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Short Review

Review of the efficacy of nanoparticle-based drug delivery systems for cancer treatment

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ABSTRACT

This review evaluates the literature on nanoparticle-based drug delivery systems for cancer treatment and assesses their efficacy. Nanoparticles have shown potential for improving anticancer agent delivery, reducing systemic toxicity, and enhancing therapeutic outcomes. Extensive studies have shown promising results in preclinical and clinical trials. However, challenges such as limited drug loading capacity, stability issues, and potential side effects need to be addressed to enhance clinical translation. Researchers are exploring strategies to improve drug loading capacity, such as modifying nanoparticle surfaces or developing novel drug encapsulation techniques. By increasing drug loading, the therapeutic efficacy of these systems can be significantly enhanced. Stability issues also pose a hurdle in clinical translation. To overcome stability issues, researchers are investigating methods to enhance the stability of nanoparticles, such as using protective coatings or optimising the formulation. Additionally, efforts are being made to minimise potential side effects by carefully selecting biocompatible materials for nanoparticle synthesis and conducting rigorous toxicity studies before moving forward with clinical trials.

1. Introduction

Nanomedicine is a promising field for developing targeted drug delivery systems for various diseases, particularly cancer cells. Lipid-based drug delivery uses nanoparticles to encapsulate and deliver drugs to specific cells or tissues, with researchers focusing on cancer cells due to their high proliferation rates and evasion of traditional treatment methods [1]. To ensure the effectiveness and safety of these nanoparticles, extensive research and optimisation efforts are being conducted to fine-tune their size, surface charge, and composition. Researchers are also investigating their potential toxicity and biocompatibility to ensure their safety in clinical applications [2]. To develop drug delivery systems that effectively deliver therapeutic agents to the desired site, minimise side effects, and maximise treatment efficacy. Interdisciplinary collaborations between chemists, biologists, and clinicians are crucial for understanding biological interactions and optimising the design of lipid-based nanoparticles [3]. Chemists can design and synthesise various lipid compositions to enhance stability and biocompatibility, while biologists study cellular uptake and intracellular trafficking. Clinicians can evaluate therapeutic efficacy and potential toxicity in preclinical models or clinical trials, providing valuable feedback for further optimisation of the nanoparticle design. However, lipid-based nanoparticles may still face challenges in terms of long-term stability and potential accumulation in certain organs [4]. The complex interplay between biological factors, such as immune response and nanoparticle clearance mechanisms, can significantly impact their performance and safety profile in vivo.

Different types of nanoparticles are used in the treatment of cancer (Fig. 1). Nanoparticles can deliver chemotherapy drugs directly to cancer cells, enhancing effectiveness and reducing side effects [5]. They can also heat and destroy cancer cells through hyperthermia. Additionally, nanoparticles can enhance medical imaging techniques, enabling better tumour monitoring and location. Overall, nanoparticles hold great potential for improving patient outcomes and advancing oncology [6]. Therefore, it is crucial to thoroughly investigate these factors and understand their influence on nanoparticle behaviour before advancing to human trials. Additionally, developing strategies to enhance nanoparticle stability and minimise organ accumulation will be essential for their successful translation into clinical applications [7]. In this review, we describe the nanodrug delivery of the cancer therapy.

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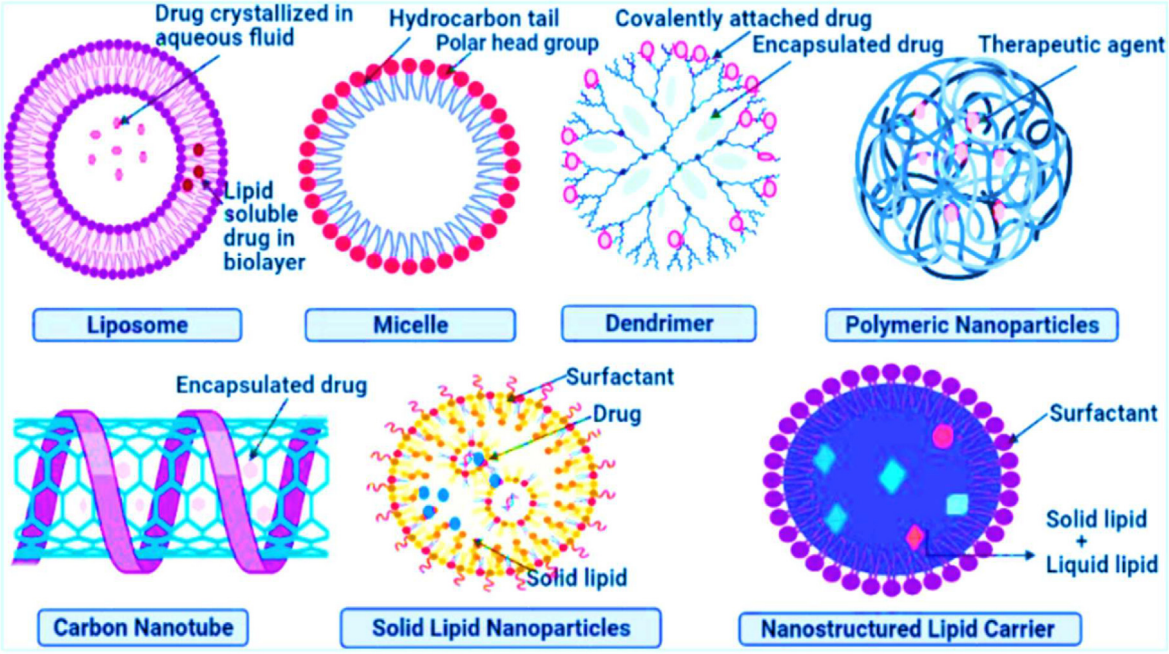

Fig. 1. Different types of nanoparticles are used in cancer treatment [1].

2. The importance of drug delivery in nanomedicine

Nanoparticles have shown great promise in improving drug delivery systems, allowing for the targeted and controlled release of medications. This has the potential to enhance the efficacy and reduce the side effects of drug therapies. Encapsulating drugs within nanoparticles protects them from degradation, delivers them directly to the target site, and releases them in a controlled manner, maximising therapeutic effects [8]. This advancement in nanomedicine has revolutionised drug delivery and holds great potential for improving patient outcomes. By using drug delivery systems based on nanoparticles, healthcare professionals can now precisely control the dosage and timing of medication release, leading to more personalised and effective treatment plans [9]. Additionally, the use of nanotechnology in drug delivery has opened up new possibilities for delivering drugs to previously inaccessible areas of the body, such as crossing the blood-brain barrier for neurological disorders. This breakthrough technology has the potential to transform the field of medicine and significantly improve patient care [10]. Personalised medicine also opens up new possibilities for nanoparticle-based treatments, tailoring treatments to individual patients based on their unique genetic makeup and disease characteristics. This targeted approach leads to more effective and precise treatments, minimising the risk of adverse reactions and optimising therapeutic outcomes. Nanoparticles have also shown promise for overcoming biological barriers that can hinder the effectiveness of traditional drug therapies [11]. Nanoparticles loaded with chemotherapy drugs can target tumour cells while sparing healthy cells, reducing the toxic side effects associated with chemotherapy. Additionally, nanoparticles can overcome the blood-brain barrier, allowing therapeutic drugs to be delivered directly to the brain for neurological disorders like Alzheimer's disease. This targeted drug delivery system has the potential to revolutionise cancer treatment by increasing the efficacy of chemotherapy while minimising its harmful effects on the body [12]. Furthermore, nanoparticles can be engineered to release drugs in a controlled manner, ensuring a sustained and prolonged therapeutic effect. One potential drawback of nanoparticles in targeted drug delivery is the development of drug resistance in tumour cells. Over time, tumour cells can adapt and become resistant to the chemotherapy drugs carried by nanoparticles, limiting their effectiveness in treating cancer [13]. Despite the potential benefits of nanoparticles in targeted drug delivery, the development of drug resistance in tumour cells can significantly reduce their effectiveness in treating cancer. This issue of drug resistance highlights the need for ongoing research and development in the field of targeted drug delivery. Scientists are actively working to find solutions to overcome drug resistance, such as combining different types of nanoparticles or using alternative delivery methods. By addressing this challenge, the potential benefits of nanoparticles in targeted drug delivery can be maximised, leading to more effective treatments for cancer patients [14].

