

Nanoformulation: Theranostic Strategies for the Treatment and Diagnosis of Cancer

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ABSTRACT

Theranostic polymeric nanoparticles (TPNs) are an advanced and very promising method for both diagnosing and treating cancer. They integrate both therapeutic and diagnostic functionalities into a single platform. This study evaluates the most recent advancements in Total Parenteral Nutrition, focusing on innovative designs and strategies, as well as the findings from case studies and clinical trials. We performed a comparative analysis of Total Parenteral Nutrition and traditional methods, highlighting their improved compatibility with living organisms, accurate dispersion, and reduced overall toxicity. Despite the advantages mentioned, there remain persistent challenges in the form of technical and clinical limitations, regulatory barriers, and ethical considerations. The proposed future study attempts to address these issues and enhance the efficacy and use of TPNs in the area of cancer.

Keywords: Biocompatibility, Cancer therapy, Nanotechnology, Polymeric nanoparticles, Theranostic

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INTRODUCTION

Cancer presents a substantial threat to human life and well-being, serving as a prominent contributor to the prevalence of disease and mortality on a worldwide scale.¹ In recent decades, substantial resources have been allocated to cancer research, yet there has been little advancement in enhancing the diagnosis and prognosis of the illness.² The main challenge is in accurately identifying cancer patients at the early stages of the illness to promptly commence personalized therapy. The majority of individuals with cancer get a diagnosis at the advanced stage of the disease since there are no usual clinical symptoms present. The standard methods used for cancer diagnosis mainly include biopsy, computed tomography (CT), magnetic resonance scanning (MRI), single photon emission tomography (SPECT), ultrasonography (US), and positron emission scanning (PET).³ Biopsy continues to be the most dependable and precise approach for diagnosis. PET imaging has limited resolution capabilities, but MRI scans may provide several false positive signals.^{4,5} Traditional cancer therapies, such as chemotherapy, radiation, immunotherapy, and surgery, have substantial challenges, such as limited ability to reach all tissues, imprecise targeting, severe side effects across the body, and the emergence of drug resistance.⁶ Therefore, it is essential to investigate more effective therapeutic strategies for treating cancer.⁷ Nano agents have attracted considerable attention because of their readily changeable hydrophobic areas and numerous functional groups, which are manufactured using nanotechnologies and nanoparticles (NPs).⁸ Nanoparticles

(NPs) primarily include metal and metal oxide-based NPs, liposomes, dendrimers, magnetic NPs, quantum dots, and polymeric NPs.⁹ Polymeric nanoparticles, particularly polymeric nano agents, have made substantial progress in the domain of cancer diagnosis and treatment.¹⁰ Because polymeric nanoparticles (NPs) are tiny in size and have a significant surface area compared to their volume, they may easily go through narrow blood arteries and surpass biological obstacles. Thus, polymeric nanoparticles may effectively accumulate in cancer cells because of the enhanced permeability and retention (EPR) effect while also regulating the dispersion of therapeutic medications throughout the body.¹¹ A multitude of polymeric nano agents have been produced because of modifying hydrophobic regions and functional groups. These agents can bind with imaging agents and therapeutic molecules, such as fluorescent dyes, photosensitizers, aptamers, peptides, antibodies, chemotherapeutic medicines, and other biological molecules.¹⁰⁻¹² Recent preclinical investigations have shown that new polymeric nano agents have better biosafety, increased selectivity, less systemic side effects, higher solubility, and greater stability.¹³ The unique properties of polymeric nano agents have allowed them to perform precise imaging and tailored therapy of malignant regions, resulting in the development of personalized polymeric theragnostic nanoplatforms. Novel polymeric nano agents for imaging provide superior temporospatial resolution in comparison to traditional imaging approaches. Various polymeric nanoparticles, such as indocyanine green (ICG),¹⁴ neodymium (Nd) lanthanide ions,¹⁵ and chlorin e6 (Ce6)-based

