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Research Article

Nanoparticle-Based Cancer Therapy: A Novel Approach

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ABSTRACT:
Nanoparticle-mediated drug delivery has shown great potential for cancer treatment, offering improved delivery of anticancer agents, reduced systemic toxicity, and enhanced therapeutic efficacy. The Novel Drug delivery system's compact size yields significant benefits, including modified pharmacokinetic profiles and enhanced payload capacity, surpassing conventional large-scale systems. Although preclinical and clinical phases have yielded positive responses, further research is necessary to overcome challenges related to stability and potential side effects, ultimately enhancing therapeutic applications. To address stability concerns, experts are exploring techniques to stabilize nanoparticles, including protective coatings and formulation optimization. Furthermore, they are selecting biocompatible materials and conducting toxicological studies to mitigate potential side effects before proceeding to clinical trials. This review provides a comprehensive analysis of existing literature on nanoparticle-based drug delivery systems, focusing on their applications and efficacy in cancer treatment.
Keywords: Nanoparticles, Anticancer drugs, Targeted therapy, Cancer treatment, liposomes, Dendrimers.

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INTRODUCTION:

Cancer is one of the most destructive diseases globally, affecting 10 million people annually (Stewart B.W., et al. 2003). Cancer is a disease where abnormal cells grow and spread uncontrollably (Ana Catarina Pinto JNM., et al. 2011). Over 100 cancer types exist, originating from various cell types (Schilsky R. L., et al. 2006). Worldwide, 3.68 million cancer cases were reported, with 2.23 million deaths in 2013 (Duong H., et al. 2013). In 2015, cancer claimed 2.8 million lives and affected 4.2 million people with new cases (Xu B., et al. 2016). The most frequent types in men are prostate, liver, lung, colorectal, and stomach cancers, while in women are breast, cervix, lung, colorectal, and stomach cancers (Chen W., et al. 2017). Cancer treatments like radiation therapy, surgery, and chemotherapy can help, but they can also harm healthy cells and cause unpleasant side effects.

Nanoparticles are transforming cancer therapeutics, offering unprecedented opportunities for targeted and effective treatments. Nanoparticles, defined as particles between 10-100 nanometres in diameter, possess substantial surface areas for conjugating therapeutic agents, although optimal delivery of select drugs necessitates larger particle sizes (De Jong, et al. 2008, Duncan R., 2003). Nanoparticles help chemotherapy reach cancer cells directly, making treatment more effective and reducing harm to normal cells (Badea,

2017). The FDA's clearance of Abraxane, an albumin-bound paclitaxel nanoparticle formulation, for breast cancer treatment has facilitated the advancement of nanoscale drug distribution technologies aimed at enhancing target tissue specificity (Perez E., 2005). Cancer is an intricate and dynamic disease characterized by unchecked cell proliferation and advancement, leading to the disruption of normal cellular function and tissue structure (Ganesh K., et al. 2021, Merriel S. W. D., et al. 2021, Sung H., et al. 2020). About one in six fatalities globally are caused by cancer, making it a global health emergency. According to data from 2020, there were 19.3 million new instances of cancer identified worldwide, and the disease claimed almost 10 million lives. There are over 100 distinct types of cancer, with the most prevalent forms being lung, cervical, prostate, liver, breast, ovarian, colorectal, and stomach cancers. For more than 60 years, conventional chemotherapy has remained the standard treatment approach for cancer. Traditional chemotherapy targets rapidly dividing cancer cells, but unfortunately, also damages healthy cells. To address this challenge, a groundbreaking approach has emerged, targeted cancer therapy utilizing nanoparticle-based drug delivery systems. This comprehensive review delves into the complexities of cancer and examines the transformative potential of nanoparticle-based drug delivery systems.

TYPES OF CANCER:

1. Lung cancer:

Lung cancer is a very frequent and aggressive disease that kills more people globally. At the cellular level, this is characterized by disrupted regulation, leading to unchecked cell growth and loss of cellular balance. The transformation from normal to malignant lung cancer cells is thought to occur through a complex, multi-step process involving the accumulation of genetic and epigenetic changes, ultimately resulting in the clonal expansion of invasive cancer cells. The progression of primary cancer is fuelled by the relentless accumulation of genetic and epigenetic alterations during tumor cell growth. This enables the cancer to infiltrate surrounding tissues, metastasize to distant sites, and develop resistance to therapeutic drugs (Nowell P. C., 1976). To improve early detection, develop tailored, focused treatments, and develop effective prevention, it is essential to comprehend the molecular mechanisms behind cancer. By combining knowledge of tumor characteristics and genetic profiles, healthcare providers can create personalized prognoses and treatment plans tailored to individual patients, transforming the landscape of precision cancer care (Pass H. I., et al. 2010).

2. Breast cancer:

The most common cancer in women worldwide, breast cancer is a complicated and multifaceted illness with a wide range of subtypes and traits. It can be categorized in multiple ways, including its clinical presentation, tumor marker expression, and histological classification, highlighting its complexity and variability. The two predominant forms of invasive breast cancer are ductal carcinoma and lobular carcinoma, highlighting the disease's heterogeneity (Li C. I., et al. 2003). Although ductal and lobular carcinomas have been extensively studied, the rarer subtypes of breast cancer, such as mucinous, tubular, and medullary carcinomas, which comprise approximately 10% of all cases, remain poorly understood. Treatment options, including medication choices, are often influenced by menopausal status. To enhance the effectiveness of anticancer therapies, various nanotechnology-based delivery systems have been developed, including liposomes, polymeric micelles, quantum dots, nanoparticles, and dendrimers, which offer promising avenues for improved cancer treatment.