3. Nanoparticle-based drug delivery systems

Nanoparticle-based drug delivery systems have shown promise in improving cancer treatment by selectively delivering drugs to cancer cells, minimising damage to healthy tissues [15]. However, drug resistance remains a major concern that needs to be addressed to fully harness the potential of these systems. Scientists are exploring ways to overcome drug resistance and enhance the effectiveness of these systems. Combination therapies involve multiple drugs being delivered simultaneously using nanoparticle-based systems, targeting different pathways and mechanisms of drug resistance [16]. Nanoparticles can also actively bypass drug-resistant mechanisms within cancer cells, allowing drugs to reach their intended targets and exert therapeutic effects. Nanoparticles can be engineered to release drugs in a controlled manner, ensuring sustained drug levels and minimising side effects. Furthermore, ongoing research is focused on improving the specificity of nanoparticle-based systems, enabling them to selectively target cancer cells while sparing healthy tissues. This holds great promise for the development of more personalised and effective cancer treatments in the future [17]. Gene therapy agents that reverse or inhibit drug resistance in cancer cells are also being investigated. Nanoparticles can encapsulate chemotherapy drugs and specifically target cancer cells while bypassing the mechanisms that make them resistant to treatment. These nanoparticles can deliver drugs directly to cancer cells, effectively overcoming drug resistance and increasing treatment effectiveness. However, not all cancer cells may respond equally to nanoparticle-based treatments, as mutations or genetic variations may render them less susceptible to the effects of nanoparticles. Some cancer cells may develop mechanisms to actively expel or neutralise nanoparticles, making them ineffective in delivering

drugs to targeted cells [18]. Additionally, the complex interaction between nanoparticles and cancer cells can lead to unforeseen side effects or toxicities, potentially causing harm to healthy tissues and organs. It is important to consider that the effectiveness of nanoparticle-based treatments can vary depending on the specific type of cancer cells being targeted [19]. Certain cancer cells may possess unique characteristics that make them more resistant to nanoparticle therapies. Also, the possibility of off-target effects and unintended results should be carefully considered before nanoparticle-based treatments are widely used in clinical settings. In addition, the delivery method of nanoparticles to cancer cells is a crucial factor to consider. The ability of nanoparticles to reach and penetrate the tumour site efficiently can greatly impact their effectiveness [20]. Moreover, understanding the potential long-term effects and safety profile of nanoparticle-based treatments is essential for ensuring patient well-being and minimising any unforeseen risks.

3.1. Structure of the nanoparticles

Nanoparticles play a crucial role in the effectiveness of immunotherapies, as their size, shape, and surface properties affect their interaction with immune cells and the delivery of therapeutic agents [21]. Researchers can optimise nanoparticle structure to improve targeting efficiency and overall immunotherapy efficacy. Stability and biocompatibility are essential factors to minimise toxic effects and ensure long-term patient safety. Biodegradable polymers like poly-lactic-*co*-glycolic acid (PLGA) and chitosan offer a safe and controlled release of therapeutic agents, allowing targeted delivery to specific immune cells or tumour sites [22]. Researchers have developed PLGA-based nanoparticles loaded with anti-cancer drugs that target tumour cells, minimising damage to healthy cells and reducing side effects. These nanoparticles allow controlled drug release over time, ensuring sustained therapeutic effects and reduced administration frequency. Chitosan-based scaffolds have been used in tissue engineering to create artificial bone or cartilage implants, providing temporary support structures while promoting tissue regeneration [23]. However, nanoparticles can still accumulate in unintended tissues and cause toxicity or adverse reactions. Additionally, chitosan-based scaffolds may not always degrade at the desired rate, leading to incomplete tissue regeneration or prolonged foreign body reactions. To address these challenges, researchers have been exploring different strategies to enhance the biocompatibility and degradation properties of chitosan-based scaffolds. For instance, surface modifications with bioactive molecules or the incorporation of growth factors can improve cell adhesion and promote tissue regeneration [24]. The development of composite scaffolds using chitosan and other biodegradable materials has shown promising results in achieving controlled degradation rates and better tissue integration.

3.2. Types of nanoparticles used in drug delivery

Nanoparticles, like liposomes, polymeric nanoparticles, and metallic nanoparticles, can be used to make different kinds of drug delivery systems that work well for certain types of cancer cells. Polymeric nanoparticles, made from biocompatible polymers, provide a safe and efficient means of drug delivery, while metallic nanoparticles, like gold or silver, offer unique optical and physical properties for targeted drug delivery and imaging [25]. These nanoparticles can be coated with specific antibodies or proteins that bind to cancer cells, allowing for targeted drug delivery. They can also be used in imaging techniques like photoacoustic imaging to detect and monitor cancer cell progression in real-time. In addition to their targeting capabilities, biocompatible polymers also offer the advantage of controlled release, allowing for a sustained and prolonged drug effect [26]. Furthermore, metallic nanoparticles have shown promising results in enhancing the efficacy of chemotherapy drugs by increasing their cellular uptake and reducing systemic toxicity. The use of metallic nanoparticles in cancer treatment may also have unintended consequences. Studies have shown that these nanoparticles can accumulate in healthy organs and tissues, leading to potential toxicity and long-term side effects. Additionally, there is limited research on the long-term effects of metallic nanoparticles on the human body, raising concerns about their safety and efficacy in clinical applications [27]. Despite their potential in cancer treatment, concerns remain about their safety and efficacy in clinical applications. It is crucial to conduct further research and rigorous testing to fully understand the risks and benefits associated with metallic nanoparticles. Additionally, regulatory agencies should establish guidelines and protocols to ensure the safe and responsible use of these nanoparticles in medical settings [28]. Furthermore, long-term studies are needed to assess the potential side effects and interactions of metallic nanoparticles with other medications or treatments. Additionally, it is important to involve multidisciplinary teams of scientists, clinicians, and regulatory experts to evaluate the ethical implications and address any potential societal concerns surrounding the use of metallic nanoparticles in cancer treatment.

3.3. Inorganic nanoparticles

Inorganic nanoparticles, like gold and silver nanoparticles, have shown great promise in cancer treatment due to their unique properties. These nanoparticles can be engineered to target cancer cells and enhance the effectiveness of other treatments like chemotherapy or radiation therapy. However, extensive research is needed to optimise their safety and efficacy profiles. Understanding the potential long-term effects of nanoparticles on the human body is crucial to preventing unintended harm to patients [18]. Researchers must also address the challenge of scaling up nanoparticle production to meet clinical applications. Standardised and cost-effective manufacturing processes are essential for the widespread availability and affordability of these promising cancer treatment options. In addition, it is important for researchers to consider the ethical implications of using nanoparticles in cancer treatment. They must ensure that the benefits outweigh any potential risks and that patients are fully informed about the use of these innovative therapies. Moreover, collaboration between scientists, clinicians, and regulatory agencies is crucial to establishing guidelines and regulations for the safe and responsible use of nanoparticles in clinical settings [14]. A clinical trial found that nanoparticles combined with chemotherapy drugs enhanced the treatment's effectiveness by targeting cancer cells while minimising damage to healthy cells. This breakthrough highlighted the importance of understanding how nanoparticles interact with other medications and paved the way for personalised cancer treatment plans tailored to individual patients. Innovative manufacturing techniques, such as continuous flow reactors, have been developed to reduce costs and ensure widespread access to this cutting-edge technology [23]. However, the limited effectiveness of nanoparticle-based cancer treatment for certain types of tumours is a significant counterexample. For example, in pancreatic cancer, dense stromal tissue surrounding the tumour hinders drug penetration, limiting the effectiveness of nanoparticles in certain tumour microenvironments. This challenge has prompted researchers to explore alternative strategies, such as combining nanoparticle-based treatments with other therapeutic approaches like immunotherapy or targeted drug delivery systems [9]. By synergistically leveraging multiple treatment modalities, scientists aim to overcome the limitations posed by dense stromal tissue and enhance the efficacy of cancer treatments in challenging tumour microenvironments.

3.4. Organic nanoparticles

Organic nanoparticles are a promising alternative to metallic nanoparticles in medical applications because they are biocompatible and can be made to have specific properties, such as the ability to deliver drugs to specific areas or be used as an imaging agent [4]. These nanoparticles have shown promise in cancer therapy, where they can selectively target tumour cells and deliver anticancer drugs directly to the disease site,

reducing side effects and enhancing treatment efficacy. They also have great potential in medical imaging, allowing for better visualisation of tissues and organs and aiding in early disease detection and diagnosis [15]. Researchers have developed nanoparticles coated with a specific protein that target breast cancer cells, delivering a potent anticancer drug directly to the tumour site. This targeted therapy approach has shown promising results in preclinical studies, effectively inhibiting tumour growth and reducing the risk of metastasis. Additionally, the use of nanoparticles in drug delivery systems allows for controlled release of the drug, ensuring a sustained and optimal therapeutic effect [12]. However, organic nanoparticles can also emit fluorescent signals when interacting with specific tissues or organs, enabling better visualisation. However, this approach has potential side effects and toxicity, as well as difficulties in accurately visualising specific tissues or organs. Research is needed to fully understand the long-term effects and potential risks associated with using organic nanoparticles in medical treatments [24]. Additionally, the use of organic nanoparticles in medical treatments raises concerns about their potential accumulation in the body over time. This accumulation could potentially lead to unintended consequences and adverse reactions. Therefore, it is crucial to conduct extensive studies to evaluate the safety and efficacy of organic nanoparticles before they can be widely adopted in therapeutic applications [29].