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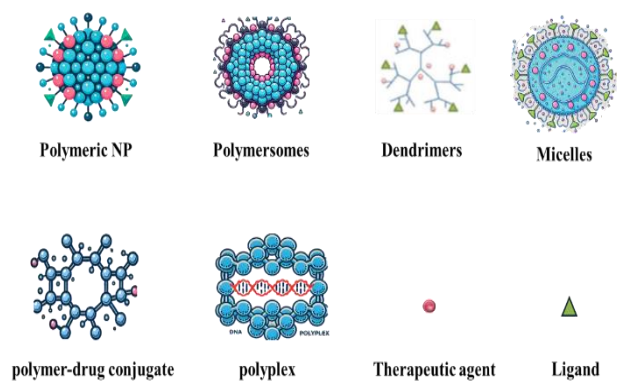


Figure 1: Various polymeric NPs as drug delivery vehicles.

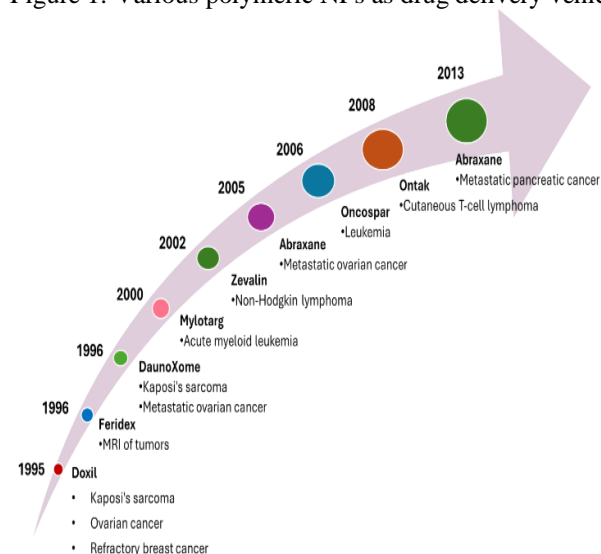


Figure 2: A chronology of the development of cancer treatments based on polymeric NPs.

nanoparticles,¹⁶ have been created to detect cancer in its early stages. Presently, novel strategies for cancer treatment include the utilization of cutting-edge polymeric nano agents for chemotherapy, gene therapy, photothermal therapy (PTT), and photodynamic therapy (PDT). PTT causes permanent protrusion of the eyeball, programmed cell death, and tissue death in cancer cells by converting near-infrared (NIR) light into heat and then raising the temperature to produce hyperthermia. PDT triggers apoptosis in cancer cells by using light energy and producing reactive oxygen species (ROS), namely singlet oxygen.¹⁷ Theranostic approaches using polymeric nano agents are recognized for their ability to be minimally intrusive, provide improved specificity, and have less off-target toxicity¹⁸. This review will outline the composition of novel polymeric nano agents and their prospective use in the early identification, treatment, and combined diagnosis and therapy of cancer.¹⁹ This debate will specifically address the outstanding challenges related to new polymeric nano agents in the field of cancer.

Polymeric nanoparticles

Nanotheranostics is an emerging area focused on rapid cancer detection, medicine administration, and treatment.²⁰⁻²² Nanoparticles typically have sizes ranging

