



Polymer-based nanoparticles in targeted cancer therapy: a review

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ABSTRACT

Tumors are the result of unchecked cell proliferation in the body, which leads to the complicated and widespread illness known as cancer. The formidable issue of providing effective cancer treatment has prompted scientists to investigate novel strategies. Using nanoparticles based on polymers tiny particles made of substances that are harmless for the body is one approach that shows promise. Strong anticancer medications are delivered to cancer cells directly via these nanoparticles, which also increase therapy effectiveness and reduce adverse effects on healthy cells. This study explores the field of targeted cancer treatment using polymer-based nanoparticles, using information from reliable sources such as PubMed, Web of Science, and Scopus. A strict and methodical procedure was followed in the selection of published articles to guarantee the inclusion of relevant and excellent research papers. Numerous production techniques, including self-assembly, emulsion/solvent evaporation, and nanoprecipitation, provide fine control over the size, shape, and properties of nanoparticles. Methods based on ligands, pH response, and stimuli response are used to promote enhanced selectivity and accumulation inside malignancies. Diverse advantages are provided by polymer-based nanoparticles for targeted cancer therapy. Their promise in targeted cancer therapy is highlighted by this comprehensive review, which also provides insights into design concepts, manufacturing techniques, and targeting strategies that open the door to individualized and successful therapies. The benefits of polymer-based nanoparticles are emphasized, including their strong drug-loading ability, prolonged half-life, and active targeting of cancer cells with the least amount of damage to healthy tissues. In order to maximize the usage of polymer-based nanoparticles in customized cancer therapies and eventually improve patient outcomes in the area of oncology, further investigation and clinical trials are necessary.

INTRODUCTION

Targeted cancer therapy has emerged as a promising approach to revolutionize the field of oncology. It aims to maximize treatment efficacy while minimizing adverse effects commonly associated with conventional cancer therapies [1]. The conventional methods which are included in chemotherapy

and radiation therapy, often lack specificity and tend to damage healthy cells along with cancerous ones leading to severe side effects. In contrast, targeted therapy aims to selectively deliver therapeutic agents to cancer cells, leaving healthy cells unharmed [2]. In their pursuit of efficient targeted drug delivery, scientists have thoroughly investigated a variety of nanocarriers, including liposomes, micelles, dendrimers, and inorganic nanoparticles. Due to their distinctive qualities and adaptability, polymer-based nanoparticles have attracted a lot of attention in this industry. Polymers such as poly [lactic-co-glycolic acid] (PLGA), polyethylene glycol (PEG), and poly [lactic acid] make up the majority of these nanoparticles [3]. It is included in biocompatible and biodegradable. These polymers have proven to be highly suitable for targeted cancer

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therapy, offering numerous advantages. One notable advantage lies in the tunable physicochemical properties of polymer-based nanoparticles. By modifying the composition, molecular weight, and structure of the polymers, researchers can precisely control the size, surface charge, and drug release kinetics of the nanoparticles [4]. This tunability allows for customization to match the specific requirements of different cancer types and therapeutic agents. Another critical aspect is the high drug-loading capacity offered by polymer-based nanoparticles. These nanoparticles have a huge surface region-to-volume proportion and enable efficient encapsulation of a diverse array of therapeutic agents. It includes small molecules, proteins, nucleic acids, and even combination therapies. The high drug-loading capacity ensures optimal delivery of therapeutic payloads, maximizing the concentration of drugs at the tumor site while minimizing systemic exposure and off-target effects.

Polymer-based nanoparticles also offer the advantage of extended circulation time within the bloodstream. A defensive layer known as the “stealth effect” is framed by changing the nanoparticle surface with hydrophilic polymers like PEG. This protective layer reduces the identification and removal of nanoparticles by the immune system, resulting in prolonged circulation and enhanced accumulation within the tumor site. Furthermore, polymer-based nanoparticles possess the capability for active targeting. Their surface can be easily tailored by attaching ligands or targeting components that specifically recognize and bind to cancer cell receptors or markers. This active targeting approach significantly improves the selectivity and accumulation of nanoparticles within the tumor, facilitating enhanced drug delivery to cancer cells while minimizing harm to healthy tissues (Fig. 1), thus Nanotechnology improves cancer detection and diagnosis [5].

This review article aims to delve into the wide-ranging application of polymer-based nanoparticles in targeted cancer therapy. It provides a comprehensive overview of the design principles underlying these nanoparticles, including their composition, size, and surface modification strategies [6]. Furthermore, it discusses various fabrication methods

employed for the synthesis of polymer-based nanoparticles which are included in nanoprecipitation, emulsion/solvent evaporation, and self-assembly techniques. The review also explores the targeting strategies employed with polymer-based nanoparticles, including ligand-based targeting, pH-responsive targeting, and stimuli-responsive targeting. It discusses the new advances in preclinical and clinical examinations that have showcased the potential of polymer-based nanoparticles in improving cancer treatment outcomes.

MECHANISMS OF TARGETED CANCER THERAPY

Targeting tumor heterogeneity

Cancer is a very varied disease because different groups of cells within the tumor exhibit different genetic profiles and behavior behaviors. Combination drugs have recently been created in targeted cancer therapy to address this tumor heterogeneity, to simultaneously target numerous genetic disorders. Researchers are also investigating strategies to target cancer stem cells, a subgroup of tumor cells that cause tumor growth and medication resistance, to produce more significant and durable therapeutic responses [7].