3.5. Hybrid nanoparticles

Hybrid nanoparticles are a promising approach to addressing concerns about organic nanoparticle accumulation by combining the advantages of organic and inorganic materials. By incorporating inorganic components like metals or metal oxides, these nanoparticles can enhance their biocompatibility and reduce the risk of long-term accumulation [11]. However, further research is needed to fully understand the potential interactions and long-term effects of these hybrid nanoparticles in the human body. The immune response to hybrid nanoparticles can vary depending on their size, shape, and surface properties [18]. While organic nanoparticles are generally considered biocompatible, the introduction of inorganic components may trigger an immune response that could potentially lead to inflammation or other adverse effects. Therefore, it is crucial to investigate the immune response to these hybrid nanoparticles and determine their safety profile before they can be widely used in medical applications [7]. A study on hybrid nanoparticles with both organic and inorganic parts found that smaller nanoparticles with a spherical shape and smooth surface were more likely to pass the immune system and be considered biocompatible [4]. However, larger nanoparticles with irregular shapes and rough surfaces triggered a stronger immune response, leading to inflammation and potential health risks. This highlights the importance of thoroughly examining the physical characteristics of nanoparticles to ensure their safety in medical applications. Gold nanoparticles, for example, have been found to activate the immune system and induce inflammation, suggesting that size and shape alone do not determine biocompatibility [13]. Additionally, certain inorganic nanoparticles with irregular shapes and rough surfaces have shown low immunogenicity, contradicting the notion that these factors always trigger a stronger immune response. Therefore, a comprehensive understanding of nanoparticle behaviour is necessary to accurately assess their safety in medical applications.

3.6. Advantages and limitations of nanoparticle-based drug delivery systems

Nanoparticle-based drug delivery systems offer numerous advantages in cancer treatment, such as improved drug targeting and penetration into tumour cells, leading to enhanced therapeutic efficacy [30]. However, these systems also have limitations, such as potential toxicity concerns and immune system recognition and clearance risks. Extensive research is needed to optimise these systems and address their limitations for safe and effective clinical applications [25]. One approach is to modify nanoparticles' surface properties by coating them with biocompatible materials, targeting ligands on the surface, and creating stimulus-responsive nanoparticles that release their cargo in response to specific cues within the tumour microenvironment [23]. Another approach is to engineer nanoparticles with controlled size and shape to enhance their circulation time in the body and improve their ability to penetrate tumour tissues. Additionally, researchers are exploring the use of multifunctional nanoparticles that can simultaneously deliver therapeutic agents, imaging agents, and targeting molecules to improve the overall efficacy of cancer treatment. Research in nanomedicine has the potential to revolutionise cancer treatment by providing more targeted and efficient therapies [16]. Nanoparticles have been developed to deliver chemotherapy drugs directly to tumour cells, reducing systemic doses and toxicity to healthy tissues. This approach has shown promising results in preclinical studies and could eventually be translated into clinical practise to improve patient outcomes [22]. However, drug resistance remains a challenge, as tumour cells can develop resistance to these treatments over time through mutations or activation of alternative signalling pathways. To overcome drug resistance, researchers are exploring combination therapies that target multiple pathways simultaneously [16]. Additionally, efforts are being made to develop nanoparticles with enhanced targeting capabilities to specifically deliver drugs to resistant tumour cells. These strategies hold great potential for overcoming the challenge of drug resistance and improving the effectiveness of cancer treatments. In addition, scientists are also investigating the use of immunotherapies to enhance the body's own immune response against resistant tumour cells [19]. By harnessing the power of the immune system, these therapies have shown promising results in overcoming drug resistance and improving patient outcomes. Ongoing research is focused on identifying biomarkers that can predict drug resistance, allowing for more personalised treatment approaches tailored to individual patients.

4. Lipid-based nanoparticles for drug delivery

Lipid-based nanoparticles are a promising approach for drug delivery due to their biocompatibility and ability to enhance drug stability, solubility, and targeting capabilities. These nanoparticles can be designed to interact with resistant tumour cells, increasing their effectiveness and overcoming multidrug resistance (MDR) in cancer treatment. Nanoparticles made of lipids can get around efflux pumps on MDR tumour cells [21]. This lets drugs build up inside the cells and kill them. This targeted drug delivery system has shown promise in preclinical studies, making chemotherapy more effective in treating resistant tumours. However, in a clinical trial involving human patients, these nanoparticles had limited efficacy in targeting MDR tumour cells, resulting in little effect on the cells and poor treatment outcomes [28]. This presents a challenge for the development of new cancer therapies and patient outcomes. Further research is needed to understand the underlying mechanisms behind the limited efficacy of these nanoparticles in targeting MDR tumour cells. Additionally, exploring alternative drug delivery systems that can overcome this challenge may lead to improved treatment outcomes for patients with resistant tumours [21]. One possible approach to overcome the limited efficacy of nanoparticles in targeting MDR tumour cells is to investigate combination therapies. By combining nanoparticles with other treatment modalities such as immunotherapy or gene therapy, it may be possible to enhance their effectiveness and improve patient outcomes [17]. Additionally, understanding the specific molecular pathways involved in multidrug resistance could help identify novel targets for therapeutic intervention and pave the way for the development of more tailored and effective cancer treatments.

4.1. Lipid-based nanoparticles for drug delivery

Lipid-based nanoparticles offer a promising alternative for drug delivery due to their biocompatibility and ability to encapsulate a wide

Table 1
Several types of lipid nanoparticles and the functions they offer.

Nanoparticles	Lipid	Surfactant	Drug	Method	Disease	References
LNPs.	Waxcetyl palmitate, DMPC.	Polysorbate 60 or 80.	Camptothecin.	Nonsolvent Emulsification.	Glioblastoma.	[31]
Mannosylated LNP.	Tristearin, stearyl Amine.	Soya-lecithin.	Doxorubicin.	Solvent injection.	Lung cancer.	[32]
Lactoferin-modified LNPs.	Glyceryl monostearate, Stearic acid.	Tween 80, Soy-lecithin.	Docetaxel.	Emulsification and solvent evaporation.	Brain tumour.	[33]
Fas ligand antibody conjugated PEGylated LNPs.	Medium chain triglyceriade, Amino-terminated polyethylene glycol monostearate.	Polysorbate 80.	3-*n*-Butylphthalide.	Solvent diffusion method.	Brain ischaemic stroke	[34]
Apo E-targeting LNPs.	Dynasan 116.	Tween 80.	Donepezil.	Homogenization sonication.	Alzheimer's Disease.	[35]
LNPs.	Stearic acid, lecithin.	Myrj 52.	Curcumin.	Emulsion solvent evaporation.	Asthma.	[36]
Chitosan-coated LNPs.	Cetyl palmitate.	Tween 80.	Rifampicin.	Micro emulsion.	Tuberculosis.	[37]
Transferrinmediated-LNPs.	Hydrogenated soya phosphatidylcholine, DSPE, Cholesterol, Triolein.	Poloxamer 188.	Curcumin.	High-speed homogenization – high pressure Homogenization.	Breast cancer.	[38]
pH-responsive LNPs.	Trilaurin, sodium Laurate.	PEG.	Doxorubicin.	Micro emulsion evaporation.	Tumour.	[39]
Self-assembled LNPs.	Monoolein.	Pluronic F127 triblock copolymers, Tween 80, 1,2-distearoyl-*sn*-glycero 3-phosphoethanolamine-PEG Mw¼3400-maleimide.	Paclitaxel.	Solvent evaporation.	Aggressive ovarian cancer.	[40]

range of drugs (Table 1). These nanoparticles can be easily engineered and manufactured using well-established techniques, making them more practical for widespread clinical use. Moreover, lipid-based nanoparticles have shown better stability and controlled release properties compared to polymeric nanoparticles [28]. However, challenges still exist in terms of their potential toxicity and clearance from the body, which need to be addressed for successful clinical application [6]. One of the main challenges in the clinical application of lipid-based nanoparticles is their potential toxicity. Although they have shown promising results in drug delivery, there is a need to thoroughly evaluate their safety profile to ensure patient well-being. This involves conducting comprehensive toxicity studies to assess any adverse effects on vital organs and biological systems [8]. Additionally, understanding the mechanisms of nanoparticle clearance from the body is crucial for their successful clinical use. Researchers might conduct toxicity studies on lipid-based nanoparticles by administering them to laboratory animals and closely monitoring their organ functions and overall health. They would analyse blood samples, perform histopathological examinations, and assess any changes in organ structure or function [17]. Also, they would look into how these nanoparticles are removed from the body, such as through renal excretion or hepatic metabolism, to figure out how they might build up or leave the body. This approach would be appropriate if the nanoparticles being studied have a unique mechanism of action that is not present in laboratory animals [11]. In such cases, administering the nanoparticles to animals may not accurately reflect how they would behave in humans, leading to misleading toxicity results [19]. Also, if the nanoparticles leave the body quickly through processes other than renal excretion or hepatic metabolism, studying how they build up or leave the body using these methods would not give accurate information. It is crucial to consider alternative methods for studying nanoparticle behaviour in humans, such as in vitro models or computational simulations, to better understand their potential toxicity [20]. Additionally, exploring novel imaging techniques that can track the distribution and clearance of nanoparticles in real-time would provide more reliable data on their behaviour within the human body.