from 1.0 to 100.0 nm, making them about a thousand times smaller than typical human cells. In addition, these nanoparticles have a high likelihood of engaging in biological interactions with cellular receptors, enzymes, and antibodies.²³ Nanoparticle modification enables their use as optimal candidates for precise diagnosis and therapy.^{24,25} The literature suggests the existence of several theranostic nanoparticle agents. These materials consist of several components, such as gold ions, silica, carbon, and others.^{26,27} These imaging probes have been examined in several animal models and have shown remarkable potential for early cancer diagnosis. However, these substances have several disadvantages, including immunogenicity, toxicity, and a sluggish rate of elimination from the body.^{28,29} Consequently, several macromolecules have been examined for these objectives. The key chemicals used for these “platforms are polylactic acid (PLA), poly(ϵ -caprolactone), poly(lactide-co-glycolide) (PLGA), poly(alkylcyanoacrylate), and polyglycolic acid. On the other hand, the natural polymers used include peptides, proteins, nucleic acids, dextran ester, and chitosan”. Undoubtedly, these compounds possess remarkable qualities but are hindered by their brief duration of effectiveness, indiscriminate dispersion rates, and restricted use due to their interactions with medication molecules. Therefore, researchers investigated synthetic, polymeric, and biodegradable nanoparticles.^{30,31} A lot of work in synthetic chemistry and modelling went into making these polymeric nanoparticles. Various synthetic biodegradable polymeric nanocarriers can be found, such as “poly(2-hydroxyethyl-L-aspartamide), poly(L-aspartate), poly(D, L-lactic acid-co-glycolic acid), poly(ϵ -caprolactone), poly(ethylene glycol) (PEG), poly(N-vinyl pyrrolidone) (PVP), poly(N-isopropyl acrylamide) (PNIPAM), poly(hydroxypropyl methacrylamide) (PHPMA), poly(methyl methacrylate), poly(ethylene glycol), poly-(chloromethyl-styrene) (PCMS)”, and others.³¹ Both diagnosis and treatment are at the heart of the theranostic method of cancer care. Hence, cancer diagnosis and cancer therapy are the two parts of this study. You can see the many types of polymeric nanoparticles that are used to deliver medications in Figure 1. Table 1 presents the details of biocompatible polymer-based cancer theranostic^{32,33} Figure 2 shows the development of polymeric nanoparticles (NPs) for cancer treatment in chronological order. Table 2 displays a range of polymeric nanoparticle-based drugs currently in clinical trials, detailing their active ingredients, nanoparticle platforms, and clinical status. It shows that products like Abraxane and ABI-009 are approved or in early phases for various cancers, while others, such as BA-003 and BIND-014, are advancing through different trial phases for specific cancer types. The table highlights diverse nanoparticle platforms, including albumin, polymeric, and cyclodextrin-based formulations, used to enhance drug delivery and targeting in cancer therapy.

Table 1: The biocompatible polymer-based cancer theranostics.

Imaging Modality	Polymers	Imaging Agents	Encapsulated Moiety	Targeting Moiety
MRI	Poly(trimethylene carbonate)-poly(L-glutamic acid) (PTMC-b-PGA copolymer)	Ultrasmall superparamagnetic iron oxides (USPIOs)	Doxorubicin	-
MRI	PTMC-b-PGA copolymer	USPIOs	Doxorubicin	HER-2
MRI	Poly(acrylic acid-co- distearin acrylate)	Superparamagnetic iron oxide nanoparticles (SPIONs)	Doxorubicin	Folic acid
MRI	PluronicR L-121 (EO5-PO68-EO5)	SPIONs	Camptothecin	Bombesin
MRI	PTAMC-b-PGA copolymer	USPIOs	Doxorubicin	-
MRI	PEO-POLGA-PEO(polyethyleneoxide-poly D, L lactide-co-glycolidepolyethyleneoxide) methoxy or folate (FA)-PEG	Iron oxide (Fe3O4)	Doxorubicin	-
MRI	114-PLA-PEG-acrylate 46 SPIO NPs PLGA	SPIONs	Doxorubicin	Folic acid
Ultrasound	(poly(D,L-lactide-coglycolide))	Fe3O4	H2O2	
Ultrasound	Poly(ethylene glycol)- poly(L-aspartic acid) (PEG-PAsp)	-	Doxorubicin Calcium carbonate	Rabies virus glycoprotein (RVG) peptide
Optical imaging	PLGA	Mercaptosuccinic acid(MSA)-coated CdTe QDs	Doxorubicin	-
Optical imaging	poly(2-hydroxyethylcooctadecyl aspartame) (PHEA-C18)	Magnetic resonance tomography (MIR) fluorescent probe, FPR-675	Folic acid	-
Optical imaging	poly(ethylene glycol)- poly(trimethylene carbonate-cocaprolactone)	Multiporphyrin near-infrared (NIR) fluorophores	-	-
Optical imaging	PPF-PLGA-PEG polymer	Rhodamine B	Folic acid	-
Optical imaging	PPF-PLGA-PEG copolymer	-	Doxorubicin	-
Optical imaging	Polytyrosine	-	Doxorubicin	-
Optical imaging	Polyethylenimine	Hematoporphyrin	-	-

