery, and the ability to activate both humoral and cellular immune responses (Wang et al., 2019). They have been shown to stimulate strong immune responses against many cancers in animal models, opening new avenues for cancer treatment. However, more extensive research is needed to maximize formulations and evaluate long-term safety and efficacy for widespread clinical utility (López-Sagaseta et al., 2016).

Although they exhibit apparent promise, the development of nano vaccines presents significant challenges, including variability in immune responses between animal species and stability issues for nanoparticle formulations. These discrepancies constrain the efficacy of vaccines and highlight the need for design improvements. Those strategies include adding toll-like receptor (TLR) agonists as an adjuvant for increasing the immunogenic potential and biomimetic materials for stabilizing efficacy. In addition, accurate tuning of the size and surface characteristics of SAPN by self-assembly may help fine-tune the target and delivery. Ongoing research in these domains is critical to provide an avenue for the future safe and effective use of nano vaccines in this arena (Wang et al., 2019).

However, increased delivery efficiency and specificity in recent years only enhance the potential of these nano vaccines. Biodegradable nanocarriers and biomimetic coatings have enhanced interactions with immune cells, improved antigen stability, and sustained release (Varma et al., 2020). Use of nanocarriers in vaccination by enhancing immunity and reducing the antigen dose. These advancements meet technological and immunological needs and contribute to improvements in total vaccine performance. Further studies are needed to continue translating these technologies into more predictable therapeutic solutions for veterinary medicine by improving upon these strategies and testing the feasibility of their use in various animal populations (López-Sagaseta et al., 2016).

A natural progression from these advancements in nanovaccine development is the exploration of integrated approaches, such as theranostics, which combine diagnostic and therapeutic functionalities to further revolutionize veterinary oncology (López-Sagaseta et al., 2016).

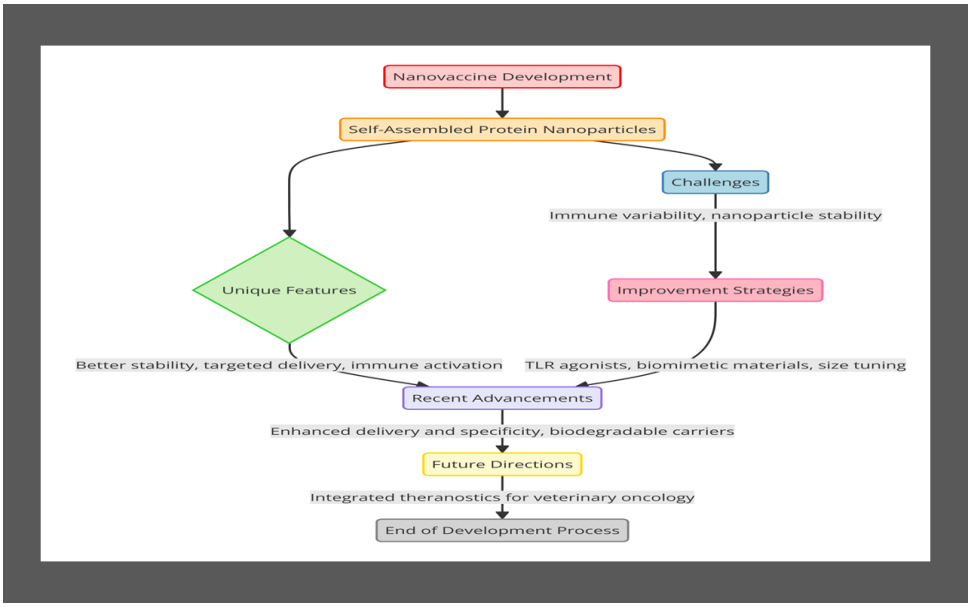

Figure 2: The flowchart defines the development process of nano vaccines, commencing with Self-Assembled Protein Nanoparticles (SAPNs), recognized for their distinctive attributes, including stability, targeted administration, and dual immune activation. It underscores problems such as unpredictability in immune response and nanoparticle durability, resulting in enhancement tactics that incorporate toll-like receptor agonists, biomimetic materials, and size optimization. These strategies contribute to recent developments such as improved delivery specificity and biodegradable nanocarriers. The flowchart finishes with future approaches, highlighting integrated theranostics as a promising approach to transform veterinary oncology.

