



**INTERNATIONAL JOURNAL OF
PHARMACEUTICAL SCIENCES**
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: <https://www.ijpsjournal.com>



Review Article

Novel Functionalised Polymer Based Nanoparticle Formulation With Anti Cancer Drug

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ARTICLE INFO

Received: 21 July 2024

Accepted: 27 July 2024

Published: 02 Aug 2024

Keywords:

Cancer, nano size particle, chemotherapy, drug delivery.

DOI:

10.5281/zenodo.13173238

ABSTRACT

A tailored and customised medication delivery method was developed to address the drawbacks of traditional dosage forms. At this time, there was a great desire for innovative medication delivery systems. One kind of targeted medicine delivery technique is nanoparticles. Colloidal particles called nanoparticles allow medications to be delivered to specified locations. While there are many distinct types of nanoparticles, polymeric nanoparticles are unique. One of the topics being researched the most right now is polymer nanoparticles. Polymer-based nanoparticles include dendrimers, ligand-based nanoparticles, polymer micelles, PEGylated nanoparticles, and other compounds. The many developments in polymeric nanoparticles and the polymers utilised in their synthesis are covered in this chapter. It provides information on the varieties of functionalized nanoparticles. Finally, using cancer and vaginal illnesses as examples, it addresses the use of various polymers in medication delivery systems to treat a variety of disorders. The final chapter also discusses the potential applications of functionalized polymeric nanoparticles. It's a flexible delivery strategy because there's a lot of room to chemically alter the polymer to create the desired build. For clinical usage, a number of therapeutic NPs based on polymers have received approval. This study sheds light on the developments targeted nanocarriers based on polymers, with, with an emphasis on their potential use in oncology therapy. The targeting mechanisms of several nanocarrier types, including organic-inorganic hybrid nanoparticles (NPs), were briefly described in this review paper. Here, the creation, advantages, and uses of polymeric nanoparticles (PNPs) in several anti-cancer treatments are highlighted. The drug delivery strategy using functionalized or encapsulated PNPs (with or without targeting ability) for therapeutic and diagnostic purposes (theranostics) has also been discussed.

INTRODUCTION

Cancer is a primary cause of mortality globally, with millions of fatalities each year. Despit major

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



breakthroughs in treatment, some problems continue that need to be addressed to enhance cancer therapy. Thus, the goal of oncological research is to find novel and inventive medications that will lessen the severe adverse effects of conventional therapies. Many of the advances have been included in clinical trials or are now being investigated. For example, creation of biocompatible materials for use in diagnostic and therapy is greatly aided by nanomedicine. Furthermore, precise targeting methodologies and tailored systems have been developed through the bioengineering of patient cells and extracellular vesicles. These developments hold potential for improving the efficacy of cancer therapies [1].

Nano medicines are a result of drug delivery using nanotechnology. Many of the problems the pharmaceutical business is now facing might be solved by these creative ideas. Nano drugs promise to open the door for the creation of cutting-edge medications with fewer adverse effects because of their many benefits [2]. This research will explore the most recent developments in theranostic methods, fundamental and applied nanotechnology. We will look at how these developments have produced nanoscale materials, which act as ground-breaking models for unique targeted cancer therapies and biological uses [3].

CHEMOTHERAPY

This research will explore the most recent developments in theranostic methods, fundamental and applied nanotechnology. We will look at how these developments have produced nanoscale materials, which act as ground-breaking models for unique targeted cancer therapies and biological uses [4,5]. Chemotherapy has a number of serious side effects that include low blood count, nausea, exhaustion, hair loss, anemia, diarrhea, constipation, and problems with reproduction. Chemotherapeutic drugs can also affect brain function directly or indirectly through several mechanisms. Chemotherapy frequently

has a major, long-lasting impact on cognitive function, even if there are systemic blood-brain barrier medicines for the brain; the precise cause is yet unknown [6]. Chemotherapy frequently involves the use of several drugs, such as gemcitabine, paclitaxel, docetaxel, azacitidine, and pemetrexed. These anticancer medications can be taken in a number of ways, including as pills, capsules, and parenteral (intramuscular and intravenous) techniques [7].