Synthesis methods

The synthesis techniques used in the production of nanogels and nanospheres have a substantial impact on their properties, including size, surface area, drug loading capacity, and release patterns.³⁴ Hence, it is essential to carefully choose a suitable synthesis technique, considering the desired characteristics of the nanoparticles. By selecting certain polymers and other materials during the synthesis process, the properties of theranostic applications in cancer treatment and diagnostics may be further modified and optimized. Nanogels and nanospheres may be manufactured using a variety of ways, which can be roughly classified into polymer dispersion and

polymerization procedures.³⁵ The techniques often used in the production of nanogels and nanospheres include evaporation of solvent, nanoprecipitation, and gelation.

Solvent evaporation method

The solvent evaporation method is a commonly adopted process for producing nanospheres, especially when using pre-made polymers such as polycaprolactone (PCL), poly(lactic-co-glycolic acid) (PLGA), or ethylcellulose (EC).³⁶ This approach comprises two primary stages. Initially, the polymer and medication are solubilized in an organic solvent, such as chloroform, dichloromethane, or ethyl acetate. Subsequently, the solution is transformed into an emulsion by combining it with an aqueous phase that

Table 2: The polymer NP-based drugs in clinical trials.

Products	Drugs	Platform (NPs)	Status	Applications
Abraxane	Paclitaxel	Albumin	Approved	Lung, breast, and pancreatic cancers
ABI-009	Rapamycin	Albumin	Phase I/II	Solid tumors
ABI-008	Docetaxel	Albumin	Phase I/II	Prostate & breast cancers
BA-003	Doxorubicin	Polymeric	Phase III	Hepatocellular cancer
BIND-014	Docetaxel	PEG-PLGA polymeric	Phase I/II	Lung cancer
CALAA-01	siRNA targeting	Cyclodextrin	Phase I	Solid tumors
DHAD-PBCA-NPs	Mitoxantrone	Polymeric	Phase II	Hepatocellular cancer
Docetaxel-PNP	Docetaxel	Polymeric	Phase I	Solid tumors
Nanotax	Paclitaxel	Polymeric	Phase I	Neoplasms
ProLindac	DACH Pt	HPMA-polymeric	Phase II/III	Ovarian cancer

contains an emulsifier such as polyvinyl alcohol (PVA) or Poloxamer-188. The emulsification procedure may be conducted using either a single emulsion (O/W) or a double emulsion (W/O/W) method, depending on the drug's hydrophobic or hydrophilic nature. Following the process of emulsification, the organic solvent is eliminated by either agitation or the application of decreased pressure, resulting in the creation of solid nanospheres. Factors such as stirring velocity, polymer content, and the kind and concentration of the emulsifier have an impact on the particle size and shape. For example, the size of particles may be reduced by using polymers with greater molecular weight or by increasing the duration of sonication in Figure 3. Conversely, bigger particles can be obtained by increasing the concentration of the polymer. The solvent evaporation approach has effectively been used for the synthesis of nanoparticles containing different medications such as Praziquantel and ibuprofen. The particle sizes achieved ranged from 100 to 200 nm, depending on the specific formulation circumstances.³⁷

Gelation method for nanogels

Nanogels are often produced using gelation techniques, which include the cross-linking of hydrophilic polymers to create a three-dimensional structure that can expand in water³⁸. Gelation may be triggered using either physical or chemical cross-linking techniques. Physical cross-linking involves the use of ionic contacts or hydrogen bonding, often with the addition of substances such as sodium tripolyphosphate (for chitosan-based nanogels) or divalent cations like calcium.³⁹ Chemical cross-linking, however, utilizes chemicals such as glutaraldehyde or genipin to create covalent connections between polymer chains. During a standard process, the polymer (such as chitosan, hyaluronic acid, or poly(N-isopropyl acrylamide)) is dissolved in a water-based solution and combined with the medicinal ingredient.⁴⁰ Subsequently, cross-linking agents are introduced to initiate gelation, resulting in the formation of a nanogel structure. One may regulate the dimensions and drug-carrying capacity of nano gels by manipulating factors such as the concentration of polymers, the concentration of cross-linkers, and the technique used to include drugs in Figure 4. For instance, nanogels created using the in-situ loading technique, in which the medication is introduced while the gel is forming, often display a more uniform distribution and a

regulated release pattern.⁴¹ The nanogels produced possess the capacity to encapsulate pharmaceuticals that are both hydrophilic and hydrophobic. The particle sizes of these nanogels usually fall within the range of 50 to 200 nm, which varies depending on the formulation used.