Chimeric antigen receptor T (CAR-T) cells and adoption-based cell therapy

Adoptive cell therapies, in particular CAR-T therapy, have grown into ground-breaking strategies in the treatment of specific cancers. CAR-T cells are designed to detect and target cancer cells that express particular surface antigens [8]. The library of targetable antigens is growing thanks to recent developments in this sector, which additionally improve CAR-T cell durability and persistence and minimize side effects.

Targeting non-coding RNAs

Non-coding long RNAs, in particular microRNAs, are key players in the emergence and spread of cancer. Modern research is identifying many non-coding RNAs as potential therapeutic targets. It is being researched how to target and alter the activity of these non-coding RNAs to stop the growth and spread of malignant cells [9]. These methods include treatments based on RNA interference and antisense oligonucleotides.

Radiolabeled therapeutics

In radiolabeled therapeutics, targeted agents such as antibodies or small compounds are joined with radioactive isotopes. These radiotherapies target and localize the killing of tumor cells by delivering radiation directly to cancer cells that express the target antigen. Modern research in radiolabeled therapeutics is expanding the repertoire of targetable antigens, and radioisotope payloads are being tailored for better therapeutic outcomes [10].

Cancer microenvironment modulation

A patient’s capacity to answer therapy is fundamentally impacted by the cancer microenvironment. Modern research aims to alter the cancer microenvironment to increase the effectiveness of targeted drugs. Among the methods utilized to boost drug absorption and immune cell infiltration are targeting

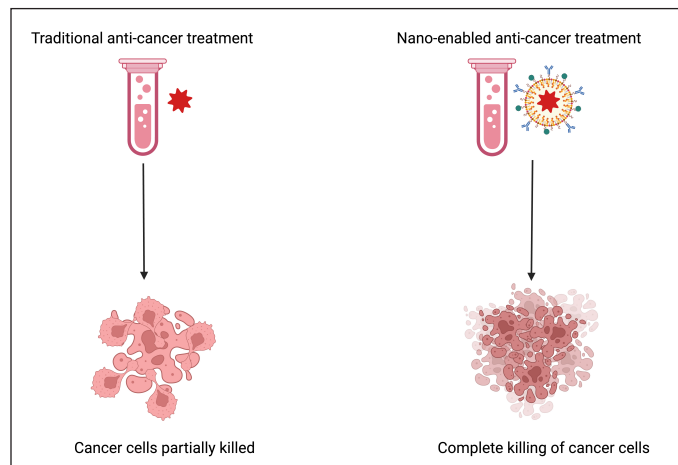


Figure 1. Nanotechnology improves cancer detection and diagnosis.

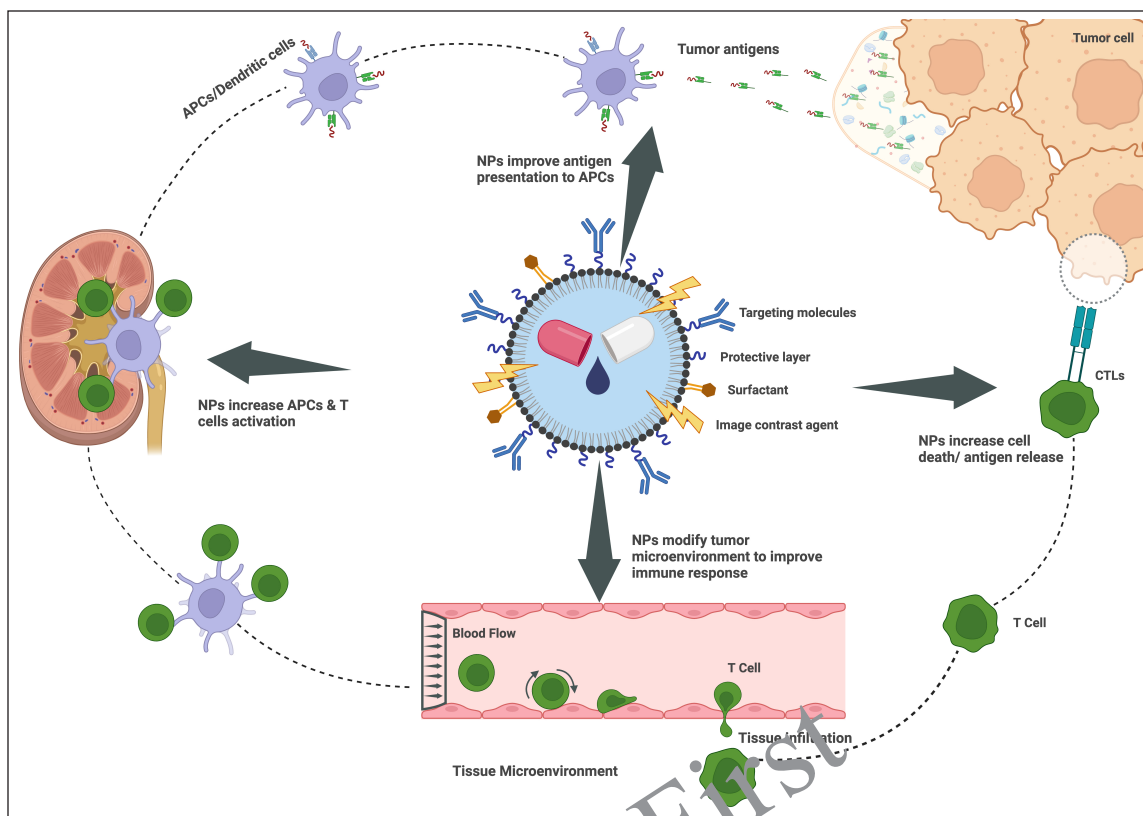


Figure 2. Schematic diagram of polymer-based nanoparticles in targeted cancer therapy working method.

immunosuppressive cells, such as regulatory T-cells and myeloid-derived suppressor cells, as well as reprogramming the cancer stroma [10].