3. Cervical cancer:

A major public health concern and a serious threat to women's health worldwide, cervical cancer is the fourth most common malignancy among women (Bray F., et al. 2018). One notable feature of cervical cancer, which contributes significantly to cancer-related mortality and morbidity, is that it usually strikes women in their 40s and 50s, when they are relatively young. Compared to ovarian, lung, and breast cancers, this occurs noticeably earlier. The human papillomavirus (HPV), specifically types 16 and 18, is the primary cause of cervical cancer. HPV DNA, which is mostly transmitted through sexual contact, is found in an astounding 90% of squamous cervical malignancies (Bosch F. X., et al. 1995, Chichareon S., et al. 1998, Ngelangel C., et al. 1998). Squamous cell carcinoma and adenocarcinoma are the two main histological subtypes of cervical cancer. Smoking also plays a role in increasing the risk, as it weakens immune function at the cellular level. In low-resource settings, radiation therapy is often the primary treatment approach, usually aimed at alleviating symptoms. However, the combination of chemotherapy and radiation (chemoradiation) has proven to be a highly effective treatment strategy, substantially improving survival outcomes for cervical cancer patients.

4. Prostate Cancer:

Prostate cancer is the most prevalent non-skin cancer among men, disproportionately affecting older adults. With the global population aging, prostate cancer cases are projected to increase. Statistics reveal that roughly 17% of men will receive a prostate cancer diagnosis during their lifetime, while approximately 3% will succumb to the disease (American Cancer Society, 2010). A significant majority, approximately 75%, of prostate cancer diagnoses occur in men aged 65 and older (Spickett I., et al. 2010). Prostate cancer is uncommon in men under 40, but its incidence increases with age. While localized prostate cancer has an excellent 5-year survival rate of over 99%, advanced prostate cancer is generally considered incurable (Moul J.W., 2004, Siegel R. L., et al. 2020). Advanced prostate cancer refers to cases where the disease has recurred after treatment. Therefore, there is a pressing need for innovative and effective treatments to combat this devastating disease.

5. Liver cancer:

Liver cancer is a highly aggressive and frequently fatal disease that usually develops in individuals with pre-existing chronic liver disease. Most primary liver cancers originate from epithelial cells, primarily hepatocytes. Globally, primary liver cancer poses a major health threat, ranking among the top 10 most common cancers, with men being fifth and women seventh most affected, and is also the third highest cause of cancer-related fatalities worldwide (Jemal A., et al. 2011). Despite progress in treatment options, liver cancer remains a difficult disease to manage. While surgery, local ablation therapies, and liver transplantation offer potential curative options for early-stage liver cancer, recurrence rates remain high even after successful treatment. Furthermore, even patients with small tumors (<3 cm) who undergo surgery face a suboptimal prognosis, with 5-year survival rates ranging from 47% to 53%. (Altekruse S. F., et al. 2012, Fong Z. V., et al. 2014, Poon R. T., et al. 2002). Non-epithelial liver cancer is a less occurring type, that accounts for a small proportion. Meanwhile, the treatment of liver cancer has become increasingly tailored, with a multidisciplinary approach that takes into account each patient's distinct needs and circumstances to create personalized treatment plans. Nanotechnology has shown great promise in enhancing the effectiveness of anticancer therapies, offering new hope for improved treatment outcomes. Innovative delivery systems, such as liposomes, and polymeric micelles, have been developed to enhance cancer therapy outcomes, offering new ways for improving treatment strategies.

6. Ovarian cancer:

Ovarian tumors are categorized based on their origin, including epithelial, stromal, and germ cell tissues. Cancers of the peritoneum and fallopian tubes are typically treated in a similar way to epithelial ovarian cancer, which makes up more than 90% of all ovarian cancers. EOC predominantly affects postmenopausal women, typically occurring between the ages of 50 and 70. Although the exact cause of ovarian cancer remains unknown, research suggests that the risk decreases with fewer lifetime ovulations. Research has found that factors that decrease ovulation frequency, such as having multiple children, extended breastfeeding, and using oral contraceptives, can reduce the risk of ovarian cancer (Hinkula M., et al. 2006, Titus-Ernst off L., et al. 2001). On the other hand, certain inflammatory conditions, including endometriosis, may increase the risk. The treatment approach for ovarian cancer is tailored to the stage of the disease and surgical results, generally involving 6-8 cycles of chemotherapy. The extent of any remaining disease is evaluated using a combination of surgical assessment, CT scans, and CA 125 blood tests. Ovarian cancer recurrence can be identified through the appearance of new symptoms, imaging tests, or increasing CA 125 levels. Ongoing clinical trials are investigating targeted biological agents for the treatment of recurrent ovarian cancer, intending to integrate effective therapies into first-line treatment options.