Nanoprecipitation method

The nanoprecipitation method, commonly referred to as the solvent displacement method, is a frequently used technique for producing nanospheres. This method entails the deposition of a polymer at the interface as it forms from an organic solvent into a non-solvent (often water) that may mix with the organic phase. During this procedure, the polymer and medicine are first dissolved in a water-soluble organic solvent, such as acetone or ethanol. The solution is then introduced in small drops to a liquid phase while being stirred continuously, resulting in the spontaneous creation of nanospheres as the polymer solidifies.⁴² The nanoprecipitation technique is very beneficial due to its simplicity and capacity to generate nanoparticles without the need for surfactants. It relies on the Ouzo effect to stabilize the particles. The size of the nanospheres is mostly influenced by parameters such as the polymer content in the organic phase, the pace at which the solvent is added, and the ratio of solvent to non-solvent shown in Figure 5.⁴³ Increasing the concentration of the polymer typically leads to the formation of bigger particles, but a quicker addition of solvent may result in the production of smaller particles that have a more uniform size distribution. Nanoparticles with diameters ranging from 50 to 300 nm have often been used to enclose different therapeutic substances, such as ibuprofen and doxorubicin.⁴⁴ These synthesis processes are very adaptable and effective, making them well-suited for creating nanogels and nanospheres. These components are crucial for developing theranostic platforms used in cancer treatment and detection.

Characterization techniques

Particle size analysis

DLS (Dynamic light scattering)

DLS is a commonly used technique for determining the size distribution of nanoparticles in a liquid solution. The method operates by examining the variations in the intensity of light scattering resulting from the random movement of the particles, known as Brownian motion. DLS offers data on the hydrodynamic diameter of

particles, providing an average spatial and polydispersity index (PDI) that reflects the homogeneity of the size distribution of nanoparticles. The number 56 is enclosed in square brackets.⁴⁵

NTA (Nanoparticle tracking analysis)

NTA visualizes and measures the size and concentration of nanoparticles based on their movement under Brownian motion. It allows for the analysis of individual particles, providing a more detailed size distribution and concentration.⁴⁶

SEM (Scanning electron microscopy)

SEM provides high-resolution images of nanoparticles, allowing for direct measurement of their size and morphology. SEM can also give insights into the surface structure and aggregation state of the nanoparticles.⁴⁷

Surface charge (Zeta potential)

ELS (Electrophoretic light scattering)

ELS quantifies the zeta potential of nanoparticles, which serves as an indication of their surface charge. Zeta potential is ascertained by the motion of charged particles in an electric field, providing valuable information on the stability of suspensions containing nanoparticles. Significant zeta potential values (either positive or negative) indicate favorable stability since the particles exhibit repulsive forces that hinder aggregation.⁴⁸

Laser doppler micro-electrophoresis

This method similarly quantifies the zeta potential by assessing the speed of particles in an electric field. This method is used to deduce the surface charge, which is crucial for comprehending the interaction between nanoparticles and biological systems, as well as their colloidal stability.⁴⁹

Morphology

TEM (Transmission electron microscopy)

TEM offers high-resolution images of nanoparticles, enabling detailed observation of their internal structure and morphology. TEM involves passing an electron beam through a thin sample, producing images that can reveal the size, shape, and arrangement of nanoparticles. It is particularly useful for examining the core-shell structures of polymeric nanoparticles.⁵⁰

SEM (Scanning electron microscopy)