Radiation Therapy

Radiation therapy is the cornerstone of cancer treatment and has a 40% cure rate for patients. The way this therapy functions is by stopping the growth of cancer cells. Radiation therapy with high energy is used to shrink tumors and destroy cancer cells. This radiation includes charged particles, gamma rays, and X-rays. It goes after and destroys the DNA molecules inside the cells, tampering with their genetic makeup and stopping them from multiplying [8,9].

Surgical Therapy

Cancer surgery saw tremendous progress around the start of the 20th century. Miles carried out the first lobectomy in 1912 and the first abdominoperineal excision in 1908. The classic Halsted surgery is being replaced by non-invasive procedures like laparoscopic colectomy and chest video-assisted technologies., modern surgical techniques have undergone significant evolution. Eliminating sentinel nodes has enhanced cosmetic results and decreased lymphedema risk. Laryngoscopy laser techniques can now be used to treat early-stage laryngeal cancer. The Da Vinci® robotic system is one of the newest developments and is utilized in procedures for prostate and kidney cancer [10-14].

Proton Therapy

There is great potential for proton therapy as a tumor treatment. Since the FDA approved proton therapy in 2001, there has been a significant increase in public interest in this treatment.



Cancers in children as well as tumors in the kidney, bladder, brain, spine, lungs, back, and legs can be effectively treated with this therapy. Proton treatment is being used more often, and facilities are always assessing whether it works for more cancer kinds [15]. However, while evaluating proton treatment, it is crucial to take into account appropriate patient preparation, in-depth scientific study, including comparisons with other technology, moral dilemmas, and financial outcomes [16].

Heating Treatment

At least 4000 years have passed since the first recorded uses of thermotherapy for the treatment and elimination of tumor masses. Tumors can be destroyed by hyperthermia, which is the application of extremely high temperatures to cancer cells, which damages the proteins and structures inside the cells. The classic Halsted surgery is being replaced by non-invasive procedures like laparoscopic colectomy and chest video-assisted technologies, including varicose vein treatment. In order to enable deep penetration, thermotherapy entails heating human tissues to as high as 113 degrees Fahrenheit [17-19].

Photodynamic Therapy (PDT)

When photodynamic therapy (PDT) was originally developed in 1903, it was primarily used to target basal cell carcinomas (BCC) using eosin. A photosensitizing substance that reacts to a certain light wavelength is employed. in PDT. The photosensitizing chemical releases a form of oxygen that kills nearby cells when it is exposed to this light. This treatment has demonstrated potential in reducing harm to healthy cells while specifically focusing on malignant areas [20, 21]. It is possible to combine photodynamic therapy (PDT) in a way that works well with other medical procedures like radiation, chemotherapy, or surgery. PDT's efficacy in treating different cancer types is presently being studied in a large number

of clinical studies [22]. It is essential to meet every need for the perfect PDT agent in order to employ nanoparticles as carriers for photosensitizing agents in PDT [23].

Laser therapy

Many malignancies and precancerous situations are treated using laser treatment, especially when it comes to reducing or completely removing tumors. Peripheral illnesses such as early-stage basal cell skin carcinoma and other malignancies among the illnesses are non-small cell lung cancer, ovarian cancer, penile cancer, and cervical cancer for which it is frequently utilized. Furthermore, blockage and bleeding are two other cancer symptoms that laser treatment can assist with. It is frequently used in conjunction with other medical procedures such radiation therapy, chemotherapy, and surgery. Additionally, One method of scanning lymph vessels is using laser therapy., which lessens tumor cell spread and edema [24].