TARGETED METHODS FOR CANCER NANOPARTICLE DRUG DELIVERY:

Targeted therapeutic approaches aim to optimize treatment specificity and minimize off-target toxicity, which are commonly linked to conventional treatments using medications. The field of nanotechnology is rapidly advancing, with ongoing research concentrated on developing novel approaches that efficiently bypass drug resistance mechanisms (Wang G., et al. 2008). Targeted systems are engineered to selectively target tumour cells, thereby enhancing efficacy while minimizing adverse effects. Researchers employ two primary approaches to ensure targeted drug delivery: passive targeting, which relies on particle size and material properties and active targeting, which utilizes ligands or antibodies (Fig. 1).

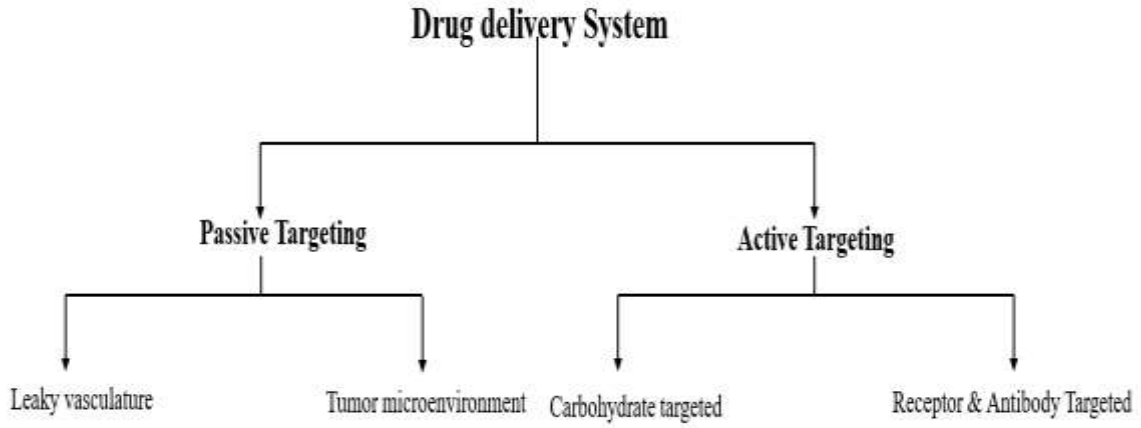

Fig. 1: Delivery of Nanoparticles occurs in two ways- Passive and Active targeting.

1. Passive Targeting:

This is a strategy for increasing the efficacy of targeted drug delivery in oncology (Fig. 2). Nanoparticle enables targeted therapy by entrapping bioactive compounds and transporting them directly to tumor sites, enhancing their efficacy and minimizing harm to normal healthy cells

(Golla K., et al. 2013). Preclinical and clinical trials demonstrate the potential of this approach to combat drug resistance and enhance cancer treatment. This strategy optimizes drug delivery and achieves sustained release profiles, leading to extended durations of therapeutic effectiveness (Nie Y., et al. 2023). By combining passive targeting with established cancer therapies, such as chemotherapy and radiation therapy, researchers aim to create a multimodal approach that significantly enhances treatment efficacy. The utilization of nanoparticles has emerged as a promising strategy to overcome limitations associated with conventional anticancer therapies, enhancing bioavailability and therapeutic efficacy. The unique properties of nanoparticles enable them to encapsulate drugs, thereby shielding them from various degradation pathways and maintaining their therapeutic potency (Chen X., et al. 2017).

a) Leaky vasculature:

By exploiting the inherent pathophysiological characteristics of tumors, including Vascular permeability and disrupted blood-lymph barrier function, this method enables selective nanoparticle accumulation within the tumor microenvironment via Enhanced Permeability and Retention Effect. The Enhanced Permeability and Retention (EPR) effect relies on two main mechanisms:

i. Malignant tissues have abnormally leaky blood vessels, enabling large molecules like nanoparticles to penetrate the tumor.
ii. Tumours lack effective lymphatic drainage, leading to prolonged retention of substances.

By linking chemotherapy agents to nanoparticles or molecular carriers using degradable bonds, these carriers can enhance the delivery of the agent to the tumor site. This targeted approach can achieve concentrations 10-100 times higher than those obtained with traditional free drug administration.

b) Tumour microenvironment:

Tumor-activated prodrug therapy represents an innovative method of passive drug targeting, leveraging the unique characteristics of the tumour microenvironment. This strategy involves conjugating a therapeutic agent to a tumour- particular protein, delivered in an inactivated state. Upon reaching the tumour site, the agent is converted into its active form through enzymatic or environmental triggers. Research has repeatedly shown that matrix metalloproteinase-2 (MMP-2) is overly active in melanoma cells, both in lab tests and patient studies. MMP-2 is a key player in breaking down the barriers that normally keep cells in place, allowing cancer cells to spread and grow, and ultimately leading to the disease spreading to other parts of the body. Scientists have taken advantage of this discovery by creating a special version of the cancer drug doxorubicin. This new form is soluble in water and contains a specific sequence of amino acids that is recognized by MMP-2. This allows the drug to selectively target and attack cancer cells that produce high levels of MMP-2 (Mansour A. M., et al. 2003). This specially designed drug-polymer combination has a strong attraction to a specific part of a protein called albumin that circulates in the blood. When the drug-polymer combination binds to albumin, it's efficiently cut by the MMP-2 enzyme, releasing the active cancer drug doxorubicin. Additionally, researchers have found that changes in acidity and oxidation levels at the tumor site can also trigger the release of the drug, ensuring it reaches the target area. The unique pH and redox profiles of the tumour microenvironment can be harnessed to activate prodrugs, ensuring the selective release of the therapeutic agent. This tumor-activated prodrug approach offers a promising strategy for enhancing the efficacy and specificity of cancer therapy, minimizing off-target effects, and improving patient outcomes (Guo X., et al. 2003.)