As mentioned earlier, SEM provides detailed images of the surface morphology and size of nanoparticles. It uses a focused beam of electrons to produce high-resolution, three-dimensional images, allowing for the examination of surface textures and topography.⁵¹

Chemical composition

FTIR (Fourier-transform infrared spectroscopy)

FTIR is used to identify the chemical composition and functional groups present in nanoparticles. It works by measuring the absorption of infrared light at different wavelengths, producing a spectrum that represents the molecular fingerprint of the sample. FTIR can confirm the

presence of specific polymers and other functional groups used in the synthesis of theranostic nanoparticles.⁵²

NMR (Nuclear magnetic resonance) spectroscopy

NMR provides detailed information about the molecular structure and composition of nanoparticles. It works by detecting the magnetic properties of certain atomic nuclei. NMR can be used to determine the chemical environment of atoms within the nanoparticles, revealing insights into the polymer composition, the presence of drugs, and other chemical modifications. Proton (¹H) and carbon (¹³C) NMR are commonly used for analyzing organic components in polymeric nanoparticles.⁵³

Theranostic applications

Dual functionality of theranostic nanoparticles

Theranostic nanoparticles integrate both therapeutic and diagnostic functions into a single platform, allowing simultaneous treatment and real-time monitoring of diseases. This dual functionality enhances the precision and efficacy of cancer therapy by ensuring targeted drug delivery while providing imaging capabilities to track treatment progress and monitor the tumor environment.⁵⁴

mechanisms of action for therapy

Drug delivery systems

Theranostic nanoparticles can encapsulate therapeutic agents, protecting them from degradation and ensuring controlled release at the target site. They exploit the enhanced permeability and retention (EPR) effect, which allows nanoparticles to accumulate preferentially in tumor tissues due to their leaky vasculature and poor lymphatic drainage.⁵⁵

Targeted therapy

Targeted therapy involves modifying the surface of nanoparticles with ligands, antibodies, or peptides that recognize and bind specifically to receptors overexpressed on cancer cells. This specificity reduces off-target effects and enhances therapeutic efficacy by concentrating the drug at the tumor site.⁵⁶

Controlled release

Controlled release mechanisms in theranostic nanoparticles are achieved through stimuli-responsive materials that release the encapsulated drug in response to specific triggers such as pH, temperature, enzymes, or magnetic fields. This ensures that the drug is released only in the desired microenvironment, minimizing side effects and improving treatment outcomes.⁵⁷

Mechanisms of action for diagnosis

Imaging modalities

Theranostic nanoparticles can be engineered with contrast agents for various imaging techniques:

MRI (Magnetic resonance imaging)

Nanoparticles can incorporate magnetic materials like iron oxide, which enhance the contrast in MRI scans, allowing

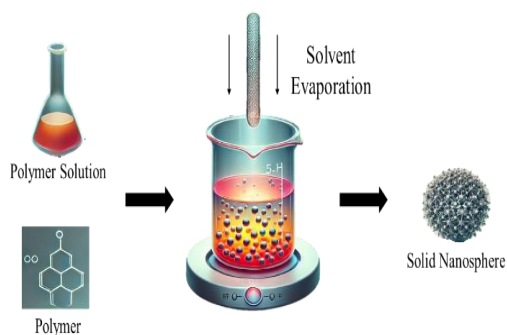


Figure 3: Synthesis of Nanospheres in a Chemical Reaction Process.



Figure 4: Formation of Cross-Linked Nanogels from a Polymer Solution using a Cross-Linking Agent.

for detailed visualization of the tumor and surrounding tissues.

CT (Computed tomography)

Nanoparticles containing heavy metals such as gold or iodine can improve the contrast in CT scans, aiding in the precise localization of tumors.