6.2 Integration of Diagnostics and Therapeutics

Diagnostic and therapeutic integration, also known as theranostics, is an exciting new opportunity for veterinary companion animals and oncology, respectively. Superparamagnetic iron oxide nanoparticles (SPIONs), as theranostic nanoparticles, integrate the functionality of MRI with targeted drug delivery, enabling real-time monitoring and therapy of the tumor. SPIONs efficiently transport chemotherapeutic agents, allowing high-resolution tumor imaging during treatment delivery and improving precision and outcome (Gao et al., 2021). In a similar approach, nanoparticles containing indocyanine green have been used for photothermal therapy, in which nanoparticle-derived heat is used for combined imaging and targeted magnetic-guided therapy to induce localized cell death (Riley & Day, 2017).

Theranostic nanoparticles are further exemplified with clinical case studies. Magnetic iron oxide nanoparticles have been utilized for simultaneous imaging and therapy (theranostics) of canine tumors, which allows real-time therapeutic monitoring (Zabielska-Koczywąs & Lechowski, 2017). Moreover, owing to their high optical absorption ability, gold nanoparticles have been utilized in photothermal therapy because they can effectively destroy cancer cells

while simultaneously providing high-contrast imaging. These examples demonstrate how theranostic nanoparticles can provide tailored treatment options that move the needle toward more effective veterinary cancer therapies (Gerosa et al., 2020).

Theranostic applications in veterinary oncology will continue to evolve, emphasizing safety, efficacy, and precision. Multiple diagnostic and therapeutic modalities are being integrated into hybrid nanoparticle systems, potentially enabling them to address specific issues in veterinary medicine (Anselmo & Mitragotri, 2019). By inducing an immune response and imaging ability, self-assembled protein nanoparticles represent dual-functional therapeutic platforms for cancer (Poilil Surendran et al., 2018). The development of these formulations for differences in physiology and pathology between animal types is an area that requires further research (Liu et al., 2018). This target specificity, focusing on species-related parameters, will improve therapeutic outcomes by maximizing the clinical use of theranostic nanoparticles.

Combined with this, theranostic improvements alongside the gratifying growth of the nano vaccine spotlight opportunities for a proprietary integrated approach to transform veterinary oncology (Vines et al., 2019). Additional studies are needed to develop the best methods of applying these strategies to different indications, ensuring they are safe, effective, and can be deployed sustainably in the clinical setting (Anselmo & Mitragotri, 2019).

7. Conclusion

This review emphasizes the revolutionary capabilities of nanoparticles and nanotechnology in veterinary oncology, concentrating on their applications in cancer treatment, diagnostics, and prospective advancements, such as nano vaccines and theranostics. Significant discoveries have highlighted the efficacy of nanoparticles in targeted drug delivery, utilizing processes including the increased permeability and retention (EPR) effect and ligand-based active targeting to enhance therapeutic accuracy while reducing systemic toxicity. Liposomes, dendrimers, and polymeric nanoparticles demonstrate considerable potential for improving drug solubility, facilitating prolonged release, and achieving targeted administration. In contrast, theranostic strategies combine diagnostics and therapies, allowing for real-time tumor surveillance and intervention. Nanovaccines, especially self-assembled protein nanoparticles, have emerged as an innovative approach to stimulate strong immune responses in animals. The wider. These findings highlight their potential to transform veterinary oncology by enhancing treatment outcomes, minimizing unwanted effects, and improving diagnostic precision. Moreover, comparative oncology connects veterinary and human health, expediting medication discovery and translational applications. Notwithstanding these advancements, considerable gaps remain. The variability of the EPR effect, species-specific physiological variations, and restricted scalability of some nanoparticle formulations hinder their broad implementation. Furthermore, nanoparticle-based therapeutics' environmental and toxicological effects necessitate additional investigations, especially regarding their bioaccumulation and permanence in ecosystems. There

is a deficiency in regulatory frameworks and standardized testing models specific to veterinary applications, which hinders clinical translation. Future research must emphasize species-specific nanoparticle designs, the creation of biodegradable and eco-friendly formulations, and methods to improve the reliability of targeting mechanisms. Moreover, cooperation among researchers, industry, and regulatory agencies is crucial for overcoming economic and logistical obstacles to clinical implementation. The scope of this review is limited by the existing literature and its focus on particular types and uses of nanoparticles. This emphasizes the capacity of nanotechnology to revolutionize veterinary oncology while promoting a comprehensive approach to its advancement, considering both animal and environmental health. By resolving current difficulties, nanotechnology has the potential to enhance precision medicine, improve patient outcomes, and influence the future of veterinary oncology.

8. References

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