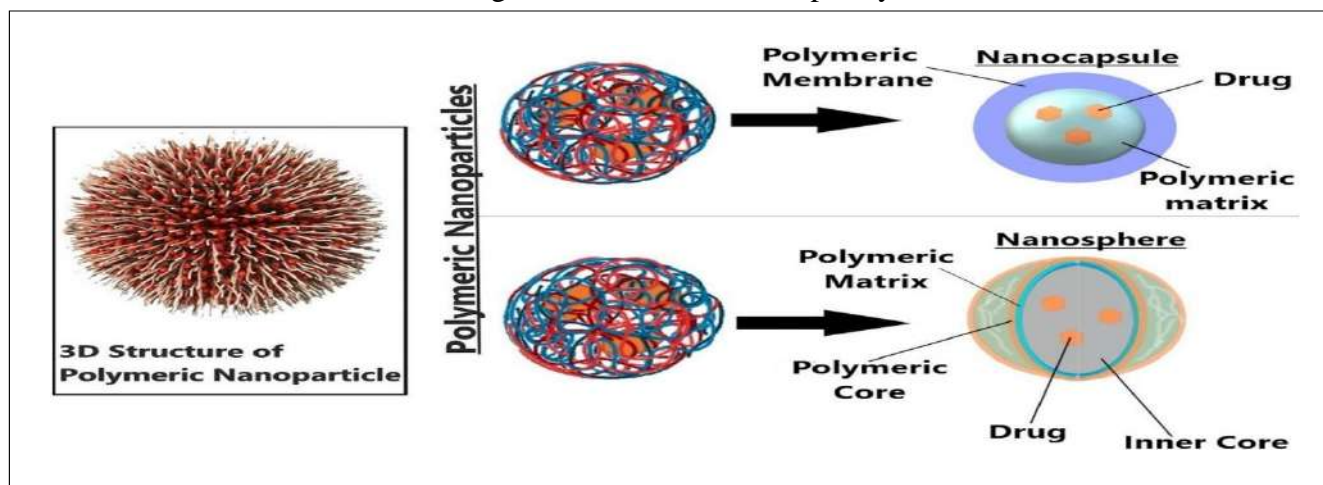
Neodymium doped yttrium aluminum garnet (Nd:YAG) lasers, xws li carbon dioxide (CO₂), argon, and thia b ntau hom lasers frequently used to treat different kinds of malignancies. Additionally, after treatment, laser therapy can evaluate nerve terminals to assist reduce pain [25]. Adoptive antitumor-infiltrating lymphocyte (TIL) treatment has been shown in recent years in clinical studies to be beneficial in causing tumor regression in around 50-75% of patients with multiple myeloma (MM) [26, 27]. Lung, brain, and kidney tumors are among the numerous malignancies that can be treated with this method. In addition, combination treatments, including DC-CIK therapy have shown promise in enhancing overall and relapse-free survival in patients with metastatic breast cancer (Dendritic Cell-Cytokine-Induced Killer). [28]. In 72% of patients with metastatic melanoma, stem cell treatment together with non-myeloablative chemotherapy and whole-body radiation therapy

led to tumor remission. Conversely, tumor regression was observed in 52% of TIL patients who had chemotherapy in addition to non-myeloablative chemotherapy. [26].

Gene therapy

An inserting antisense oligonucleotides, tiny interfering RNA, DNA, and RNA into certain targets or tissues., gene therapies seek to treat illnesses and restore lost functioning. Effective

vectors created to sustain sustained, controlled gene expression without having negative side effects are used to deliver these therapeutic genes [29]. One of the most crucial parts of gene therapy is the creation of bacteria that carry the genes that cells need. to cause apoptosis or stop cancerous rowths, new genes are incorporated into the surrounding tissue or tumor cell by gene transfer, a contemporary method of cancer treatment [3



POLYMER-BASED NPS (PNPS)

Biodegradable or non-biodegradable polymers, which can be natural or manufactured, can be used

1. Nano-spheres:

Generally speaking, drug particles are evenly distributed inside a polymeric matrix system to generate nanospheres. The concentration of the polymer utilized in the production or preparation of the nanoparticles regulates the rate at which the medication is liberated from this polymeric matrix.