Synthetic lethality and vulnerability screens

Advances in high-throughput screening technologies have made it simpler to identify synthetic lethal interactions in cancer cells. Synthetic lethality is the process of killing cancer cells by simultaneously shutting down two genes, neither of which is required in and of itself to induce cancer (Fig. 2). It could be able to eliminate cancer cells without harming healthy cells by concentrating on synthetic deadly interactions.

CURRENT STRATEGIES IN TARGETED CANCER THERAPY

Small molecule inhibitors

Small molecules are designed to inhibit specific proteins involved in cancer growth and survival [11]. Examples: Imatinib targeting breakpoint cluster region-abelson in chronic myeloid leukemia, vemurafenib targeting mutant v-Raf murine sarcoma viral oncogene homolog B (BRAF) in melanoma.

Monoclonal antibodies

Monoclonal antibodies recognize specific cancer cell surface proteins and interfere with their function or trigger

immune-mediated destruction. Examples: Trastuzumab targeting HER2 in breast cancer, rituximab targeting CD20 in B-cell lymphomas.

Immune checkpoint inhibitors

These drugs target molecules that suppress the immune response, allowing the immune system to recognize and attack cancer cells more effectively. Examples: Pembrolizumab targeting PD-1 in various cancers, nivolumab targeting PD-1 in melanoma and lung cancer.

RNA THERAPIES

Spherical nucleic acids (SNAs)

Nanostructures with a spherical arrangement of nucleic acids are called SNAs. Small interfering RNA (siRNA) and other RNA medicines may be delivered to cancer cells using these structures. Treatments for brain cancer based on RNA have the potential to be more effective using this method [12].

siRNA using polybetformin nanoparticles

The potential of polybetformin nanoparticles as vehicles for the delivery of siRNA has been investigated. Treatment accuracy and efficacy may be improved by using these nanoparticles to shield therapeutic RNA from degradation and enhance its targeted delivery to cancer cells.

NANOPARTICLE-BASED DRUG DELIVERY SYSTEMS

Liposomal delivery systems

Encapsulating medications or nucleic acids in lipid nanoparticles called liposomes improves their delivery to cancer cells and protects them from destruction. Several therapeutic medicines have been explored for delivery to brain tumors using this method.

Polymeric nanoparticles

It is possible to immobilize therapeutic payloads, such as RNA treatments, in nanoparticles manufactured from biocompatible polymers. Neurocognitive disorders are notoriously difficult to treat, but these nanoparticles can be made to cross the blood-brain barrier.

PERSONALIZED MEDICINE

Genomic profiling

Recent developments in genetic profiling have made it possible to tailor cancer treatments to individual patients. Customized medicines may be developed to target the distinct features of a patient's tumor by identifying certain genetic abnormalities or changes in their cancer cells [13].

TARGETING CANCER STEM CELLS

Stem cell-targeted therapies

Because of their significance in tumor development, progression, and recurrence, cancer stem cells are the focus of current research efforts to find new treatments. Preventing cancer recurrence and improving long-term results are the goals of targeting these cells.

COMBINATION THERAPIES

Combinatorial approaches

Combination treatments aim to tackle the cancer cells' adaptability and heterogeneity by combining several targeted

drugs or modalities. The goals of this strategy are to increase reactivity to therapy and decrease resistance.

PREPARATION OF POLYMERIC NANOPARTICLE

Polymeric nanoparticle synthesis

Nanoparticle synthesis methods are essential in the development of polymer-based nanoparticles for targeted cancer therapy [14]. These methods enable scientists to create tiny particles. These particles can carry therapeutic drugs to specific sites in the body, such as tumor tissues. There are several techniques commonly used for nanoparticle synthesis.

Emulsion/solvent evaporation

Imagine mixing oil and water in a bowl. In this method, the polymer is dissolved in an organic solvent, such as oil. Then, it is emulsified in an aqueous solution, like water. The emulsion is made by vivaciously blending the two fluids. Afterward, the organic solvent is removed, leaving behind nanoparticles that contain the polymer and any therapeutic drugs [15].

Nanoprecipitation

Picture pouring a colored liquid into clear water. Nanoprecipitation involves mixing a polymer solution with a nonsolvent, which causes the formation of nanoparticles [15]. This happens because the polymer can no longer dissolve in the mixture and forms tiny particles instead. The resulting nanoparticles can encapsulate the therapeutic drugs within their structure [16].

Self-assembly

Think of building blocks fitting together to form a structure. Self-assembly is a method that takes advantage of the natural properties of the polymer to form nanoparticles. The polymer molecules arrange themselves into organized structures, such as micelles [like tiny spheres] or aggregates, which can encapsulate the therapeutic drugs [17].