2. Active Targeting:

The integration of active targeting technologies into drug delivery systems has emerged as a transformative approach, enhancing the precision and therapeutic impact of treatments. To achieve targeted cancer therapy, nanoparticles are modified with specific ligands or antibodies that recognize and bind to distinct receptors on the surface of cancer cells. By providing localized delivery of drugs to the targeted cells, this approach ensures optimal therapeutic efficacy while minimizing unnecessary exposure to healthy cells (Jin R., et al. 2022). Creating nanoparticles that can attach to multiple targets on cancer cells at the same time is a promising area of research, as it could greatly improve the delivery of cancer treatments to the cells that need them. Advancing the development of precise and potent drug delivery systems has led to the exploration of numerous biological ligands for actively targeting nanoparticles (NPs) to specific cells. These biological ligands have demonstrated a remarkable ability to bind selectively to specific receptors on the surface of target cells, thereby facilitating enhanced cellular uptake of drug-loaded NPs and augmenting therapeutic efficacy. Research has revealed that increasing the density of ligands on NPs offers a distinct advantage in Amplifying cell attachment and entry through a cooperative binding effect. This phenomenon enables NPs to engage multiple receptors simultaneously, leading to amplified targeting efficiency and reduced off-target effects. A diverse array of ligand types has been employed to functionalize NPs, including proteins, polysaccharides, nucleic acids, peptides, and small molecules. These ligands can be categorized based on their molecular structure, binding specificity, and functional properties. The functionalization of NPs with biological ligands can be achieved through two primary strategies. The first approach involves chemically conjugating or physically adsorbing ligands onto pre-formed NPs. This method allows for precise control over ligand density and orientation, ensuring optimal targeting efficiency. The second approach entails integrating ligands with NP components, such as polymers, during the NP formation process. This strategy enables the creation of NPs with tailored surface properties and ligand densities, facilitating the design of

optimized drug delivery systems. By leveraging the specificity and diversity of biological ligands, researchers can develop NPs that selectively target cancer cells, reduce off-target effects, and enhance therapeutic outcomes. Targeted cancer therapies leverage the specificity of antibodies to selectively bind to cancer cells displaying unique surface receptors, ensuring accurate delivery of therapeutic agents (Chen F., et al 2020). While, this approach faces limitations when targeting cancers lacking these receptors, resulting in reduced drug delivery and efficacy. To address current limitations, researchers are seeking novel solutions to advance this technology's clinical utility. By developing nanoparticles capable of concurrent binding to multiple surface receptors, researchers aim to enhance the specificity, efficacy, and delivery of therapeutic agents to cancer cells (Gencer A., et al. 2021). The application of nanotechnology in oncology promises tailored treatments targeting specific tumors. By harnessing the power of research and development, scientists are crafting innovative cancer treatments that prioritize personalized and optimized care (Wang G., et al. 2008).

a) Carbohydrate-Directed Targeting:

Lectin-carbohydrate interactions have emerged as a promising strategy for active drug targeting. Cell surface carbohydrates play a crucial role in mediating tumor cell interactions with normal cells and the extracellular matrix, thereby influencing metastatic spread and growth. Lectins, a family of binding proteins, recognize specific carbohydrate patterns and mediate these interactions. Recent discoveries have expanded our understanding of endogenous lectins, highlighting their role in innate and adaptive immunity. Notably, certain lectins can identify "foreign" carbohydrate patterns on tumor cells, impacting tumour cell survival, adhesion, vascularization, and other processes critical for metastasis. Building on this knowledge, researchers have developed nanoparticles that exploit specific lectin-carbohydrate binding. Two approaches have been explored: direct lectin targeting, where nanoparticles bearing carbohydrate moieties target specific lectins, and reverse lectin targeting, where lectins incorporated into nanoparticles target cell surface carbohydrates (Yamazaki N., et al. (2000). Although initial drug delivery systems based on this interaction have focused on targeting whole organs, potentially harming normal tissues, lectins remain an attractive tool for enhancing nano-drug delivery. Their unique affinity for sugar moieties on tumor tissue surfaces makes them an appealing target for the development of "smart carrier" molecules.

b) Receptor & Antigen-Directed Targeting:

Cancer cells' unique characteristic of overexpressing specific receptors or antigens offers a strategic opportunity for targeted medication delivery through receptor-mediated endocytosis. This mechanism allows external particles to penetrate the cell's interior, facilitating efficient absorption of therapeutic agents. In this approach, a medication is attached to a polymer carrier, which is then absorbed into the cell through interactions between ligands and receptors. Once positioned at the cell surface, the targeted medication-polymer complex can exert its therapeutic effect either at the cell membrane or after being internalized. The release of the free medication into the cell's cytosol can occur through various mechanisms, including detachment from the polymer in the external environment, at the cell surface, or within cellular compartments through enzymatic breakdown (Olsnes S., et al. 1988). This approach ensures that the therapeutic agent is delivered to the cancer cells, and minimizes harm to healthy tissues. Effective targeted drug delivery requires the integration of three essential components: (a) biocompatible polymers that can be conjugated to the therapeutic agent, (b) ligands or antibodies that bind with high affinity to specific receptors or antigens on the tumour cell surface, and (c) the receptors or antigens themselves, which must be recycled and returned to the cell surface after delivery of the drug is completed.

