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Utilization of Liposome nanoparticles in the treatments and diagnosis of cancer in Bovines

AUTHORS DETAIL

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Abstract

Liposome nanoparticles are considered as the novel tool for chemotherapeutic medicines used in the treatment of cancer in cows. The use of liposome nanoparticles enhances pharmacokinetic characteristics, allows for regulated and prolonged medication release, and reduces disease toxicity. Liposomal nanoparticles are frequently employed to gain attention in the medical profession due to their commercial availability. Recent years have seen significant progress in liposome technology, which is thought to be the most effective cancer treatment. This chapter examines the current knowledge on nanotechnologies and their role in the treatment of cancer. Despite the limitations of the majority of cancer treatments and therapies, cancer still remains as one of the most severe diseases. New and improved materials for biomedical applications, with an emphasis on therapy and diagnostics, have been made possible by nanotechnology. Metal nanoparticles are increasingly being used in cancer research as alternatives to chemotherapy medications. Metallic nanoparticles are very helpful because metals have anticancer characteristics that are either intrinsic or surface-induced. Metal nanoparticle development is advancing in a variety of ways, providing new therapeutic approaches and enhancing the effectiveness of numerous cancer treatments.

Keywords: Liposomes, nanoparticles, Bovines, Cancer, Pharmacokinetic

1. Introduction

Nanotechnology holds significant potential in medical diagnosis and therapy driven by advancements that have led to improved nanomaterials for biomedical use. Nanoparticles (NPs) are widely applied due to their unique properties. Multifunctional Nanoparticles have various capabilities that enhance drug delivery and therapeutic outcomes. They can transport hydrophobic compounds that carry water insoluble drugs which improving their solubility and bioavailability. It facilitate the advancement in drug formulations diagnostic and personalized medicine. NPs are particularly valued for their distinctive features including quantum properties, a high surface to mass ratio and their ability to absorb and transport proteins and drugs. Their composition varies with materials such as dextran, chitosan, biological lipids, phospholipids, lactic acid, silica, metals, carbons and other polymers which serve as building blocks. These attributes make NPs as a cornerstone of modern medical applications (Ma and Yang, 2016).

The root cause of cancer lies in mutations within specific genes inside cells. These genetic changes disturb the production of certain biomolecules leading to uncontrolled cell division. This results in the formation of a mass of abnormal cells in a

particulate tissue or organ referred as tumor. If the tumor cells remain confined to their original locations. It is termed as benign. However, if the tumor invades surrounding tissues it is termed as malignant. Most cancer diagnostic and treatment methods aim to halt the division of carcinomas. Early and precise detection of cancer is crucial for effective treatment and is typically achieved through methods such as ultrasound, Positron Emission Tomography (PET), Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) (Li et al., 2012). The current imaging as well as diagnostic tools fall short in providing comprehensive clinical insights into various types and stages of tumor, thus complicating successful treatment and patient recovery. Many existing anticancer therapies fail to distinguish between healthy and cancerous cells causing systemic toxicity and unwanted side effect. A significant challenge in imaging cancer is its late detection and it is often not diagnosed until it has progressed to metastatic stages (Magaye et al., 2012).

2. Nanoparticles

Nanoparticles are tiny particles with dimensions typically ranging from 1 to 100 nanometers. Due to their small size and high surface area to volume ratio they exhibit unique physical, chemical and biological properties that differ from bulk materials. Metal nanoparticles (NPs) address key limitations of traditional cancer treatments. They enhance targeting gene silencing and drug delivery efficiency. Functionalized with specific ligands, metal NPs enable precise energy deposition in tumors. Therapeutic particles play a crucial role in cancer imaging which aids in both diagnosis and treatment. The functionalized metal nanoparticles engineered the targeted cancer cells which reduce the damage to healthy tissues. Nanotechnology and NPs have recently gained traction in cancer therapy due to their precision and efficiency in overcoming many challenges of conventional chemotherapy. Traditional methods face challenges like ineffective drug delivery to target sites and limitations posed by cellular and non-cellular processes in tumors leading to higher recurrence and mortality rates. Metal NPs hold promise in revolutionizing cancer care by addressing these challenges (Akhter et al., 2013).