These synthetic methods allow scientists to control the size, shape, and properties of the nanoparticle [18]. These are important factors for efficient drug delivery. By using these techniques, researchers can create polymer-based nanoparticles that can transport therapeutic drugs to targeted cancer cells, enhancing the effectiveness of cancer treatment.

Encapsulating therapeutic agents

Encapsulating therapeutic agents is a crucial method in using polymer-based nanoparticles for targeted cancer therapy Schematic representations of the therapeutic nanoparticles [19,20]. It involves incorporation of the drugs into the nanoparticles to enable controlled release and targeted delivery to cancer cells. There are different techniques used for encapsulation, including attaching the drugs chemically to the nanoparticles (covalent conjugation) (Fig. 3), trapping them physically within the nanoparticle structure [physical entrapment], or using electrostatic interactions to attract charged drugs to the nanoparticle surface [21].

Covalent conjugation connects the drugs to the nanoparticles through chemical bonds, ensuring a strong and

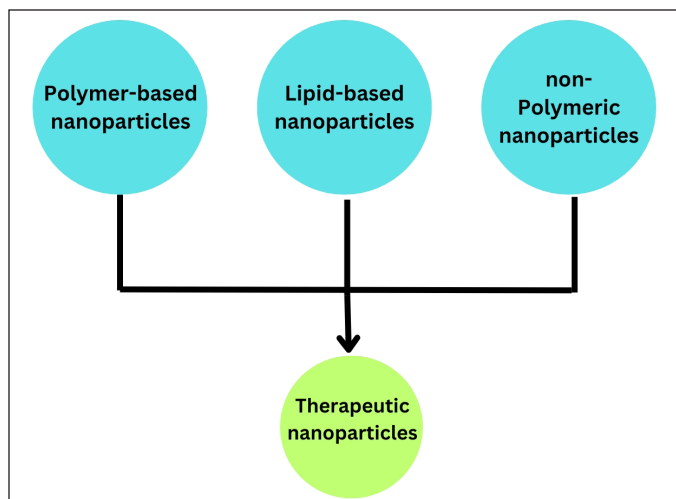


Figure 3. Representation of the therapeutic nanoparticles.

long-lasting attachment. Physical entrapment involves capturing the drugs within the nanoparticles using physical interactions like sticking them together or trapping them in small spaces. Electrostatic interactions occur when the drugs have an electric charge and are drawn to the opposite charge on the nanoparticle surface. Encapsulating the drugs within the nanoparticles brings several benefits for targeted cancer therapy [22]. It shields the drugs from degradation, improves their solubility, and enables precise delivery to the tumor site. By encapsulating the drugs, they can avoid getting eliminated by the body's natural defense systems and accumulate more effectively at the tumor, while minimizing harm to healthy tissues [23]. Overall, encapsulating therapeutic agents within polymer-based nanoparticles offers a promising approach for targeted cancer therapy. It provides a versatile platform to develop personalized treatments that deliver drugs directly to cancer cells, improving the effectiveness and reducing side effects for cancer patients [24].

SURFACE MODIFICATION TECHNIQUES

Surface modification techniques play a vital role in the application of polymer-based nanoparticles for targeted cancer therapy. These techniques involve modifying the outer surface of nanoparticles to enhance their ability to target cancer cells, improve stability, and optimize drug delivery [24]. Two commonly used surface modification strategies are ligand conjugation and stealth coating.

Ligand conjugation is a method where specific molecules like antibodies or peptides are attached to the nanoparticle surface (Fig. 4). These molecules can recognize and bind to specific markers present on the surface of cancer cells [25]. By attaching these molecules, the nanoparticles can actively target and accumulate at the tumor site. This targeted approach improves the precision of drug delivery to cancer cells, making the therapy more effective while minimizing harm to healthy tissues [26].

Stealth coating, also called PEGylation, is a method where a layer of a polymer called PEG [27] is applied to the surface of nanoparticles. PEG is a safe polymer that attracts water and creates a protective shield around the nanoparticles. This shield helps the nanoparticles to avoid detection and removal by the immune system, allowing them to stay in the

bloodstream for a longer time. By escaping the immune system, the nanoparticles can gather at the tumor site by utilizing a process called the enhanced permeability and retention (EPR) effect. This effect takes advantage of the special characteristics of blood vessels in tumors, enabling the nanoparticles to specifically accumulate within the tumor tissues [28].

Surface modification techniques offer several benefits in targeted cancer therapy. They enhance the targeting ability of nanoparticles, ensuring they reach cancer cells more effectively while minimizing damage to healthy cells [29]. Moreover, surface modifications improve the stability of nanoparticles and their circulation in the body, enabling sustained release of drugs and better accumulation at the tumor site [30]. These modifications also provide opportunities for personalized medicine by tailoring the nanoparticles to specific types of cancer or individual patient requirements [31]. In conclusion, surface modification techniques, such as ligand conjugation and stealth coating, are crucial for optimizing the performance of polymer-based nanoparticles in targeted cancer therapy. These modifications improve targeting efficiency, enhance stability, and enable controlled drug delivery, promising more effective and personalized treatments for cancer [32].