4.2. Advantages and limitations of lipid-based nanoparticles for drug delivery

Lipid-based nanoparticles offer advantages for drug delivery, such as biocompatibility, release control, and protection from degradation. However, their limited efficacy in targeting MDR tumour cells requires further research to understand their mechanisms and explore alternative drug delivery systems [17]. Nanocarriers like liposomes, polymeric nanoparticles, and dendrimers have shown promise in enhancing drug delivery to resistant cancer cells. These nanocarriers can be engineered to target MDR tumour cells, increase drug efficacy, and be loaded with multiple drugs for combination therapy [18]. Liposomes can be loaded with chemotherapy drugs and equipped with targeting Liposomes to target specific receptors on MDR tumour cells. Polymeric nanoparticles can encapsulate different anticancer drugs in separate compartments, enabling simultaneous delivery of multiple drugs to combat drug resistance mechanisms in MDR tumours [9]. However, there are limitations to polymeric nanoparticles, such as conflicting mechanisms of action, time-consuming and expensive engineering and manufacturing processes, and limited practicality for widespread clinical use. Additionally, the potential toxicity of polymeric nanoparticles and their clearance from the body pose challenges in clinical application [10]. The complex interactions between different drugs within the nanoparticles may affect their efficacy and overall therapeutic outcome [5]. Furthermore, the stability and long-term storage of polymeric nanoparticles can be a concern, as they may degrade or lose their effectiveness over time. Additionally, scaling up the production of polymeric nanoparticles for large-scale clinical use can be challenging due to the need for precise control over particle size and distribution [1].

5. Polymer-based nanoparticles for drug delivery

Polymer-based nanoparticles offer a promising approach to overcome limitations in drug delivery systems. These nanoparticles can be designed with a controlled release mechanism, allowing for sustained drug release over time. The size and surface properties can be tailored to enhance stability in biological environments and targeting capabilities [25]. This allows researchers to accurately study drug behaviour and toxicity in

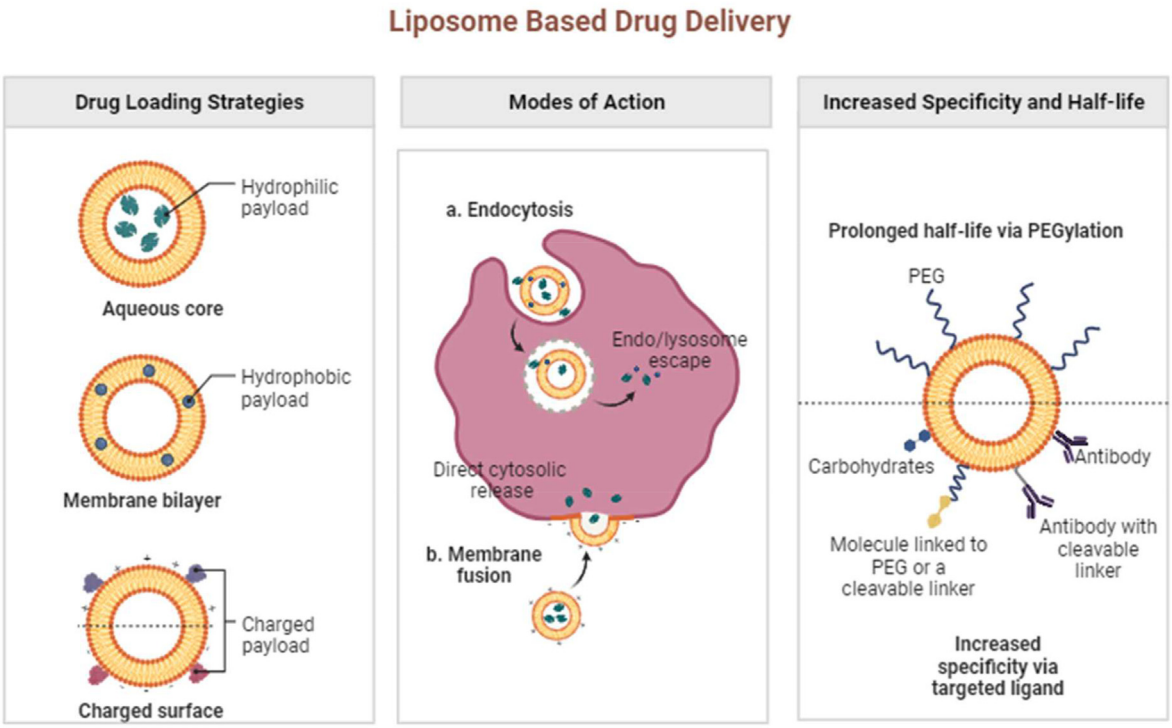

Fig. 2. Liposome based drug delivery.

Table 2
Polymeric micelles are used to carry drugs, contain drugs, and treat the diseases for which they are administered.

Types of Nano Particles	Nano Particle Composite	Drug Delivery	Treatment	References
Polymeric Micelles	PLGA/PVA.	Fenofibrate.	Choroidal neovascularization, retinal dysfunctions, retinal leukostasis, retinal vascular leaks, overexpression of VEGF, and retinal leukostasis.	[58]
	PLGA/PVA/PEI.	Dexamethasone.	Neovascularization of the choroidal stroma.	[59]
	PLGA/Tween 80, poloxamer. 188	Brinzolamide.	Inflammation of the eyes.	[60]
	PLGA/Pluronic F127.	Dexamethasone.	Rejection of the transplant due to an immune response.	[61]
	Bevacizumab-coated PLA NPs embedded in PLGA microparticles.	Bevacizumab.	Macular aging and degeneration.	[62]
	PEG–PCL–PEG	Triamcinolone acetonide.	Inflammation of the eyes.	[63]
	Tween80/polyoxyethylene stearate.	Everolimus.	Immune-mediated rejection, non-infectious uveitis, neovascularization of the cornea, and autoimmune uveoretinitis.	[64]
	Cationic CH grafted methoxy poly (ethylene Glycol)-poly (ε-caprolactone).	Diclofenac.	Inflammation of the eyes.	[65]
	Methoxy poly (ethylene glycol)-poly (lactide) block Copolymer.	Cyclosporine A.	Syndrome of the dry eye.	[66]
	CH/PVA/sodium deoxycholate.	Prednisolone.	Ocular inflammation	[67]
	Stearic acid and valylvaline functionalized CH.	Dexamethasone.	VEGF overexpression, choroidal neovascularization, retinal dysfunctions, retinal leukostasis, retinal vascular leakage, and inflammation of the eye.	[68]
Cyclodextrins	Propylamino-β-Cyclodextrin	latanoprost	Glaucoma	[69]
	α-Cyclodextrin/Soluplus/Pluronic P103	natamycin	Fungal keratitis	[70]
	γ-Cyclodextrin and randomly methylated β-cyclodextrin	celecoxib	Age-related macular degeneration and diabetic retinopathy	[71]
Polymeric vesicles	DOTAP/DOPE/DSPE–PEG	siRNA sequences/ chlorhexidine	Keratitis caused by *Acanthamoeba*	[72]
	Precirol® ATO 5/castor oil/Span® 80/mPEG-2K-DSPE	natamycin	Fungal keratitis	[73]

PLGA stands for poly(lactic-*co*-glycolic acid), PVA for poly(vinyl alcohol), VEGF for Vascular Endothelial Growth Factor, PEI for poly (ethyleneimine), PVP for poly (vinylpyrrolidone), CH for chitin, PCL for poly(-caprolactone), and PEG for poly(ethylene glycol). DOTAP is short for 1,2-dioleoylsn-*glycero*-3-trimethylammonium propane. DOPE is short for 1,2-di-(9E-octadecenoyl)-*sn*-glycero-3-phosphoethanolamine. DSPE–PEG is short for 1,2-distearoyl-*sn*-glycero-3-phosphoethanolamine-N-[methoxy(polyethylene glycol-1,2-distearoyl-*sn*-glycero-3- phosphoethanolamine.

humans, leading to safer and more effective therapies. Polymer-based nanoparticles can be easily functionalized with ligands or antibodies to specifically target diseased cells or tissues [29]. This targeted drug delivery approach minimises off-target effects and improves therapeutic efficacy. Additionally, the biocompatibility and biodegradability of these nanoparticles make them suitable for long-term drug delivery applications without causing adverse reactions in the body [16]. Nanoparticles offer several advantages over traditional drug formulations, such as

Table 3
Polymer nanoparticles used to treat cancer are arranged by the type of cancer they treat.