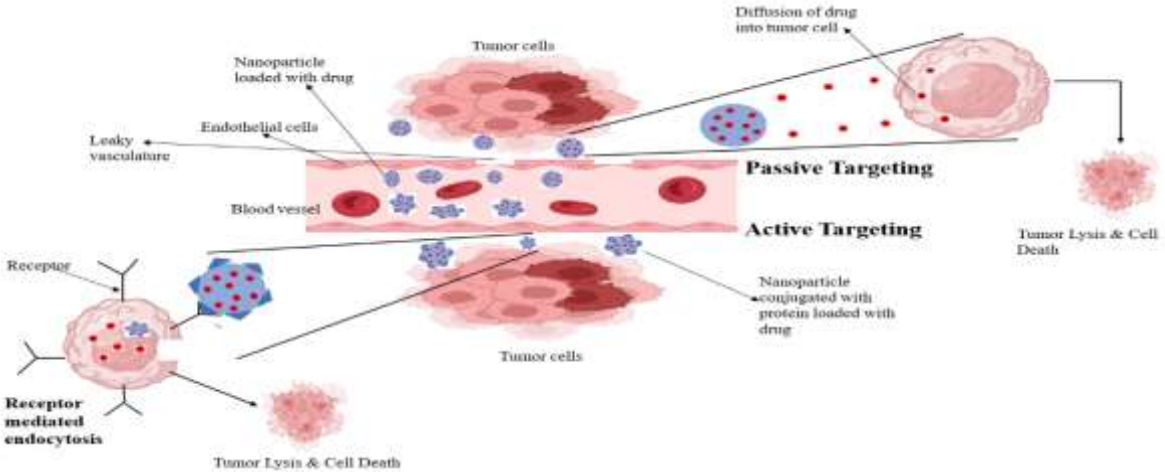

Fig. 2: Schematic representation of passive and active targeting (credits, Biorender).

TREATMENT AVAILABLE FOR VARIOUS CANCERS:

Taxanes are a powerful class of cancer medications, with paclitaxel showing remarkable effectiveness in a wide range of cancer types. Taxanes are commonly utilized in the treatment of various cancers, including breast, lung, and ovarian cancers, due to their efficacy in inhibiting cell division and promoting apoptosis.

Abraxane, an anti-microtubule agent, functions by stabilizing microtubules. This microtubule stability disrupts the microtubules essential for cell division and mitosis. The active ingredient, paclitaxel, induces abnormal microtubule arrangements and multiple asters during cell division. Research has demonstrated that Abraxane used alone or in combination with gemcitabine, can reduce pancreatic stroma in pancreatic cancer models, showcasing its potential therapeutic advantages (Lim E. K., et al. 2018). The Genexol-Pm is a Cremophor EL-free nanoscale preparation of paclitaxel, consisting of a sterile, lyophilized polymeric micelle. Furthermore, the formulation demonstrated enhanced biodistribution, achieving two- to three-fold higher concentrations in various tissues, including the liver, spleen, kidney, lung, and notably, in cancer cells.

DaunoXome is a cancer medication that inhibits the growth of tumor cells. Its active ingredient, daunorubicin, is encapsulated in liposomes, making it a unique formulation. DaunoXome is a targeted treatment for Kaposi's sarcoma, a rare and aggressive cancer that primarily affects the skin, lungs, and gastrointestinal tract (Ki. D. W., et al. 2007).

DESIGN OF NANOPARTICLE:

Nanoparticles Structure, & Physical characteristics crucially influence their reaction with the immune system and distribution of potent drugs, impacting immunotherapy efficacy (Trigueros S., 2016). The structural configuration of nanoparticles can be developed to optimize targeting specificity and potency. The optimization of stability and biocompatibility is crucial for mitigating toxicological effects and promoting long-term patient safety. Nanoparticle behavior can be tailored through surface modification and size optimization.

Surface Parameters:

Surface modification of nanoparticles influences their ability to evade macrophage capture, impacting circulation duration and therapeutic efficacy. To escape macrophage capture, the surface of nanoparticles should have a hydrophilic nature (Moghimi, et al. 2003). Coating nanoparticles with polyethylene glycol (PEG) and designing surfaces that repel plasma proteins are two effective strategies to prevent opsonization and prolong circulation. Nanoparticles can be engineered from block copolymers that contain distinct hydrophilic and hydrophobic domains, facilitating self-assembly and nanoparticle formation (Harris J. M., et al. 2001).