CONTROLLED DRUG RELEASE

Controlled drug release is an important method used in the application of polymer-based nanoparticles for targeted cancer therapy. It involves creating nanoparticles that can release therapeutic drugs in a controlled and gradual manner at the tumor site (Fig. 5). This controlled release helps to ensure

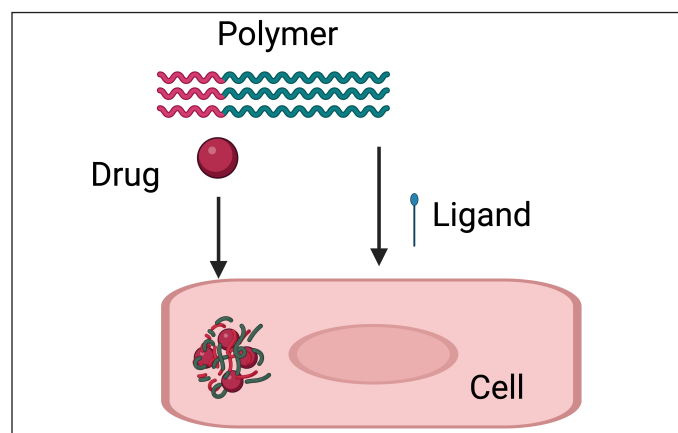


Figure 4. Ligand conjugation.

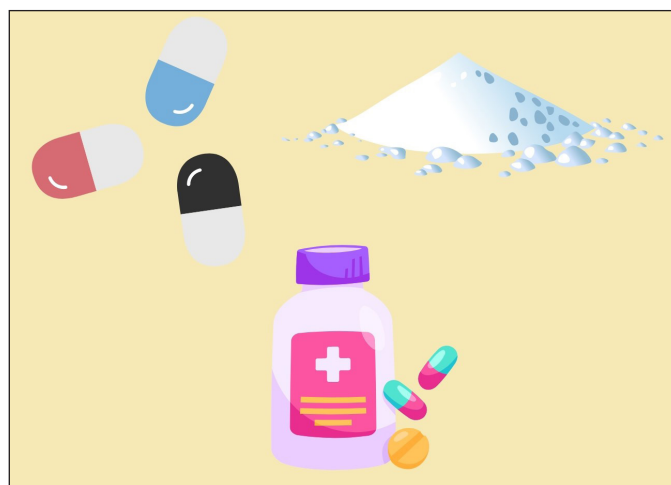


Figure 5. Forms of drugs.

Table 1. Natural and synthetic polymer.

Natural polymer	Synthetic polymer	Co-natural polymer
Chitosan	PLGA	Chitosan-Gelatin
Alginate	PEG	Alginate-hyaluronic acid
Gelatin	Poly[ε-caprolactone] (PCL)	Gelatin-dextran
Hyaluronic acid	Polyvinyl alcohol (PVA)	Hyaluronic acid-chitosan
Dextran	Polycaprolactone (PCL)	Dextran-alginate

Table 2. Advantages and disadvantages of natural and synthetic polymers [36].

Natural polymer [advantages and disadvantages]	Synthetic polymer [advantages and disadvantages]
Advantage: Natural polymers are generally biocompatible and less likely to cause immune reactions or toxicity in the body.	Advantages: Synthetic polymers can be precisely engineered to achieve specific properties, allowing better control over nanoparticle characteristics.
Disadvantage: Natural polymers may have limited control over their properties, leading to variations in nanoparticle characteristics.	Disadvantages: Some synthetic polymers may raise biocompatibility issues, requiring additional modifications or coatings to improve safety.
Advantage: Many natural polymers can be easily broken down by the body, reducing the risk of long-term accumulation.	Advantages: Synthetic polymers often exhibit enhanced stability, ensuring a longer shelf life and consistent performance.
Disadvantage: The properties of natural polymers can vary between batches, affecting reproducibility.	Disadvantages: Certain synthetic polymers may be non-biodegradable, leading to potential long-term accumulation in the body.
Advantage: Natural polymers can be sourced from renewable resources, making them environmentally friendly.	Advantages: The release of drugs or therapeutic agents from synthetic polymer nanoparticles can be finely tuned for sustained and controlled delivery.
Disadvantage: Natural polymers might be susceptible to degradation or instability under certain conditions.	Disadvantages: The production of some synthetic polymers can be costly, impacting the overall cost of nanoparticle preparation.

Table 3. Techniques and types of polymeric nanoparticles.

Techniques	Type of polymeric nanoparticles
Emulsion polymerization	Polymeric micelles
Solvent evaporation/extraction	Nanospheres
Nanoprecipitation	Nano capsules
Self-assembly techniques [e.g., Micelles, Nanogels]	Dendrimers
Electrospinning [for nanofiber-based nanoparticles]	Nanogels

that the drugs are delivered effectively to the cancer cells maximizing their effectiveness while minimizing side effects [33].