2. Nano-hydrogels:

Because of their superior strength and elasticity over conventional PNPs, nano-hydrogels are becoming recognized as a major invention, particularly in the field of cancer theranostics. In essence, these Made of a cross-linked (chemical or physical) polymer network, nanohydrogels are hydrophilic nanoparticles. [31]. Historically, hydrophilic drug delivery has been the exclusive

to create polymeric nanoparticles (PNPs), which have a range of 1 to 1000 nm in size. PNPs are split into two classes, as Figure 1 illustrates use of nano-hydrogels. However, new methods have been devised to integrate these medications into hydrogels since many commercially available pharmaceuticals are hydrophobic [32].

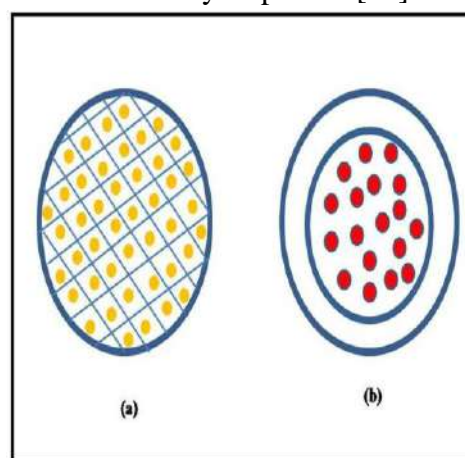


Figure 2. shows two different kinds of polymeric nanocarriers: nanocapsules and nanospheres. The essential oil of the nanocapsule, in which the majority of the medicine dissolves, is encircled by a polymer shell that modifies the drug release profile. The medicine is able to stay in the matrix or adsorb on the surface of the nanosphere structure because of the continuous polymer that makes up that structure.

Following tumor removal, local cancer recurrences can lead to a variety of health issues. After surgery, painkillers can have dangerous adverse effects. But because of their exceptional flexibility, biodegradability, biocompatibility, and multifunctionality, nanohydrogels have garnered a lot of interest as a potential platform for local cancer therapy. Furthermore, there are a lot of benefits to using nano-hydrogel composite systems for building hierarchical structures that improve the synergistic effects of combination treatment and enable the regulated multistage release of different medicinal substances [33,34]. When compared to other forms of nanoparticles, polymeric nanoparticles (NPs) have a number of advantages, including water solubility, biodegradability, non-toxicity, cost-effectiveness, ease of integration, and high shelf life [35]. The term "shelf life" describes the amount of time that polymeric nanoparticles (PNPs) are appropriate for sale, use, or consumption. The stability of PNP is influenced by several key parameters, including as temperature, pH, light exposure, molecular weight, and nanoparticle size. By reducing instability in suspension, lyophilization is used to improve PNPs' long-term stability for drug delivery applications. Using the right cryoprotectants and molecular imaging can help overcome restrictions and increase shelf life. Tumor-targeting ligands and other small compounds are frequently added to PNPs to help in target identification. Polyether block polymers are used in ultrasonic medication delivery from micelles. Ultrasound breaks down cavitation

bubbles to produce shear stress and shock waves that liberate medication from micelles. The nanoparticles can enter tumor tissue because of their modest size. The multitude of medications and genes that may be noninvasively administered to specified tissues makes ultrasonic delivery of pharmaceuticals and genes from nanocarriers extremely promising. Therapeutic or imaging agents are usually conjugated on the surface, or they are adsorbed or dispersed uniformly inside the pores or polymeric matrix of nanosphere systems. Alternatively, theranostic drugs are contained within an oily or aqueous cavity in nanocapsules, which have a core-shell structure and are protected from the outside world by a polymeric compartment. Important variables influencing the release of nanocapsules include the thickness and permeability (pore size) of the shell as well as the characteristics of the inside substance. Typically ranging in size from 10 to 100 nm, nanomicelles are spherical formations made up of self-assembling amphiphilic molecules with both hydrophilic and hydrophobic regions. Reverse micelle structures, including a hydrophobic crown and a hydrophilic core, can be formed by nanomicelles when their concentration above the critical micelle concentration (CMC). Hydrophilic polar heads make up the corona layer of nanomicelles in aquatic environments, whereas hydrophobic tails make up the inner core. Micelles' hydrophilic tails make them more soluble in the surrounding water, while their hydrophobic portions use hydrophobic interactions to bind hydrophobic substances like medicines. Different techniques (e.g., oil-in-water alone/double emulsions, dialysis, film casting, direct detonation) can be employed, depending on the molecular weight and solubility of the copolymer blocks composing the core and corona. can be used to manufacture micellas of varied sizes and forms. Premature drug release from micelles can occur as a result of interactions or absorption by circulating