Polymer	Active Principle	Type of Cancer	Experimental Model/Route	Size (nm)	References
PLA–PEG–maleimide.	Paclitaxel.	breast cancer (TNB).	In vitro: MDA-MB-231 cells In vivo: BALB/c homozygous nude mice Intravenous injection. Tail vein.	212	[74]
PLGA–Cyanine.	Doxorubicin.	Glioblastoma.	In vivo: C6 Glioma cells in Wistar rats and nude mice Tail vein.	114	[75]
PBCA	doxorubicin	glioblastoma	In vitro: U87 glioblastoma human cells line	260	[76]
Lip–BSA	paclitaxel	various	In vivo: 4T1 cells in BALB/c mice Tail vein	116.2	[77]
PLGA–PEG	paclitaxel	glioma	In vivo: gliosarcoma 9L cells in Fischer F344 rats Direct injection	121	[78]
PCL–PEG	camptothecin	glioma	In vivo: 4T1 cells in BALB/c mice Tail vein	274	[79]
PEI–PLA	paclitaxel	lung cancer	In vivo: A549 cells in BALB/c mice. Tail vein	67.31	[80]
mPEG–PLGA–PGlu	doxorubicin–curcumin	breast cancer	In vivo: LM2 cells in BALB/c homozygous nude mice Tail vein	107.5	[81]
PCL–PEGPEG–PCL	paclitaxel	lung cancer	In vivo: MCF-7/ADR cells in BALB/c nude miceIntravenous injection	168	[82]
TPGS–PLGA	doxorubicin	breast cancer	In vivo: MCF-7 cells in nude mice Tail vein	87	[83]
Gal–pD–TPGS–PLA	docetaxel	liver cancer	In vivo: MCF-7 cells in BALB/c mice Orthotopic injection	209.4	[84]

protecting the drug from degradation, increasing shelf life and bioavailability, and allowing efficient drug delivery to specific target sites. This targeted approach minimises exposure to healthy tissues and reduces the required dosage, minimising potential side effects [30]. Additionally, nanoparticles can be incorporated with various therapeutic agents, such as proteins, genes, and imaging agents, further enhancing their potential for personalised medicine. Nanoparticles have been shown to cause adverse reactions in patients, such as immune system reactions and inflammation, leading to unexpected side effects and complications. This highlights the need for further research and development in nanoparticles to improve drug delivery and patient outcomes [28]. In recent years, researchers have been exploring different strategies to mitigate the adverse effects of nanoparticles. One approach involves modifying the surface of nanoparticles to make them less likely to trigger immune responses or inflammation. Additionally, efforts are being made to develop targeted delivery systems that can specifically deliver nanoparticles to the desired site, minimising off-target effects and improving overall treatment efficacy [16]. These advancements hold promise for addressing the current limitations and maximising the potential benefits of nanoparticles in personalised medicine.

5.1. *Polymer-based nanoparticles for drug delivery in clinical use*

Liposomes, spherical vesicles made of lipid bilayers, are biocompatible and can encapsulate various therapeutic agents (Fig. 2). They are biocompatible and can enhance drug stability and bioavailability, improving patient outcomes. Dendrimers and polymeric micelles are two other types of polymer-based nanoparticles being studied for clinical use (Table 2). Dendrimers have a highly branched structure, allowing for a large surface area and precise drug release control. They can be modified with various functional groups to interact with specific biological targets [11]. When amphiphilic block copolymers self-assemble into a core-shell shape with a hydrophobic core and a hydrophilic shell, this makes polymeric micelles. Polymeric micelles have shown promise in delivering hydrophobic drugs to tumour sites (Table 3), as the hydrophobic core can encapsulate the drug and protect it from degradation. Additionally, the hydrophilic shell allows for prolonged circulation time in the bloodstream, enhancing drug delivery efficiency. These unique properties make polymeric micelles a potential solution for improving targeted drug delivery and enhancing patient outcomes [74].

This unique structure allows them to encapsulate hydrophobic drugs within their core while maintaining stability in aqueous environments. Dendrimers can be engineered to target cancer cells by adding ligands or antibodies that recognise cancer cell markers to the surface of dendrimers. This targeted delivery system reduces side effects and increases drug delivery efficiency [75]. However, tumour delivery systems have the potential for off-target binding as they may bind to healthy cells that express similar markers as tumour cells, leading to toxicity and damage to healthy tissues, negating the desired specificity of the delivery system. To address this challenge, researchers are exploring various strategies to enhance the selectivity of targeted delivery systems. One approach involves utilising advanced imaging techniques to accurately identify and characterise cancer cells, allowing for the development of more precise ligands or antibodies that specifically recognise tumour markers [76]. Additionally, advancements in nanotechnology are being leveraged to design multifunctional dendrimers that can actively target cancer cells while avoiding healthy tissues, further minimising off-target binding and potential side effects [77].

5.2. *Advantages and limitations of polymer-based nanoparticles for drug delivery*

Polymer-based nanoparticles offer versatility in drug delivery by encapsulating various therapeutic agents, such as small molecules, proteins, and nucleic acids. These nanoparticles can be easily modified to control their size, surface properties, and drug release kinetics, making them highly customizable for specific drug delivery applications [78]. However, there are limitations to consider, such as the potential for toxicity and immunogenicity, as well as the challenge of precise control over drug release kinetics. Additionally, the degradation of polymers can vary depending on factors like pH, temperature, and enzymatic activity, complicating drug release kinetics. Researchers are constantly exploring new strategies and technologies to overcome these limitations and enhance the performance of polymer-based drug delivery systems [79]. One example is the development of pH-responsive polymer nanoparticles for targeted drug delivery. These nanoparticles release the drug payload in response to changes in pH levels within the body, such as those found in tumour microenvironments [80]. By adding pH-sensitive polymers to the nanoparticle formula, researchers can control the rate at which drugs are released and ensure therapeutic doses reach the site where they are needed. This approach not only improves drug efficacy but also minimises potential side effects on healthy tissues [81]. However, pH levels in tumour microenvironments can vary significantly among different types of tumours and within the same tumour, making consistent and targeted drug release challenging. Additionally, pH-sensitive polymers may not effectively respond to subtle changes in pH levels, leading to inadequate drug release or premature release in non-targeted areas [34]. To address these challenges, researchers have been exploring novel strategies to enhance the responsiveness of pH-sensitive polymers. One promising method is to add “stimulus-responsive moieties” to the structure of the polymer. This lets the drug be released more precisely and in response to specific pH changes. Another strategy involves combining pH-sensitive polymers with other targeting mechanisms, such as ligand-receptor interactions or magnetic targeting, to further improve drug delivery accuracy and efficiency [43]. These advancements hold great potential for improving the effectiveness of pH-sensitive polymer-based drug delivery systems.

6. Drugs are loaded into nanoparticles

Drug loading methods in nanoparticle synthesis include encapsulation, adsorption, and drug conjugation. Encapsulation allows controlled drug release, while adsorption involves drugs being adsorbed onto the surface of pre-formed nanoparticles [49]. Encapsulation can be achieved through techniques like coacervation, co-precipitation, or self-assembly [51]. Coacervation involves the formation of a polymer-rich phase that encapsulates the drug, while co-precipitation involves the simultaneous precipitation of both the drug and the polymer [52]. Self-assembly utilises the inherent properties of certain polymers to form nanoparticles that encapsulate the drug [54]. Drug conjugation, on the other hand, involves chemically attaching the drug to the nanoparticle surface, allowing for targeted delivery and controlled release [54–56]. These various methods provide flexibility in loading drugs into nanoparticles and offer potential for optimising therapeutic efficacy. By utilising co-precipitation, self-assembly, and drug conjugation, researchers can tailor the drug-loading process to specific drugs and desired release profiles [59]. This versatility is crucial in achieving maximum drug loading efficiency and ensuring the nanoparticles effectively deliver the drug to the intended site of action. Additionally, these methods allow for the incorporation of targeting ligands onto the nanoparticle surface, enabling specific delivery to diseased tissues or cells [60]. As nanoparticles continue to be explored as drug delivery systems, the optimisation of drug loading techniques will be instrumental in advancing the field of nanomedicine.

Encapsulation also protects the drug from degradation and enhances its stability. Nanoparticles can be modified to improve their interaction with biological systems, making them easier for cells to absorb and enhancing therapy effectiveness [63]. Researchers have developed lipid-based nanoparticles for cancer treatment that enhance drug stability, solubility in water, and selective delivery to tumour cells while minimising toxicity to healthy tissues. Furthermore, nanoparticles can be engineered to target specific cells or tissues, allowing for more precise drug delivery and reducing potential side effects [64]. This targeted approach has shown promising results in improving the efficacy of various therapies, including chemotherapy and gene therapy. As nanomedicine continues to advance, these advancements hold great potential for revolutionising the treatment of various diseases and improving patient outcomes [66]. However, the development of drug-resistant tumour cells could render the targeted delivery approach ineffective and limit its long-term impact on cancer treatment. The complexity and potential cost of manufacturing these nanoparticles at a large scale could pose challenges for widespread implementation in clinical settings [70].