There are different ways to achieve controlled drug release from polymer-based nanoparticles. One way is to use special polymers that respond to specific conditions found in tumors, such as changes in pH or temperature. When exposed to these conditions, the polymers change shape and release the drug. Another approach is to use biodegradable polymers that break down over time, slowly releasing the drug [34]. The rate of degradation can be adjusted to control the release of the drug. Nanoparticles with tiny pores or a porous structure can also be used for controlled drug release. These pores are designed to allow the drug to pass through based on its size. By controlling the size of the pores, the release of the drug can be managed. Additionally, external stimuli like light, heat, or magnetic fields can be used to trigger drug release from the nanoparticles. Controlled drug release has many benefits. It allows for precise control over when and how much drug is released, ensuring the best treatment outcomes [31]. It also reduces the exposure of healthy tissues to the drug, minimizing side effects. This method also enables the use of potent drugs that may have limited solubility or stability, as the nanoparticles provide a protective environment for the drug. In conclusion, controlled drug release is a key method in the use of polymer-based nanoparticles for targeted cancer therapy. It involves designing nanoparticles that release drugs in a controlled manner, improving treatment effectiveness and minimizing side effects [35]. This approach offers greater precision, prolonged drug action, and improved outcomes in cancer treatment.

The natural and synthetic polymers are mentioned in Table 1.

The advantages and disadvantages of natural and synthetic polymers are mentioned in Table 2.

The techniques and types of polymeric nanoparticles in Table 3.

POLYMER-BASED NANOPARTICLES IN THE TREATMENT OF CANCER

Polymeric-based nanoparticles stand out in the field of malignant growth treatment because of their extraordinary properties and expected applications. These nanoparticles are regularly made out of biocompatible and biodegradable polymers that can exemplify or form with remedial specialists, taking into consideration focused on and controlled conveyance to malignant growth cells. This is an outline of the way polymeric-based nanoparticles are utilized in the therapy of disease [36].

Drug delivery

Polymeric nanoparticles can embody different sorts of helpful specialists, for example, chemotherapy drugs, little particles, and, surprisingly, natural specialists like siRNA or miRNA. The nanoparticles shield these specialists from debasement in the circulatory system and work with their aggregation in cancer tissues. This designated drug diminishes fundamental poisonousness and upgrades the adequacy of the treatment by concentrating the helpful payload at the cancer site [37].

Targeted therapy

Functionalization of polymeric nanoparticles with a focus on ligands, like antibodies or peptides, empowers the dynamic focusing of disease cells. These ligands perceive explicit markers overexpressed on the outer layer of malignant growth cells, permitting the nanoparticles to tie to and enter these cells specifically. This approach upgrades the particularity of the treatment and limits harm to solid cells [38].

EPR effect

Polymeric nanoparticles can exploit the EPR impact, which is a trademark element of growth vasculature. Cancers

Table 4. Polymer-based nanoparticles in the treatment of cancer.

Polymer	Drug	Cancer cellline	Invitro and <i>in vivo</i> studies	Reference
PLGA	Docetaxel	Breast cancer cells	<i>In vitro</i> cytotoxicity, <i>In vivo</i> tumor regression	[33]
Chitosan	Doxorubicin	Ovarian cancer cells	Improved drug take-up <i>in vitro</i> , cancer development hindrance <i>in vivo</i>	[41]
PCL	Paclitaxel	Lung cancer cells	Sustained drug discharge release <i>in vitro</i> , <i>in vivo</i> antitumor activity	[6]
PEG	Cisplatin	Colon cancer cells	<i>In vitro</i> cellular take-up, <i>in vivo</i> tumor suppression	[42]
Alginate	Methotrexate	Leukemia cells	Controlled drug discharge <i>in vitro</i> , <i>in vivo</i> therapeutic efficacy	[43]
PLGA	Paclitaxel	Prostate cancer cells	Enhanced cellular take-up <i>in vitro</i> , <i>in vivo</i> tumor growth inhibition	[44]
Chitosan	Methotrexate	Melanoma cells	Controlled drug discharge <i>in vitro</i> , <i>in vivo</i> tumor regression	[45]
PCL	Doxorubicin	Pancreatic cancer cells	<i>In vitro</i> cytotoxicity, <i>in vivo</i> therapeutic efficacy	[46]
PEG	Irinotecan	Gastric cancer cells	Sustained drug discharge <i>in vitro</i> , <i>in vivo</i> antitumor activity	[47]
Alginate	5-Fluorouracil	Esophageal cancer cells	<i>In vitro</i> cellular take-up, <i>in vivo</i> tumor suppression	[48]
PLGA	Gemcitabine	Bladder cancer cells	Enhanced drug take-up <i>in vitro</i> , <i>in vivo</i> tumor growth inhibition	[49]
Chitosan	Etoposide	Hepatocellular carcinoma cells	Controlled drug discharge <i>in vitro</i> , <i>in vivo</i> therapeutic efficacy	[26]
PCL	Bleomycin	Cervical cancer cells	<i>In vitro</i> cytotoxicity, <i>in vivo</i> tumor regression	[50]
PEG	Mitomycin C	Endometrial cancer cells	Sustained drug discharge <i>in vitro</i> , <i>in vivo</i> antitumor activity	[51]
Alginate	Vinblastine	Neuroblastoma cells	<i>In vitro</i> cellular uptake, <i>in vivo</i> tumor suppression	[52]
PLGA	Epirubicin	Thyroid cancer cells	Enhanced cellular take-up <i>in vitro</i> , <i>in vivo</i> tumor growth inhibition	[53]
Chitosan	Camptothecin	Head and neck cancer cells	Controlled drug discharge <i>in vitro</i> , <i>in vivo</i> therapeutic efficacy	[54]
PCL	Fluorouracil	Colorectal cancer cells	<i>In vitro</i> cytotoxicity, <i>in vivo</i> therapeutic efficacy	[55]
PEG	Methotrexate	Leukemia cells	Sustained drug release <i>in vitro</i> , <i>in vivo</i> antitumor activity	[56]
Alginate	Cisplatin	Lung cancer cells	<i>In vitro</i> cellular uptake, <i>in vivo</i> tumor suppression	[57]
PLGA	Doxorubicin	Ovarian cancer cells	Enhanced drug uptake <i>in vitro</i> , <i>in vivo</i> tumor growth inhibition	[58]
Chitosan	Paclitaxel	Breast cancer cells	Controlled drug discharge <i>in vitro</i> , <i>in vivo</i> therapeutic efficacy	[59]
PCL	Gemcitabine	Pancreatic cancer cells	<i>In vitro</i> cytotoxicity, <i>in vivo</i> tumor regression	[60]
PEG	Irinotecan	Gastric cancer cells	Sustained drug discharge <i>in vitro</i> , <i>in vivo</i> antitumor activity	[61]
Alginate	Etoposide	Bladder cancer cells	<i>In vitro</i> cellular take-up, <i>in vivo</i> tumor suppression	[62]
PLGA	Bleomycin	Hepatocellular carcinoma cells	Enhanced cellular take-up <i>in vitro</i> , <i>in vivo</i> tumor growth inhibition	[63]
Chitosan	Mitomycin C	Cervical cancer cells	Controlled drug release <i>in vitro</i> , <i>in vivo</i> therapeutic efficacy	[64]
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PLGA	Gemcitabine	Pancreatic cancer cells	Enhanced cellular uptake <i>in vitro</i> , <i>in vivo</i> tumor growth inhibition	[71]