Optimization of Size:

The size of nanoparticles plays a crucial role in their effectiveness, beyond surface properties. The size of nanoparticles is essential for successful delivery, as they must be small enough to evade capture by fixed macrophages yet large enough to prevent leakage into blood capillaries. Research has shown that the size of gap junctions between endothelial cells lining tumour blood vessels can vary significantly, ranging from approximately 100 to 600nm (Yuan F., 1995). To ensure efficient accumulation in tumour tissues, nanoparticles should be designed with a diameter of up to 100nm, allowing them to pass through the leaky vascular structure's characteristic of tumours.

DIFFERENT DRUG DELIVERY SYSTEM FOR NANOPARTICLE:

Different drug delivery systems that are effective against specific types of cancers has been formulated by using different types of nanoparticles (Fig. 3) such as inorganic or metallic, organic, lipid based and Polymeric nanoparticles. The incorporation of inorganic nanoparticles has been shown to optimize chemotherapy delivery, resulting in improved treatment outcomes. Inorganic nanoparticles like gold and silver have optical and physical characteristics that make them useful for targeted approaches and bioimaging (Lin M., et al. 2015). To achieve selective targeting of cancer cells, nanoparticles can be functionalized with specific proteins or antibodies, enabling precise drug delivery. A secure and effective method of drug delivery is offered by polymeric nanoparticles composed of biocompatible polymers (Huang L., et al. 2016). A multidisciplinary approach, incorporating scientists, physicians, and regulatory specialists, is crucial for evaluating ethical considerations and mitigating societal concerns surrounding nanoparticle-based cancer therapies.

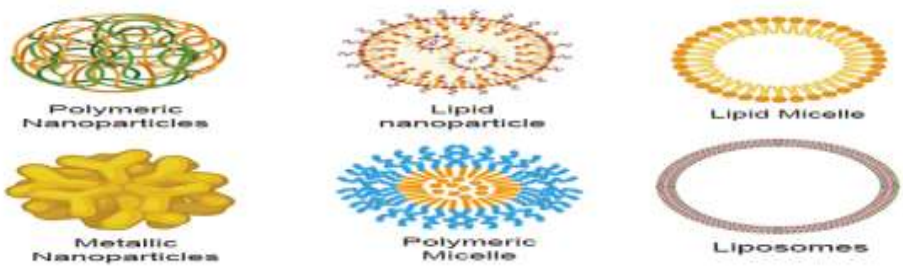

Fig. 3: Different types of nanoparticles for drug delivery (created by Bio render).

1. Inorganic Nanoparticles:

Inorganic nanoparticles, including gold, silver, and silica, have demonstrated significant potential in cancer therapy. These nanoparticles play a major function in optimizing chemotherapy and radiation therapy, ensuring that cancer cells are targeted while minimizing damage to surrounding cells. Studies have revealed that nanoparticle accumulation in non-target tissues and organs can lead to harmful toxicities and long-term consequences. Thus, rigorous investigation is essential to optimize the safety and efficacy of nanoparticles. Understanding the lasting impact of nanoparticles on human health is critical to protecting patients from harm and preventing unforeseen complications (Li P., et al. 2022). Optimized and Affordable manufacturing methods are important for the extensive accessibility of these types of treatments. Researchers must conduct thorough risk-benefit analyses and provide comprehensive informed consent to patients undergoing innovative therapies. Researchers must carefully weigh the benefits of nanoparticle-based cancer treatment against potential long-term effects (Singh D., 2017). Clinical trials have demonstrated that nanoparticle-mediated drug delivery enhances therapeutic efficacy by selectively targeting cancer cells while minimizing harm to normal cells. This groundbreaking discovery emphasized the crucial role of nanoparticle-medication interactions in cancer treatment, enabling personalized therapy plans.

2. Organic Nanoparticles:

Organic nanoparticles exhibit considerable potential as a replacement for metallic nanoparticles in medical applications, leveraging their biocompatibility and functional properties, such as site-specific drug delivery and imaging (Venkatraman S., et al. 2014). By selectively targeting cancer cells, these nanoparticles enable directed delivery of anticancer agents, reducing adverse effects and optimizing therapeutic outcomes. Furthermore, these nanoparticles are helpful in medical imaging, enabling enhanced visualization of tissues and organs, which facilitates early disease detection and diagnosis (Viswanadh M. K., et al. 2018). A novel nanoparticle platform, coated with a breast cancer-specific protein, had been made to distribute potent anticancer therapeutics directly to carcinogenic sites. Preclinical investigations have demonstrated the efficacy of this targeted approach, significantly inhibiting cancer growth and decreasing the likelihood of metastatic spread. The integration of nanoparticles into drugs enables optimized and sustained release, optimizing therapeutic efficacy (Doleyres Y., 2020). In-depth research is essential to fully grasp the extended implications and safety concerns related to the use of these approaches in healthcare (Juneja R., 2018).

3. Lipid-based nanoparticles:

Lipid-based nanoparticles have emerged as a promising drug delivery system, offering enhanced biocompatibility, improved drug stability, and increased solubility. The drugs accumulate intracellularly, inducing cytotoxicity and ultimately leading to cancer cell destruction. Preclinical research indicates that this targeted drug delivery system boosts chemotherapy's efficacy in combating resistant tumors. These nanoparticles offer more precise and optimized drug release than polymer-mediated drug delivery systems (Sahay G., 2019). Despite promising developments, challenges persist regarding the toxicity and elimination of drugs from the body, which must be overcome to achieve good therapeutic outcomes. Lipid-based nanoparticles entrap a wide range of therapeutic agents (Table 1). Liposomal formulations have demonstrated efficacy in treating breast cancer and AIDS-related Kaposi's sarcoma, leading to regulatory approval (Malik N., 1999, Markman M., 2006). The next generation of liposomal therapeutics, immunoliposomes, facilitates selective and targeted delivery of drugs to specific sites of action (Rosenthal E., et al. 2002).