6.1. Nanoparticle targets a tumour

Nanoparticles' targeting of tumours depends on their design and composition. One common approach is to attach targeting molecules to the nanoparticle's surface that recognise and bind to receptors on tumour cells [57]. This allows the nanoparticle to selectively accumulate in the tumour, enhancing its efficacy while minimising damage to healthy cells [41]. Additionally, some nanoparticles can be engineered to release their therapeutic payload in response to specific stimuli, such as changes in pH or temperature [49]. By adding these properties that change in response to a stimulus, the nanoparticles can be more targeted and make sure that the therapeutic payload is released at the right place. This approach not only improves the effectiveness of cancer treatment but also reduces potential side effects associated with non-specific drug distribution [43]. Stimulation-responsive nanoparticles are designed to release their therapeutic payload in response to specific stimuli, such as changes in pH or temperature. This allows researchers to create a system that selectively releases the drug at the tumour site, increasing its efficacy while minimising side effects on healthy cells [48]. This approach holds great potential for improving cancer treatments and reducing patient burden. By targeting the drug delivery specifically to the tumour site,

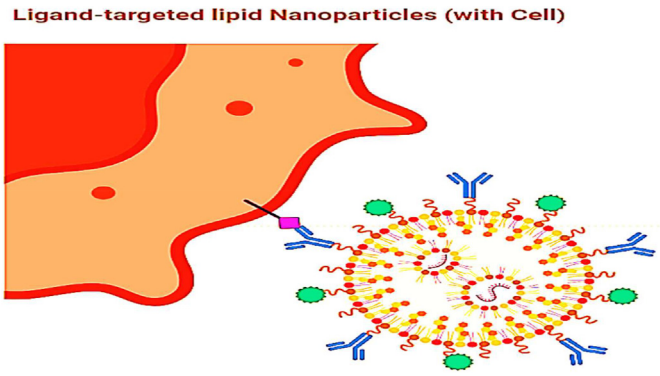

Fig. 3. Ligand-targeted lipid Nanoparticles.

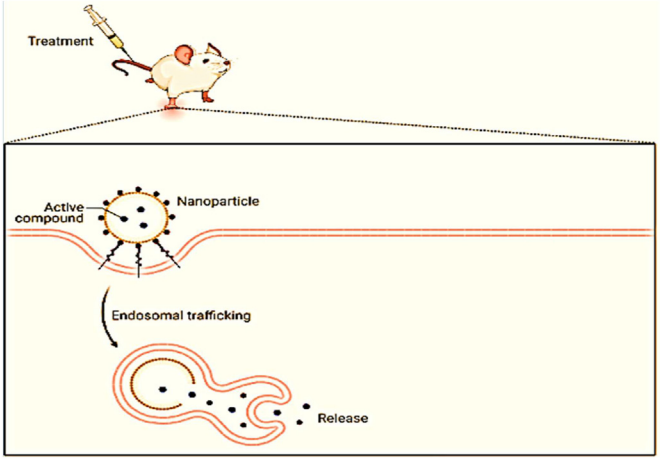

Fig. 4. Nanoparticles drug release Mechanism.

stimulation-responsive nanoparticles can minimise the damage to healthy cells and tissues surrounding the tumour [42]. This not only improves the effectiveness of cancer treatments but also enhances patient quality of life by reducing the adverse effects commonly associated with traditional chemotherapy [45–47]. Nanoparticles that are responsive to changes in pH within the tumour microenvironment release the drug payload when they encounter acidic conditions in tumours, effectively targeting and killing cancer cells while sparing healthy tissues [53]. This not only improves treatment efficacy but also minimises harmful side effects experienced by patients undergoing chemotherapy. Nanoparticles may also affect healthy tissues if they encounter acidic conditions outside of the tumour, potentially leading to unintended harm and compromising the goal of minimising side effects in patients [36]. Therefore, it is crucial to develop targeted delivery systems that ensure nanoparticles only activate in the acidic environment of tumours. Additionally, ongoing research focuses on improving the specificity of these nanoparticles to further reduce any potential harm to healthy tissues [50].

6.2. Mechanisms of nanoparticles targeting cancer cells

Nanotechnology is being used in various applications, including targeted delivery systems, cancer imaging, and diagnostic tools [35]. These systems use ligands or antibodies to bind to overexpressed receptors in cancer cells, allowing nanoparticles to accumulate in tumour tissue and avoid healthy cells (Fig. 3). Additionally, pH-responsive nanoparticles can sense the acidic environment of tumours and release their cargo only in specific locations, improving the effectiveness and safety of cancer treatments [38]. Nanotechnology-based diagnostic tools, such as biosensors and lab-on-a-chip devices, are being developed to detect cancer

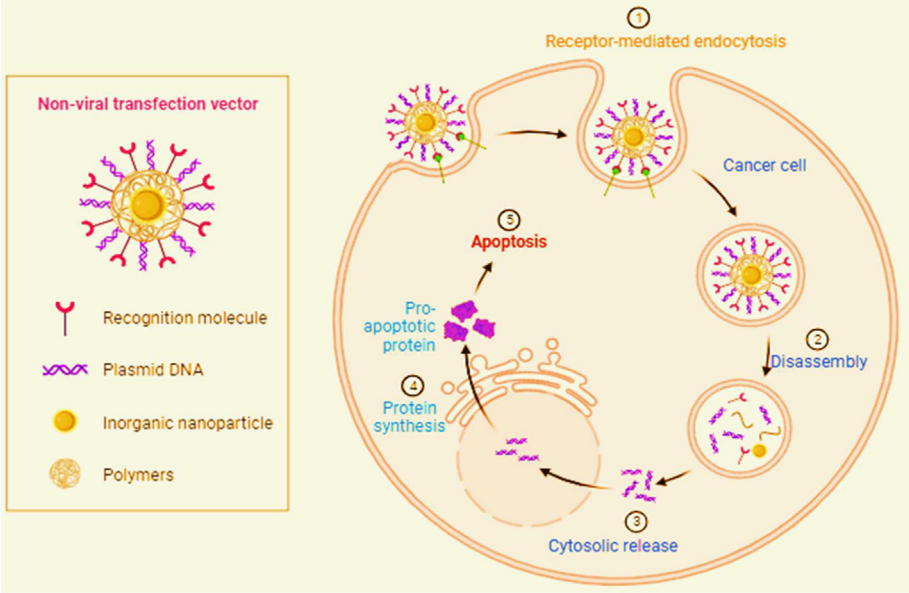

Fig. 5. Nano system in death induced gene therapy for cancer.

biomarkers in body fluids, allowing for early detection and personalised treatment strategies. These advancements have the potential to revolutionise cancer diagnosis and treatment, with nanosensors detecting tiny traces of a specific cancer biomarker in a patient's blood, increasing the chances of successful treatment and improving patient outcomes [44]. Drug delivery systems are also being developed to target cancer cells specifically, minimising side effects and maximising chemotherapy drug effectiveness (Fig. 4). However, not all cancer biomarkers are specific to a specific type of cancer, leading to potential false positives or misdiagnosis [49]. Furthermore, the use of nanotechnology in drug delivery systems may introduce new risks and complications, such as toxicity and immune response that need to be thoroughly investigated before widespread implementation.

7. Targeted nanoparticle drug delivery

Nanoparticle systems coated with pH-sensitive polymers can address challenges in cancer treatment by delivering drugs directly to the tumour site, increasing drug efficacy, and reducing side effects on healthy tissues [82]. Advanced nanoparticle systems with improved sensitivity to pH changes can ensure precise and controlled drug release, overcoming the limitations of current pH-sensitive polymers. One promising approach is the use of nanogels, three-dimensional networks of crosslinked polymers that can encapsulate drugs and respond to changes in pH. These nanogels can be designed to release drugs in a pH-dependent manner, allowing for targeted drug delivery to the tumour site [83]. Researchers are also exploring stimulus-responsive nanoparticles that can respond to other