PET (Positron emission tomography)

Nanoparticles labelled with radioactive isotopes can be used for PET imaging, providing functional information about the tumor's metabolic activity.⁵⁸

Biomarker detection

Theranostic nanoparticles can be functionalized with probes that recognize specific biomarkers associated with cancer. These probes can bind to cancer-specific antigens, enzymes, or other molecular markers, facilitating early detection and diagnosis of cancer through imaging techniques or biosensors.⁵⁹

Real-time monitoring

The integration of diagnostic agents within theranostic nanoparticles allows for real-time monitoring of therapeutic efficacy. Changes in imaging signals can indicate the progression or regression of the tumor, enabling clinicians to adjust treatment strategies promptly. This real-time feedback is crucial for personalized medicine, where treatments are tailored based on the patient's response.⁶⁰

Recent advances in theranostic polymeric nanoparticles

Innovative strategies and designs

Recent advancements in theranostic polymeric nanoparticles have focused on developing multifunctional systems that can simultaneously deliver therapeutic agents and provide diagnostic imaging. Innovations include:

Multifunctional core-shell nanoparticles

These nanoparticles have a core that carries the therapeutic agent and a shell that provides diagnostic functions or controlled release properties. The core can be made of materials such as gold or iron oxide for imaging, while the shell can be functionalized with targeting ligands or stimuli-responsive polymers.

Stimuli-responsive nanoparticles

These nanoparticles are designed to respond to specific

internal (pH, enzymes, redox conditions) or external (temperature, magnetic fields, light) stimuli, triggering drug release or enhancing imaging contrast in the tumor microenvironment. This ensures that the therapeutic agent is released at the right time and place, increasing treatment efficacy and reducing side effects.

Hybrid nanoparticles

Hybrid nanoparticles combine organic and inorganic materials to leverage the advantages of both. For example, incorporating magnetic nanoparticles within a polymeric matrix can provide magnetic targeting and MRI contrast, while the polymeric component can offer biocompatibility and controlled drug release.

Biodegradable polymers

Using biodegradable and biocompatible polymers like "PLGA (poly(lactic-co-glycolic acid)) and PEG (polyethylene glycol)" enhances the safety profile of theranostic nanoparticles. These materials degrade into non-toxic byproducts, minimizing long-term toxicity concerns.⁶¹

Case studies

Multiple case studies and clinical trials have shown the promise of theranostic polymeric nanoparticles in the treatment and detection of cancer:

Case study 1

A study on PLGA nanoparticles loaded with the chemotherapy drug doxorubicin and iron oxide for MRI contrast showed that these nanoparticles effectively targeted tumors in mice, providing both therapeutic and diagnostic benefits. The MRI allowed real-time tracking of the nanoparticles, confirming their accumulation in the tumor site.⁶²

Case study 2

Another study involved nanoparticles made from PEGylated poly(amidoamine) dendrimers loaded with a photosensitizer for photodynamic therapy and a fluorophore for fluorescence imaging. These nanoparticles exhibited targeted delivery to cancer cells and provided simultaneous imaging and therapy, resulting in significant tumor reduction in animal models.⁶³

Clinical trials

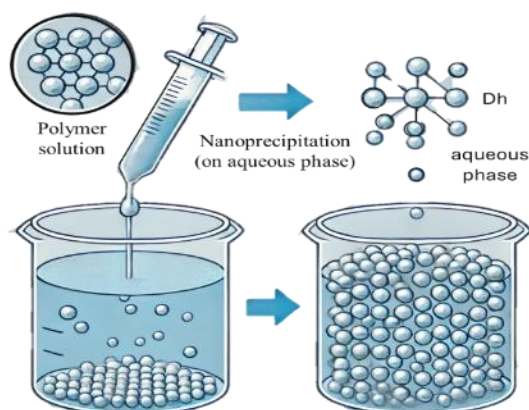


Figure 5: Nanoprecipitation Process for Polymer Nanoparticle Formation.