will generally have flawed veins and debilitated lymphatic waste, prompting the collection of nanoparticles inside the growth tissue. This detached focus on the procedure considers special amassing of nanoparticles in the growth, further working on the restorative result [39].

Combination therapy

Polymeric nanoparticles can convey various remedial specialists, empowering mix treatment draws near. This is particularly valuable for conquering drug opposition or focusing

on various pathways associated with disease movement at the same time [40].

Here is the table of polymer-based nanoparticles in the treatment of cancer in Table 4.

CHALLENGES AND FUTURE DIRECTIONS

Polymer-based nanoparticles have emerged as promising drug delivery systems in targeted cancer therapy, offering enhanced drug stability, controlled release, and improved tumor-specific targeting.

Biocompatibility and safety concerns

Guaranteeing the biocompatibility and well-being of polymer-based nanoparticles is a critical challenge in their clinical application. Some polymers may trigger immune responses or cause toxicity limiting their therapeutic use [72]. Advanced research focuses on developing biocompatible polymers and surface modifications. It is used to minimize adverse effects and enhance nanoparticle clearance from the body.

Drug loading and releasing kinetics

Efficient loading of therapeutic agents into polymer-based nanoparticles and controlled release at the tumor site are critical factors influencing treatment efficacy. Advanced research aims to optimize drug loading techniques and tailor releasing kinetics to match the drug's pharmacokinetics and therapeutic window, ensuring sustained drug exposure at the target site [73].

Biomarker identification

Identifying the reliable biomarkers for patient selection and predicting response to targeted therapies is crucial for maximizing treatment efficacy. Advances in genomic profiling and liquid biopsies are aiding in this area. Examples: Testing for EGFR mutations to predict response to EGFR inhibitors in lung cancer, and HER2 amplification testing to guide HER2-targeted therapy in breast cancer [74].

Personalized nanoparticle design

Each cancer patient's tumor exhibits unique characteristics, necessitating personalized treatment approaches. Advanced research is moving towards tailoring polymer-based nanoparticles based on patient-specific factors, such as genetic mutations, tumor heterogeneity, and treatment response. Personalized nanoparticle design aims to maximize treatment efficacy while minimizing off-target effects, fostering the development of precision medicine in cancer therapy [75,76].

Combination therapies combining therapies

Combining targeted therapies with other treatment modalities, like chemotherapy, radiation therapy, or immunotherapy, holds promise for improved outcomes. The rational design of combination regimens is an active area of investigation [28]. Examples: Combining BRAF and MEK inhibitors in BRAF-mutated melanoma, combining immune checkpoint inhibitors with other immunomodulatory agents.

DISCUSSION

Targeted cancer therapy using polymer-based nanoparticles has emerged as a potential approach in the field of oncology. This study has covered a wide range of topics related to the use of polymer-based nanoparticles in targeted cancer [77] therapy, which includes design principles, manufacturing processes, targeting strategies, and most recent advancements [78].

The design principles of polymer-based nanoparticles are crucial for their successful application in targeted cancer therapy [79]. By changing the composition, molecular weight, and structural characteristics of polymers, it is possible to

precisely control the nanoparticles' size, surface charge, and drug release kinetics [80]. This tunability is essential to increase drug delivery to cancer cells while avoiding off-target effects [81]. The advantages of polymer-based nanoparticles are their high loading and drug-loading capacity, biocompatibility, and biodegradability. Their capacity to incorporate proteins, nucleic acids, small chemicals, and combination therapies makes them a flexible platform that can support a variety of therapeutic approaches.