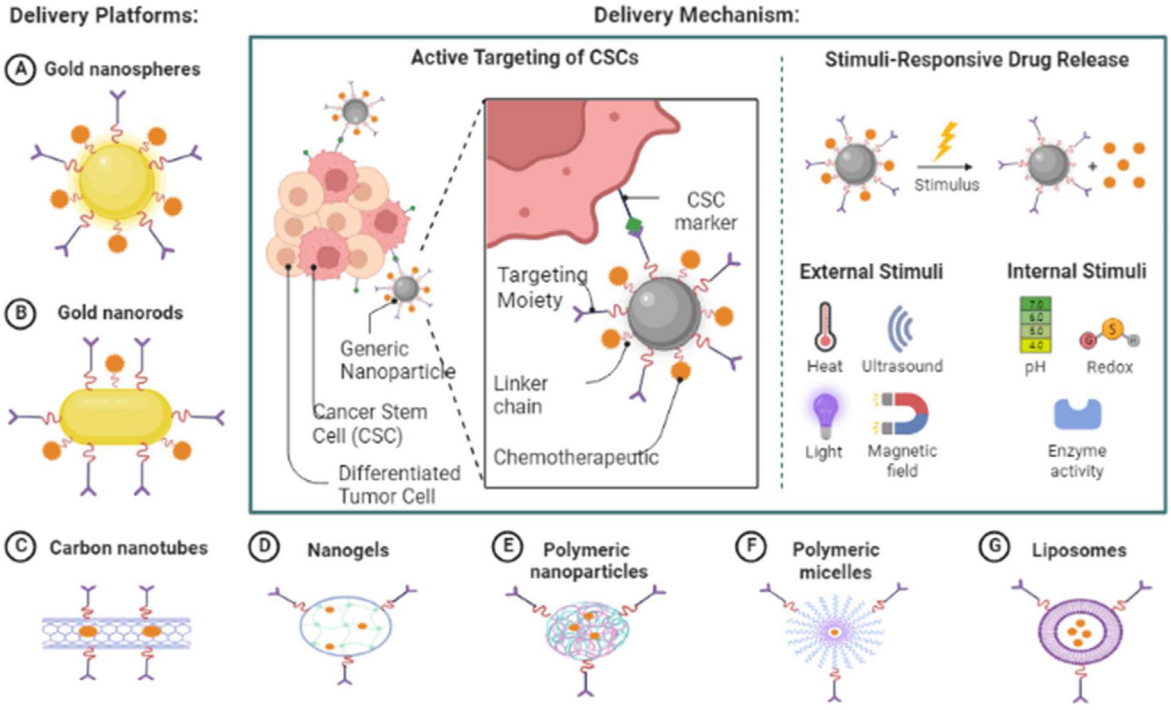

Fig. 6. Nanoparticle-mediated targeted drug delivery to cancer cells.

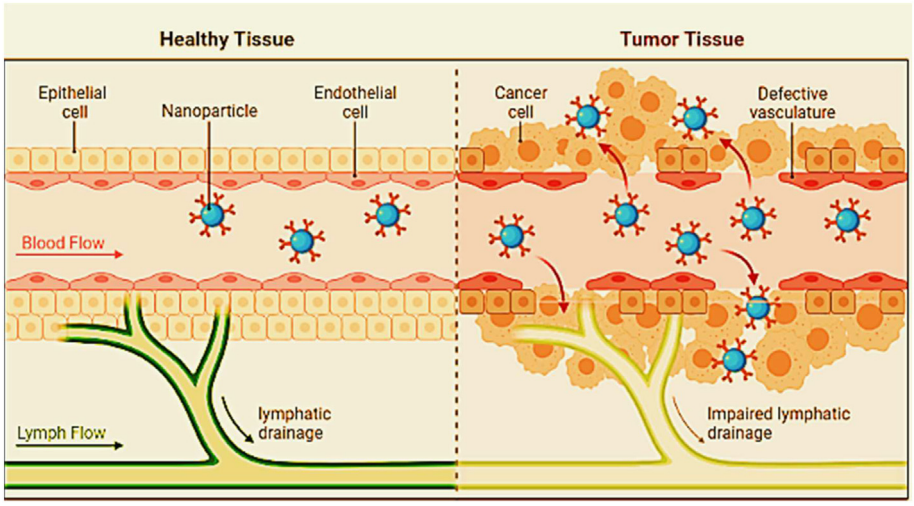

Fig. 7. Passive Targeting of Nanoparticles to cancer cells.

factors, such as temperature or enzymatic activity, to enhance drug release specificity. These advancements hold great potential for revolutionising cancer treatment and improving patient outcomes. pH-responsive nanogels can be loaded with chemotherapy drugs and injected into the bloodstream, targeting cancer cells while minimising damage to healthy tissues. This targeted drug delivery system increases treatment effectiveness and reduces side effects associated with chemotherapy [84]. However, there is a risk of drug resistance in cancer cells, which can develop mechanisms to resist the effects of nanogels. Combination therapy, where multiple drugs are administered simultaneously to combat drug resistance, has shown promising results in overcoming resistance and improving chemotherapy efficacy. Researchers are also exploring alternative strategies like immunotherapy and gene therapy to address drug resistance and enhance targeted drug delivery systems [85]. These alternative strategies aim to harness the power of the immune system or modify the genetic makeup of cancer cells to make them more susceptible to treatment. Additionally, nanotechnology continues to advance, with ongoing research focused on developing more efficient and targeted drug delivery systems that can bypass drug resistance mechanisms and improve treatment outcomes [86].

7.1. Methods used for targeted drug delivery

Nanoparticles, liposomes, and antibody-drug conjugates (ADCs) are innovative drug delivery systems being explored in cancer research to improve drug delivery specificity and efficacy. Nanoparticles can release drugs at the tumour site, minimising side effects on healthy tissues [87]. Liposomes encapsulate drugs and deliver them directly to cancer cells, while ADCs are monoclonal antibodies conjugated with chemotherapeutic agents. These methods aim to enhance treatment outcomes and overcome drug resistance [88]. Gene therapy, where genetic material is delivered to cancer cells to alter their behaviour and make them more susceptible to treatment, holds great potential for revolutionising cancer treatment and improving patient outcomes. Researchers have developed nanoparticles loaded with chemotherapy drugs and coated with antibodies specific to cancer cells that can circulate in the bloodstream, selectively targeting cancer cells while sparing healthy ones [89]. Gene therapy has shown promise in modifying cancer cells to produce proteins that make them more vulnerable to radiation or chemotherapy (Fig. 5), increasing sensitivity, and improving patient response rates [90]. However, not all cancer cells express the same surface markers targeted by the nanoparticles, which may lead to undetected and untreated cancer cells. Gene therapy may have unintended consequences, such as off-target effects or the development of resistance mechanisms in cancer cells, ultimately reducing its effectiveness in treating the disease. Furthermore, the use of nanoparticles in cancer treatment may also pose challenges in terms of their delivery to specific tumour sites (Fig. 6). The complex biological barriers within the body can hinder the efficient targeting and accumulation of nanoparticles, limiting their therapeutic potential [91]. Additionally, the long-term effects of gene therapy on normal cells and tissues are still not fully understood, raising concerns about potential side effects that could impact overall patient well-being.

7.2. Passive targeting

Passive targeting is a method for improving targeted drug delivery in cancer treatments (Fig. 7). By utilising nanoparticles or liposomes, drugs can be encapsulated and delivered directly to the tumour site, increasing their concentration and reducing toxicity in healthy tissues [92]. This strategy has shown promise in preclinical and clinical studies, offering a potential solution to overcome drug resistance and improve cancer treatment efficacy. Passive targeting takes advantage of the enhanced permeability and retention effect, which allows nanoparticles or liposomes to accumulate in the tumour due to its leaky blood vessels and impaired lymphatic drainage. This approach not only enhances drug delivery but also enables sustained release of the drug, leading to prolonged therapeutic effects [93]. Additionally, passive targeting can be combined with other treatment modalities, such as chemotherapy or radiation therapy, to further enhance the overall efficacy of cancer treatment. Also, nanoparticles and liposomes can be made to actively target cancer cells by attaching specific targeting molecules, like antibodies or peptides, to the surface of the nanoparticles [94]. These molecules can recognise and bind to overexpressed receptors or markers, allowing for selective drug delivery and minimal damage to healthy tissues. Additionally, nanoparticles coated with antibodies specific to a specific type of cancer cell can selectively bind to cancer cells, delivering targeted chemotherapy drugs directly to the tumour while sparing healthy cells [95]. This targeted drug delivery approach not only enhances the efficacy of chemotherapy but also reduces the side effects commonly associated with conventional chemotherapy. Moreover, the small size of nanoparticles enables them to penetrate deep into tumour tissues, reaching areas that are difficult to access with traditional drug delivery methods. The nanoparticles may not bind exclusively to cancer cells, leading to unintended binding to healthy cells and toxicity [96]. Additionally, relying on specific triggers for drug release may result in inconsistent or delayed release, reducing overall treatment efficacy. Furthermore, the use of nanoparticles in drug delivery has shown promising results in improving the bioavailability and therapeutic efficacy of anticancer drugs. This is due to their ability to enhance drug stability and protect it from degradation in the body [97]. However,

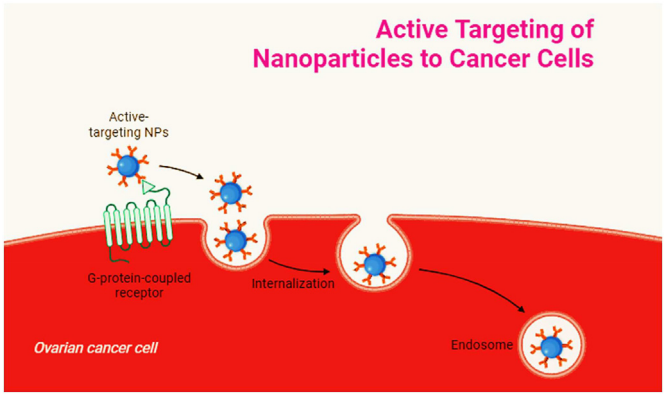

Fig. 8. Active Targeting of Nanoparticles to cancer cells.

careful consideration must be given to the selection of nanoparticles and their surface modifications to minimise off-target effects and maximise targeted drug delivery to cancer cells.