2.1. Classification of Nanomaterials

Nanomaterials are the foundational components of nanotechnology. These materials are characterized by having at least one dimension within Nano scale range typically less than 100 nanometers (Li et al., 2012). Depending on their dimensional properties nanomaterials are categorized into four main types:

a. Zero-Dimensional Nanomaterials (0-D): These have all three dimensions confined within the Nano scale. It includes Quantum dots, fullerenes and nanoparticles (Shapira et al., 2011).

b. One- Dimensional nanomaterials (1-D): These have one dimensions outside Nano scale range. It includes nanotubes, nano-fibers, nano-rods, nanowirs and nanohorns (Magaye et al., 2012).

c. Two-dimensional nanomaterials (2-D): These have two dimensions outside the nanoscale range. Examples include nanosheet, Nano films and nanolayers (Akhter et al., 2013).

d. Three- dimensional nanomaterials (3-D) or bulk nanomaterials: These materials are not limited to nanoscale in any dimension. Examples: It include bulk powders, dispersion of nanoparticles and array of nanowires or nanotubes (Asharani et al., 2009).

2.2. Classification of NPs

Based on their composition, NPs are generally placed into three classes including organic, Carbon-based and inorganic anoparticles (Singh et al., 2016).

2.2.1 Organic NPs: This category includes nanoparticles (NPs) composed of proteins, carbohydrates, lipids, polymers or other organic compounds. It includes dendrimers, liposomes, micelles and protein complexes like ferritin. These nanoparticles are non-toxic, biodegradable, in some cases feature as a hollow core (Kong et al., 2017)

2.2.2 Carbon-based NPs: This category includes nanoparticles composed entirely of carbon atoms. Notable examples are fullerenes, carbon black nanoparticles and carbon quantum dots. Fullerenes are carbon molecules with a distinctive symmetrical closed cage structure. For instance, C60 fullerenes consists of 60 carbon atoms arranged in a soccer ball shape although other forms like C70 and C540 fullerenes also exists (Liu et al., 2024).

2.2.3 Inorganic NPs: This category includes nanoparticles composed of materials other than carbon or organic compounds (Khan et al., 2022). Common examples include metal, ceramic and semiconductor nanoparticles:

a) Metal Nanoparticles: These are formed purely from metal precursors and can be monometallic or bimetallic. Bimetallic NPs may consist of alloys or layered structures (Core-shell). They exhibit unique optical and electrical properties due to localized surface plasmon resonance. Additionally some metal NPs have distinctive thermal, magnetic and biological characteristics making them valuable in developing nanodevices for diverse applications (Kim and Hyeon, 2013).

b) Semiconductor nanoparticles: These are made from semiconductor materials. These NPs exhibit properties intermediate between metals and non-metals. They feature wide bandgaps and show significant property changes through bandgap tuning compared to their bulk counterparts. These properties make them essential for applications in photo catalysis, optics and electronic devices (Yang and Wang 2018).

c) Ceramic nanoparticles: These are inorganic solids made from compounds like carbonates, carbides, phosphates and metalloid oxides such as titanium and calcium. These are typically synthesized by the process of heating and cooling. The ceramic NPs can exist in forms like amorphous, polycrystalline, dense, porous or hollow. They are widely used in biomedical applications due to their high stability and load capacity as well as in catalysis, dye degradation, photonics and optoelectronics (Singh et al., 2016).

2.3. Different types of Nanoparticles used in Anti-cancer therapy

2.3.1 Solid lipid NPs (SLNs): Solid lipid nanoparticles (SLNs), also called lipospheres or solid lipid nanospheres, are solid at human body temperature (37°C) and range in size from 50 to 1000 nm. They are composed of various lipids, including mono-, di-, and triglycerides, fatty acids, waxes, or their combinations. SLNs are created by replacing the liquid lipid (oil) in an oil-in-water emulsion with a solid lipid. These nanoparticles are biodegradable, biocompatible, and suitable for human use due to their low toxicity (Pardeike et al., 2009). SLNs provide a highly lipophilic matrix that allows drugs to be incorporated for controlled release (Kong et al., 2017). Drug loading into the SLN matrix depends on several factors which include; The drug's solubility in the lipid (it must be lipophilic), The chemical and physical properties of the lipid or lipid mixtures, The crystalline characteristics of the lipid at body temperature, The polymorphic form of the lipid used (Zada et al., 2020)

Using a mixture of different lipids creates an imperfect crystalline structure, enabling larger gaps for higher drug loading. SLNs have shown potential in delivering anticancer drugs, with preclinical studies in mice suggesting they could address multidrug resistance (MDR) in cancers (Vieira et al., 2018). For example, (Serpe et al., 2014). demonstrated the effectiveness of SLNs in delivering drugs like doxorubicin, cholesteryl butyrate, and paclitaxel to colon cancer cells in vitro. One notable development involved loading mitoxantrone a topoisomerase inhibitor that blocks DNA replication, into SLNs. In vivo studies using local injections in mice to treat breast cancer and lymph node metastases showed a nearly threefold reduction in lymph node size compared to free mitoxantrone, marking a significant improvement over existing treatments. SLNs present a promising alternative platform for drug delivery in cancer therapy. However, further in vivo studies are necessary to advance their application for human treatments (Serpe et al., 2004).