While making polymer-based nanoparticles for targeted malignant growth treatment, fabrication techniques are crucial. Techniques that are frequently employed include self-assembly, emulsion/solvent evaporation, and nanoprecipitation. A polymer solution and a nonsolvent are combined in nanoprecipitation, which results in the creation of nanoparticles. A polymer that has been dissolved in an organic solvent must be emulsified with an aqueous solution before the organic solvent is evaporated [82]. Self-assembly creates nanoparticles by arranging polymer molecules into well-organized structures, taking advantage of the intrinsic qualities of polymers. These production techniques offer important control over the nanoparticles' size, shape, and other characteristics.

Targeting strategies are employed to enhance the specificity and accumulation of polymer-based nanoparticles within tumor while minimizing harm to healthy tissues. Ligand-based targeting involves attaching specific molecules, such as antibodies or peptides, to the nanoparticle surface. These molecules recognize and bind to receptors or markers present on the surface of cancer cells, facilitating active targeting and accumulation at the tumor site [70]. This approach improves the selectivity of drug delivery and reduces the impact on healthy tissues. pH-responsive targeting takes advantage of the acidic tumor microenvironment to trigger drug release from the nanoparticles. Stimuli-responsive targeting utilizes external stimuli, such as light, heat, or magnetic fields, to trigger drug release at specific sites. These targeting strategies enable precise drug delivery, ensuring that therapeutic agents reach the intended location within the tumor [83].

Recent advances in preclinical and clinical studies have demonstrated the potential of polymer-based nanoparticles in targeted cancer therapy. These studies have highlighted the efficacy of polymer-based nanoparticles in delivering therapeutic agents to targeted cancer cells [84]. Stealth coating is accomplished by applying a layer of PEG to the nanoparticle surface and broadens expanding the dissemination season of nanoparticles in the circulation system. It permits in for improved aggregation at the growth site through the EPR impact. It allows enhanced accumulation at the tumor site through the EPR effect. Ligand conjugation improves active targeting and accumulation of nanoparticles within the tumor by specifically recognizing and binding to cancer cell receptors or markers. PH-responsive and stimuli-responsive strategies provide controlled and precise drug release, maximizing treatment effectiveness and minimizing side effects. These advances have shown promising results in preclinical and clinical settings. They are demonstrating the potential of polymer-based nanoparticles to improve cancer treatment outcomes [85].

Combination therapies and personalized medicine are emerging as important areas of research in the field of targeted cancer therapy using polymer-based nanoparticles [86]. Combining targeted therapies with other therapy modalities, like chemotherapy, radiation treatment, or immunotherapy, holds promise for improved outcomes. The rational design of combination regimens aims to enhance treatment effectiveness and overcome resistance mechanisms. Personalized medicine focuses on tailoring nanoparticle-based treatments to specific cancer types or individual patient requirements. This approach considers factors such as biomarkers, genomic profiling, and the unique characteristics of each patient's tumor, allowing for personalized and optimized treatment strategies.

The application of polymer-based nanoparticles in targeted cancer therapy offers a personalized and effective approach to the treatment of various cancers. The designated principles, fabrication methods, targeting strategies, and recent advancements are discussed in this review emphasizing the potential of polymer-based nanoparticles maximize treatment efficacy while minimizing adverse effects. Further research and clinical studies are necessary to fully explore the capabilities of these nanoparticles and optimize their use in personalized cancer treatments. Continued advancements in the field of targeted cancer therapy using polymer-based nanoparticles hold great promise for improving patient outcomes and revolutionizing the field of oncology.

CONCLUSION

In conclusion, polymer-based nanoparticles have arisen as a promising tool in targeted cancer therapy. These nanoparticles offer tunable physicochemical properties, high drug-loading capacity, extended circulation time, and active targeting capabilities. Their design principles, fabrication methods, and surface modification techniques contribute to their efficacy in delivering therapeutic agents to cancer cells while minimizing harm to healthy tissues. Controlled drug release mechanisms further enhance their effectiveness by ensuring precise and gradual drug delivery at the tumor site. Recent advances in preclinical and clinical studies have demonstrated the potential of polymer-based nanoparticles in improving cancer treatment outcomes. The combination of targeted therapies, personalized medicine, and optimized treatment strategies holds promise for further advancements in the field. In summary, the application of polymer-based nanoparticles in targeted cancer therapy offers a personalized and effective approach to the treatment of various cancers. These nanoparticles can be precisely engineered to deliver therapeutic agents to specific tumor sites, minimizing side effects and maximizing treatment efficacy. Continued research and clinical studies are needed to fully explore their capabilities and optimize their use in personalized cancer treatments. With further advancements, polymer-based nanoparticles have the potential to revolutionize cancer therapy, providing patients with more effective and tailored treatments.

AUTHOR CONTRIBUTIONS

All authors made substantial contributions to the conception and design, acquisition of data, or analysis and

interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agreed to be accountable for all aspects of the work. All the authors are eligible to be an author as per the International Committee of Medical Journal Editors (ICMJE) requirements/guidelines.

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CONFLICTS OF INTEREST

The authors report no financial or any other conflicts of interest in this work.

ETHICAL APPROVALS

This study does not involve experiments on animals or human subjects.

DATA AVAILABILITY

All data generated and analyzed are included in this research article.

USE OF ARTIFICIAL INTELLIGENCE (AI)-ASSISTED TECHNOLOGY

The authors declares that they have not used artificial intelligence (AI)-tools for writing and editing of the manuscript, and no images were manipulated using AI.

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