Several theranostic nanoparticles are currently in clinical trials. For example, a trial involving iron oxide nanoparticles coated with a polymer and loaded with chemotherapeutic drugs is being tested for its ability to target brain tumors while providing MRI contrast. Preliminary results indicate enhanced targeting and imaging capabilities with promising therapeutic outcomes.⁶⁴

Comparison with traditional methods

Theranostic polymeric nanoparticles provide several benefits over conventional cancer therapy and diagnosis. One major advantage is tailored delivery. By functionalizing these nanoparticles with ligands, antibodies, or peptides that have an affinity for cancer cell receptors, it is possible to specifically target cancer cells. This process of selectivity focuses therapeutic medications specifically at the site of the tumor while minimizing the amount of exposure to healthy tissues. Chemotherapy and radiation treatment, which damage both malignant and healthy cells, may cause nausea, hair loss, and immunosuppression.⁶⁵ Controlled and targeted therapeutic drug release via theranostic nanoparticles reduces negative effects. This tailored strategy reduces systemic toxicity and side effects associated with standard cancer therapies, which distribute medications non-specifically.⁶⁶ Real-time monitoring is another strength of theranostic nanoparticles. These nanoparticles integrate diagnostic agents, enabling real-time imaging and monitoring of medication distribution and treatment response utilizing MRI, CT, and PET. Clinicians need this real-time input to change treatment tactics depending on effectiveness. However, traditional approaches involve separate imaging and treatment processes, making real-time therapy efficacy monitoring problematic.⁶⁷ Therapeutic and diagnostic capabilities on one platform simplify treatment using theranostic nanoparticles. This may decrease clinician visits, simplify treatment processes, and improve patient compliance. Traditional procedures use different therapy and diagnostic modalities, which are more complicated and time-consuming.⁶⁸ Theranostic polymeric

nanoparticles have various drawbacks. Their complicated synthesis is a major issue. Creating nanoparticles with exact size, shape, surface functionalization, and multifunctionality is difficult and resource-intensive. Traditional techniques include simpler manufacturing procedures and well-established norms, making them easier to create.^{69,70} Regulatory obstacles are another disadvantage. Theranostic nanoparticles must fulfil strict therapeutic and diagnostic regulatory standards, complicating approval and delaying clinical translation. Traditional approaches have more established regulatory routes, making approval easier.⁷¹ Theranostic nanoparticles may be hazardous. However, biocompatible and biodegradable, several components employed in their fabrication may provide long-term toxicity issues that need more exploration.⁷² Traditional procedures have established toxicities and side effects, improving management and mitigation.^{73,74} Complex multifunctional nanoparticle research and manufacture may be costly, increasing treatment costs. Traditional techniques tend to be cheaper due to production processes and economies of scale.⁷⁵ Highly specialized nanoparticles are difficult to produce on a large scale and may require significant investment in new technologies and infrastructure, whereas traditional methods are easier to produce with existing manufacturing facilities.⁷⁶

Challenges and future perspectives

Theranostic polymeric nanoparticles face several technical and clinical challenges, including the complexity of their synthesis and ensuring consistent production at a large scale. Clinically, there are concerns regarding their long-term biocompatibility and potential toxicity. Regulatory and ethical considerations also pose significant hurdles, as these multifunctional nanoparticles must meet stringent requirements for both therapeutic and diagnostic purposes, complicating their approval process. Ethical issues related to patient safety and the long-term impact of nanomaterials must also be addressed. Despite these challenges, potential future developments in this field are promising. Research is focused on creating more efficient and safer nanoparticles, improving targeting and controlled release mechanisms, and integrating advanced imaging techniques. Future directions include exploring biodegradable and biocompatible materials, enhancing personalized medicine approaches, and conducting more extensive clinical trials to validate the efficacy and safety of theranostic nanoparticles in cancer therapy and diagnosis.

CONCLUSION

TPNs have the potential to greatly improve cancer detection and therapy by providing both therapeutic and diagnostic functions. Compared to conventional approaches, their ability to precisely target and release drugs in a regulated manner decreases the toxicity to the whole body and enhances the effectiveness of therapy. Nevertheless, obstacles such as intricate synthesis procedures, regulatory obstacles, and possible long-term

toxicity continue to be substantial impediments. To tackle these problems, it is necessary to conduct continuous research that focuses on enhancing the design of nanoparticles, guaranteeing their compatibility with living organisms, and confirming their effectiveness in clinical studies. TPNs (Total Parenteral Nutrition) have a bright future in cancer care since developments are expected to improve customized therapy and make treatment procedures more efficient. This will eventually lead to better patient outcomes and adherence to treatment.

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