2.3.2 Polymer-based NPs: Polymeric nanoparticles (NPs) are widely explored such as delivery of drug carriers. These nanoparticles typically consist of a polymeric backbone made from biodegradable monomers derived from simple, biocompatible organic molecules. They also include functional groups for active targeting integrated into their structure (Sharma et al., 2021). Drug loading can be achieved through two primary methods:

i. **Entrapment:** Involves encapsulating an aqueous drug phase within nanoscale structures like cages or capsules formed by the polymer (Mukherjee et al., 2023).
ii. **Chemical Bonding:** It involves attaching drug molecules to the polymer backbone using ester or amide bonds that can be hydrolyzed in the body (Zhang et al., 2024)

Advanced polymeric NPs incorporate polar groups to create hydrophobic and hydrophilic regions, enabling drug adsorption and targeted delivery. Prominent synthetic polymers such as polylactide (PLA), poly(D,L-lactide-co-glycolide) (PLGA), and polyethylene glycol (PEG) are widely studied. . These polymers are biodegradable and break down in vivo. Additionally, biological polysaccharide-based polymers like chitosan, cyclodextrin, and dextrans have been extensively investigated. Combining different polymers forms co-polymers, such as PLA-block-PEG, which harness the properties of both materials, including PEG's anti-opsonization effects (Prabha et al., 2020) .

Ligands can be attached to nanoparticles to facilitate active targeting, either through direct covalent bonding with the polymer backbone or by using biologically inert spacers. These ligands are designed to target specific cancer cell antigens. For instance, RNA A10 aptamers targeting the prostate-specific membrane antigen have been conjugated onto PLA-block-PEG co-polymers, significantly improving drug delivery to prostate tumor cells compared to non-targeting nanoparticles. This approach holds promise for non-surgical prostate cancer treatment (Bajpai et al., 2008).

In breast cancer chemotherapy, paclitaxel formulations like Taxol® rely on the organic solvent Cremophor EL, which often causes severe hypersensitivity reactions. PEGylated PLGA copolymer nanoparticles achieved 70% encapsulation efficiency for paclitaxel and induced similar levels of apoptotic cancer cell death as Taxol® in HeLa cell studies. Importantly, PEGylated PLGA nanoparticles showed no toxicity, offering an alternative formulation for patients sensitive to Cremophor EL® without sacrificing chemotherapeutic effectiveness (Zensi et al., 2009).

Cisplatin, another anticancer drug, has been incorporated into PLGA–methoxy-PEG (PLGA–mPEG) nanoparticles. In vitro studies demonstrated passive targeting of LNCaP prostate cancer cells, with reduced cytotoxicity compared to free cisplatin solution while minimizing systemic toxicity. Fluorescence microscopy confirmed nanoparticle internalization, and in vivo mouse studies revealed prolonged and sustained therapeutic cisplatin blood levels after intravenous administration (Kim and Martin, 2006).

Polymeric nanoparticles remain in the preclinical stage but show immense potential for delivering anticancer drugs due to the ease of attaching targeting ligands. These developments could revolutionize cancer treatment by providing safer, more effective drug delivery options (Prabha et al., 2020).

2.3.3 Gold NPs: Gold nanoparticles (NPs) are composed within a central atom of gold surrounded by single layer of functionalized molecules containing (SH) groups. These molecules can include ligands designed for active targeting as well as glyconanoparticles, peptides, or phosphonioalkyl selenoates. Gold NPs are typically created by reducing gold salts ($AuCl_4^-$) with sodium borohydride ($NaBH_4$) in the presence of thiol-containing molecules. These molecules form a protective monolayer around the gold core, with the process depending on the gold-to-thiol ratio. The resulting nanoparticles partake widths extending from 1 to 150 nm (JF, 2006).

2.3.4 Liposome nanoparticles: The bilayer of liposomes can consist of synthetic or natural phospholipids. Their corporeal, biochemical possessions, as well as penetrability, ion mass are determined by characteristics for phospholipids that make up the bilayer (Malam et al., 2016). Drugs can be incorporated into liposomes using several methods: Forming liposomes in an aqueous solution containing the drug, Using organic solvents with solvent exchange techniques, Incorporating lipophilic drugs, and Employing pH gradient techniques. Liposomes reach their target through passive or active targeting strategies, typically by extravasating from the bloodstream into interstitial spaces. Modifications to the liposome surface, such as adding molecules to the lipid bilayer, allow precise targeting. To overcome rapid clearance by the mononuclear phagocyte system (MPS), PEGylation is employed, which reduces opsonization and extends circulation time (Malam et al., 2009).