Table 1: types of lipid nanoparticles as drugs to treat diseases.

Lipid	Nanoparticle	Drug	Disease treated	Reference
Tristearin, Stearyl Amine.	Mannosylated LNP.	Doxorubicin.	Lung cancer.	(Oh Y. K., et al. 2016)
Glyceryl monostearate, Stearic acid.	Lactoferrin-modified LNPs.	Docetaxel.	Brain tumour.	(Fattal E., et al. 2021)
Dynasan 116.	Apo E-targeting LNPs.	Donepezil.	Alzheimer's disease.	(Nance E., et al. 2019)
Cholesterol, Triolein.	Transferrin mediated-LNPs.	Curcumin.	Breast cancer.	(Liu Q., et al. 2016)
Monoolein.	Self-assembled LNPs.	Paclitaxel.	Ovarian cancer.	(Nguyen T. M., et al. 2014)
Alkyl-Lys phospholipids.	-	Edelfosine.	Leukaemia.	(Abuasal B. S., et al. 2012)

4. Polymeric Nanoparticles:

Polymeric nanoparticles emerge as a promising tool to revolutionize drug delivery systems and tackle existing obstacles. By integrating controlled release systems, these can be tailored to deliver medicinal agents at a predetermined rate, maintaining optimal drug concentrations over an extended period. The size and surface properties of nanoparticles can be engineered to optimize their stability in biological fluid and enhance the efficacy of drugs (Lin M., et al. 2015). Functionalization of polymer nanoparticles with targeting ligands/antibodies enhances specificity and efficacy in cancer therapy (Puri S., et al. 2023) (Table 2). Nanoparticle technology out performs traditional

formulations by safeguarding drugs from degradation extending shelf life and optimizing bioavailability. The highly branched structure of dendrimers creates a large surface area, allowing for the attachment of multiple drug molecules and precise control over their release. The strategic addition of functional groups to nanoparticle surfaces enables precise control over site-specific interactions. Polymeric micelles have emerged as a versatile and efficient platform for delivering hydrophobic anticancer agents, overcoming solubility limitations, and enhancing tumor targeting.

Table 2: Polymer-based nanoparticles used for cancer treatment.

Polymer	Active principle	Treatment	Reference
PEG maleimide.	Paclitaxel.	Breast cancer.	(Xu X., et al. 2020)
PEI-PLA.	Paclitaxel.	Lung cancer.	(Hirani A., et al. 2014)
Gal-TPGS-PLA.	Docetaxel.	Liver cancer.	(Qiu F., et al. 2019)
TPGs-PLGA.	Doxorubicin.	Breast cancer.	(Liu J., et al. 2019)
PCL-PEG.	Camptothecin.	Glioma tumor.	(Huang J., et al. 2018)

The hydrophobic core of polymeric micelles serves as a protective compartment, encapsulating pharmaceutical agents and safeguarding them against degradation. The hydrophilic shell of polymeric micelles facilitates extended bioavailability in the blood, thereby enhancing drug delivery and bioavailability. The distinctive properties of polymeric micelles render them a promising platform for enhancing site-specific drug delivery (Xu X., et al. 2020). Ongoing research focuses on designing targeted nanoparticle delivery systems to selectively deliver therapeutic agents to specific sites, reducing off-target effects (Vyas K., et al. 2023).

Table 3: Nanoparticle types: size characteristics, advantages and disadvantages.

Type of nanoparticle	Size	Advantages	Disadvantages
Inorganic nanoparticle.	40-100 nm	Enhance tumor imaging and radiotherapy, Theranostic use, High drug loading capacity, and Imaging capabilities.	Metal toxicity, Potential for accumulation in organs, Storage issues, Limited control over particle size and shape.
Liposomes.	200-1 µm	Biocompatibility, Decreased drug toxicity, Potential for combination therapy, Improved pharmacokinetics.	Slow drug delivery, liposome degradation, Rapid clearance, Limited loading capacity, and Instability.
Dendrimers.	50-100 nm	Controlled drug release, self-assembly, well-defined size and shape, Targeted delivery,	Cytotoxicity, hematological toxicity & immunological reaction, Limited understanding of long-term effects
Micelles.	20-150 nm	Good biocompatibility, good drug solubilization, and reduced degradation,	Possibility of cytotoxicity, Instability in certain environments, and Scalability challenges.
Polymers.	20-300 nm	Improved drug solubility, reduced toxicity, Biocompatibility, Controlled release	Inflammatory response, cytotoxicity, degradation, Instability, High cost.