7.3. Active targeting

Active targeting is a promising way to improve targeted drug delivery (Fig. 8). This method involves putting specific ligands or antibodies on the surface of nanoparticles so that they can bind to specific cancer cell receptors. This allows for more precise and efficient drug delivery while minimising exposure to healthy cells [98]. Researchers aim to develop nanoparticle-based therapies that selectively eradicate cancer cells while sparing healthy tissues, revolutionising cancer treatment. These therapies use antibodies to specifically target cancer cells expressing specific surface receptors, allowing therapeutic agents to reach the tumour site [99]. However, this approach may not be effective for cancers that do not express specific surface receptors targeted by the nanoparticles, leading to limited drug delivery and limited efficacy in treating the cancer. Further research is being conducted to optimise this strategy for clinical use. One potential solution being explored is the development of nanoparticles that can target multiple surface receptors simultaneously, increasing the chances of effectively delivering therapeutic agents to cancer cells [100]. Additionally, researchers are also investigating alternative delivery methods such as nanocarriers or gene therapy to enhance drug delivery and improve the overall efficacy of cancer treatments. These advancements in drug delivery systems have the potential to revolutionise cancer treatment by minimising the side effects of chemotherapy and increasing the specificity of targeted therapies [82]. Moreover, the utilisation of nanotechnology in cancer treatment holds promise for personalised medicine, as nanoparticles can be designed to specifically target the unique characteristics of individual tumours. With continued research and development, these innovative approaches may lead to more effective and personalised treatment options for cancer patients in the future [86].

8. Recent developments in nanoparticle-based drug delivery

Nanoparticle-based drug delivery systems have shown promise in overcoming limitations in traditional cancer therapies. Researchers have successfully used nanoparticles to deliver chemotherapy drugs directly to cancer cells, reducing side effects on healthy tissues. These advancements can be designed to target specific molecular markers in cancer cells, increasing treatment effectiveness while minimising harm to healthy cells [77]. These advancements have the potential to significantly improve cancer patient outcomes. By specifically targeting cancer cells, drug delivery systems can enhance the efficacy of treatment and potentially reduce the risk of tumour recurrence [89]. Additionally, the ability to minimise harm to healthy cells can improve patients' quality of life during and after treatment. In addition to nanoparticle-based drug delivery, immunotherapies are another promising area of research [73]. These therapies harness the immune system's ability to recognise and destroy cancer cells, potentially treating existing tumours and preventing future cancer recurrence. Immune checkpoint inhibitors, which block proteins that prevent immune cells from attacking cancer cells, allow the immune system to recognise and destroy cancer cells more effectively [86]. Some patients with advanced melanoma have shown remarkable responses, with their tumours shrinking or disappearing completely. These promising results have led to the approval of immune checkpoint inhibitors for the treatment of various types of cancer, including lung, bladder, and kidney cancer [82]. However, it is important to note that not all patients respond equally well to these therapies, and further research is needed to understand why some individuals benefit more than others [93]. However, not all patients experience positive outcomes with immune checkpoint inhibitors. In some cases, the treatment fails to elicit a significant response from the immune system, resulting in minimal or no tumour regression. This highlights the need for further research and a better understanding of factors influencing the effectiveness of immunotherapies in different individuals [96]. It is important to consider that immune checkpoint inhibitors can also lead to immune-related adverse events in some patients. These adverse events can range from mild to severe and may require additional medical intervention. Therefore, it is crucial for healthcare professionals to closely monitor patients undergoing immunotherapy and develop strategies to manage any potential side effects [101].

9. Cancer nanodrug delivery challenges

Immunotherapies, which use the immune system to target and destroy cancer cells, have revolutionised cancer treatment. However, there is still a need to understand how these therapies may affect a woman's risk of developing breast cancer [102]. Researchers aim to optimise treatment strategies and ensure patient safety by studying the long-term effects of immunotherapies and their impact on breast cancer risk factors. One concern is whether immunotherapies could potentially increase the risk of developing breast cancer in women. Understanding the impact of immunotherapies on breast cancer risk factors can help healthcare professionals make informed decisions about treatment options and provide personalised care. Additionally, identifying potential associations between immunotherapy and breast cancer risk can help develop strategies to mitigate risks and improve patient outcomes [103]. A detailed study could involve evaluating the long-term effects of a specific immunotherapy drug on breast cancer risk factors in a sample of breast cancer patients. The study would track patients' progress over several years, monitor changes in their risk factors, and compare them to a control group that did not receive the immunotherapy [104]. A detailed counterexample could be a subset of patients who received the immunotherapy drug but showed a decrease in risk factors instead of an increase. This could be due to lifestyle changes, genetic variations, or an individual's response to the drug. Researchers should consider these confounding variables before drawing definitive conclusions about the drug's effects on breast cancer risk factors. It is important for researchers to conduct further studies to investigate the underlying factors contributing to the decrease in risk factors among certain patients who received immunotherapy [105]. By examining potential lifestyle changes, genetic variations, and individual responses to the drug, a more comprehensive understanding of the drug's effects on breast cancer risk factors can be obtained. This will enable researchers to draw more accurate conclusions and recommendations regarding the use of immunotherapy in breast cancer treatment [106].

Cancer nanodrug delivery faces significant challenges due to the immune system's ability to eliminate nanoparticles or build them up in unintended tissues, reducing their effectiveness. The dense extracellular matrix and abnormal blood vessels in a tumour's microenvironment make it difficult for nanodrugs to reach and spread through the tumour [107].

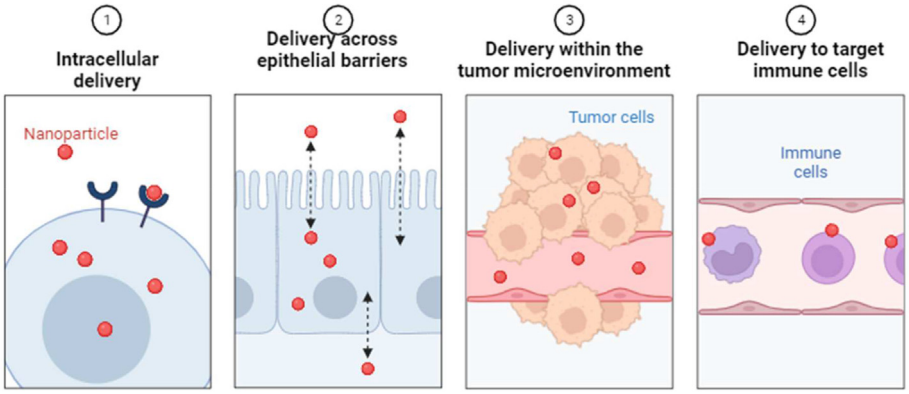

Fig. 9. Targeted drug delivery of Nanoparticles.

To overcome these obstacles, targeted drug delivery systems are developed by incorporating targeting ligands onto nanoparticle surfaces that specifically recognise and bind to tumour cell receptors (Fig. 9). This approach enhances therapeutic efficacy while minimising off-target effects. Various targeting ligands, such as antibodies, peptides, and aptamers, have been explored for this purpose [108]. Antibody-targeted drug delivery involves monoclonal antibodies engineered to bind to antigens on tumour cells and conjugated to nanoparticles loaded with chemotherapeutic drugs. This approach maximises the drug's impact on cancer cells, reduces damage to healthy tissues, improves patient outcomes, and minimises side effects [109–115]. However, this approach is counterproductive in cases where tumours exhibit heterogeneity, with different cells expressing varying levels of the targeted antigen. Additionally, tumour microenvironments that make it difficult for antibodies to enter or nanoparticles to reach the tumour can make targeted drug delivery systems less effective.

10. Conclusion

Targeted drug delivery systems have shown promise in enhancing cancer treatment, but tumour heterogeneity and microenvironmental difficulties limit their efficacy. Further research and development are needed to optimise targeted therapy delivery. Nanotechnology offers a promising strategy for the precise targeting of cancer cells while minimising damage to healthy tissues. Nanoparticles can carry therapeutic agents directly to the tumour site, bypassing barriers posed by the tumour microenvironment. Modifications to nanoparticle surfaces can enhance stability, circulation time, and cellular uptake, further improving their efficacy. The use of nanoparticles in targeted therapy can also overcome challenges such as drug resistance and limited drug penetration into solid tumours. These nanoparticles can be engineered to release the therapeutic agents in a controlled manner, ensuring sustained and effective treatment. Furthermore, ongoing advancements in nanotechnology hold the potential to revolutionise cancer treatment by enabling personalised medicine approaches tailored to individual patients' needs.

Declaration of competing interest

The authors have no conflict of interest to declare.

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