Formulations of Liposomes cancer treatment medicines is already in clinical use. For example, a liposomal form Doxil offers better efficacy and reduced cardiotoxicity, attributed to passive targeting through greater absorbency as well as effect of retention (EPR) and lower drug concentrations within healthy tissues. Evidence suggests that Doxil is metabolized differently by leukemia cells compared to free doxorubicin, contributing to its improved performance. Doxil is also being trialed for breast cancer treatment (Qiu et al., 2008).

3. Diagnosis of Cancer

A veterinarian may suspect cancer in the animal based on observable clinical symptoms and following techniques.

a) Clonally analysis for lymphoma: Clonality analysis for lymphoma is a laboratory test that examines the genetic rearrangement within patients lymphocytes to determine if a cancerous clone exists that is crucial for diagnosis and monitoring lymphoma by identifying a unique genetic signature present only in malignant cells which confirms the presence of a lymphoma and distinguish it from benign lymphoid proliferation.

b) PARA test identifies a unique signature to determine whether lymphocyte population originates from a single celled (monoclonal) or multiple cells (polyclonal). Lymphocytes acquire unique antigen receptors through antigen receptors through DNA rearrangement process enabling them to defend the body against various infectious agents encountered throughout life. The diversity of lymphocytes ensures precise clonal signatures (Chaturvedi et al., 2019).The PARA test uses PCR to amplify sequences from all lymphocytes in a sample. The results indicate whether most sequences are identical (clonal) or diverse (polyclonal). Lymphocytes expand clonally when activated normal lymphocytes create a polyclonal response while malignant lymphocytes exhibit a single clonal population. This test sensitivity is almost 75% and around 94%. (Chaturvedi et al., 2019).

c) Mutation of P-glycoprotein: This test is designed to identify dog carrying a mutation in the ABCB1 gene which encodes the P- glycoprotein (PgP) or multi- drug resistance protein. ABCB1 belongs to a family of genes responsible for producing specialized Proteins that transport nutrients into cells and expel toxins. Pgp was initially recognized for its role in chemotherapy resistance in cancer where it often overproduced in tumors, effectively removing drugs from cancer cells before they can take effect. However this protein also plays a critical role in protecting the body by preventing harmful drugs from entering sensitive organs (Roy et al., 2013)e.

d) RECAF OncoPet Analysis: OncoPet diagnostics and BioCurex have recently introduced a blood test for detecting cancer in companion animals. This test works by identifying a protein in the blood that resembles the alpha fetoprotein receptors. Alpha-fetoprotein plays a role in regulating growth and immune function while the receptor itself is not fully understood. The reagent used in this test was developed from a membrane extract of human breast cancer cells and recognizes one of the proteins that bind to alpha-fetoprotein (Xiao et al., 2009).

4. Chemotherapy by Nanoparticles

Traditional cancer treatments rely on biological agents including terpenoids, plant alkaloids, anti-metabolites and DNA damaging alkylating agents. Modern Chemotherapy encounters significant limitations primarily due to its lack of target specificity and leading to inconsistent clinical outcomes. Since Chemotherapy drugs cannot between cancerous cells and normal cells, they harm healthy tissues in areas such as bone marrow, digestive tract, macrophages and hair follicles (Davis et al., 2008).

Liposomes are widely utilized as drug delivery systems (DDS) for cytrostatic drugs, they also serve as innovative nanocarriers for immunotherapy and gene delivery. Clodronate a first generation biophoisphate is commonly used in clinical settings to prevent bone metastases, manage excessive bone resorptions and treat inflammatory conditions such as osteoarthritis. Recently encapsulated clodronate in liposomes shown advances in suppressing tumor growth and metastasis by depleting tumor-associated macrophages (TAMs) (Wang et al., 2019).

5. Conclusion

The use of NPs with liposomes is common. Early preclinical and clinical experimental data indicates that liposomes and NPs have a lot of potential for general use in the treatment of cancer. Biocompatibility, minimal toxicity, reduced clearance rates, tissue targeting, and controlled release of medications are some of its appealing qualities. The approval of Abraxane1 and Doxil1 shows that they have many advantages over traditional chemotherapy that uses free medication treatment. Both of these formulations of current medications based on nanomaterials provide improved pharmacokinetic characteristics and reduced systemic toxicity of the chemotherapeutic medications they administer.

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