LIMITATIONS:

The successful translation of nano-therapeutic strategies into clinical practice for cancer treatment faces significant challenges, primarily due to regulatory hurdles and ongoing efforts to standardize these approaches. To overcome these obstacles, healthcare professionals must establish a comprehensive regulatory framework, conduct rigorous preclinical studies, and develop sophisticated computational models. By achieving this goal, researchers can substantially mitigate the risks and adverse effects associated with nanoparticle-based cancer therapies. Moreover, a streamlined development process will accelerate the progression of these therapies into clinical trials, ultimately paving the way for their widespread adoption. The harmonization of regulatory frameworks, preclinical testing protocols, and computational modeling will facilitate the seamless translation of nano-therapeutic strategies from bench to bedside. This concerted effort will enable researchers to harness the full potential of nanoparticle-based cancer therapies, leading to improved treatment outcomes and enhanced patient care. Nanoparticle-based cancer treatment faces challenges due to immune-mediated elimination (or) off-target deposition, which minimizes the pharmacological action. The tumor microenvironment's dense extracellular matrix and aberrant vascularization pose significant obstacles to nano drug penetration and distribution (Venkatesan P., et al. 2014). Furthermore, the potential toxicity and clearance kinetics of nanoparticles present significant challenges in their clinical translation and application (Yurkin S.T., 2019). The complexation between nanoparticles and various therapeutic agents can influence their effectiveness and overall treatment success (Badea, 2017). Over time, polymeric nanoparticles may degrade, losing their therapeutic potency

APPLICATIONS:

1. Nanoparticle-based drug delivery platforms enable site-specific targeting and controlled release of

anticancer therapeutics and help to achieve maximum pharmacological action with minimum side effects.
2. Nanoparticles are helpful in the diagnosis, imaging, and treatment of cancer cells, gold nanoparticles are used as a novel therapeutic platform for cancer and other diseases, with ongoing clinical investigations.
3. Nanotechnology-mediated vaccine delivery systems are being developed to enhance immunogenicity and eliminate needle-associated risks.
4. Nanoparticles can bypass the body's natural barriers, delivering therapeutic agents directly to cells, blood vessels, stomach, and brain and they offer site-specific, sustained-release formulations for optimized drug delivery.

FUTURE PERSPECTIVE OF NANOPARTICLES IN CANCER TREATMENT:

Nanoparticle-mediated transport system offers potential solutions to overcome challenges in conventional cancer treatments. By selectively attacking tumor cells, these systems optimize therapeutic effects and minimize the likelihood of tumor reoccurrence. Furthermore, the capacity to minimize cytotoxicity to healthy cells contributes significantly to improved patient quality of life. In addition to this, Multifunctional nanoparticles enable simultaneous cancer imaging and treatment. Multiplex nanoparticles promise a breakthrough in cancer treatment, combining accurate detection, visualization, and targeted elimination with reduced toxicity. The integration of nanotechnology and multidisciplinary expertise will illuminate new pathways for cancer diagnostics and therapy. Furthermore, immunotherapies have emerged as a promising area of research. These innovative treatments harness the power of the immune system to identify and eliminate cancer cells, providing promising solutions for treating existing tumors and preventing future cancer growth. Immune checkpoint inhibitors, in particular, have shown remarkable results in patients with advanced melanoma, leading to approvals for treating various cancer types. However, individual responses to immunotherapies vary, and further research is necessary to understand the factors influencing treatment effectiveness.

Nanotechnology is transforming clinical research by enhancing the delivery of pharmaceuticals and enabling the development of innovative medications with unique properties inherent to nanomaterials. The distinct physical characteristics of nanoparticles, such as their capacity for energy absorption and re-radiation, can be leveraged for novel applications like thermal ablation and laser therapy. These therapies harness the unique properties of nanoparticles to selectively disrupt diseased tissue. Nanoparticles play a dual role in cancer treatment, encapsulating both radionuclides and active therapeutic agents. Their diminutive size enables them to accumulate at cancer sites, facilitating targeted treatment. Furthermore, nanoparticles can be formulated with ligands like DNA or RNA, including those that exhibit anti-cancer properties. This functionalization enables nanoparticles to selectively target cancer cells, enhancing treatment efficacy. The FDA employs a risk-based approach to evaluate the safety and efficacy of nanomedicines. This approach involves a thorough characterization of nanoparticles and toxicity assessments to inform decision-making. The categorization of nanotherapeutics as drugs, biologics, or medical devices necessitates distinct selection criteria, as each category has unique requirements. In conclusion, nanotechnology is revolutionizing clinical research by enabling the development of innovative medications and enhancing the delivery of pharmaceuticals.

CONCLUSION:

The field of nanotechnology is rapidly growing. This field is expected to yield innovative, multifunctional solutions capable of detecting cancer cells and precisely delivering therapeutics. In this review, we presented a detailed overview of Nanoparticles-mediated drug delivery for oncology. Nanoparticles containing anticancer drugs have revolutionized cancer therapy by offering targeted, efficient, and personalized therapy. These nanocarriers overcome traditional chemotherapy limitations, enhancing drug delivery, reducing toxicity & improving patient outcomes. Nanotechnology breakthroughs are revolutionizing cancer treatment, enabling personalized medicine that customizes therapies to each patient's unique needs and profile. Emerging trends in cancer research point to a future where predictive oncology takes center stage, with nanotechnology playing a pivotal role in enhancing early detection, precision medicine, and overall patient outcomes. The integration of diagnostics and therapeutics through nanotheranostics is poised to revolutionize cancer treatment, yielding more targeted, minimally invasive, and effective interventions.

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