plasma proteins. Cross-linked polymer micelles have been created as a solution to this problem [36,37]. Site-specific ligands can be added to the surface of micelles in cancer theranostics to enable active tumor targeting. Furthermore, stimuli-responsive substances can be used to functionalize the corona or core of micelles, allowing them to carry an anticancer medication at a certain concentration for regulated or triggered release. This system generates signals within the body and initiates medication release in response to pH changes, enzyme transformation, temperature differences, or redox processes [38, 39]. PNPs' distinctiveness is the main reason for their increasing significance over alternative delivery systems, which begs the issue of why. By means of surface engineering or modification, PNPs can increase their targeting efficacy by demonstrating a greater affinity for target organs, tissues, cells, or organelles. PNPs also work well as sustained or controlled drug delivery systems (DDS), delivering medications gradually and under strict supervision over long periods of time. The capacity of PNPs-based drug delivery systems (DDSs) to control drug release has been thoroughly studied, regardless of whether they take the shape of nanospheres or nanocapsules. Systems for sustained medication administration based on PNPs are an improvement over traditional drug delivery techniques. They guarantee a stable and sufficient medication concentration in the blood and cells, therefore removing the need for frequent dosage adjustments and meeting specific body needs. These PNPs are biocompatible and biodegradable; their unique geometries and surface features allow them to target specific locations for drug administration, extend the duration of circulation, and lessen the physiological or biological effects that infections in the body may produce. Particularly in targeted delivery technologies that effectively transport different chemotherapeutic

agents, diagnostic tools, multimodal imaging agents, and drug or gene delivery systems as part of the next-generation drug delivery systems, PNPs-based sustained drug delivery systems hold considerable therapeutic potential. Nanotechnology holds the potential to transform cancer research in both diagnosis and treatment, despite the fact that polymer assemblies for medicines are mostly focused on tumor therapy. Among other cancer treatments, PNP-based nanomedicines can be utilized for photodynamic therapy, targeted drug delivery to tumors, and generation of hyperthermia [40]. Materials based on polylactic-glycolic acid (PLGA) copolymers are frequently employed in these systems. This idea has to do with how PLGA nanoparticles (NPs) work and how they are directed toward tumor locations. There is also discussion of many multimodal strategies that improve NP accumulation and treatment effectiveness. The wealth of research on PLGA NPs in cancer treatment highlights their promise as efficient drug carriers and encourages more translational studies in this area [41]. Among the greatest biodegradable polymer nanoparticles (NPs) is PLGA. Its natural breakdown, minimal toxicity, controllable and prolonged release, and compatibility with tissues and cells have led the US FDA to allow its usage in drug delivery systems (DDS). Features of PLGA NP goods' design and technology, anti-cancer medications, cancer or cancer, and different release techniques. The result is a perfect illustration of ongoing progress. The promise of PLGA NPs in the treatment of cancer is demonstrated by their great effectiveness and a few negative effects. [42].

VARIOUS NANOCARRIERS APPLIED TO DRUGS DELIVERY

1. Organic NPs:

The development and study of nanoparticles (NPs) utilizing organic components including lipids, proteins, carbohydrates, and other



organic substances has been going on for a number of years. In addition to dendrimers, polymer-based NPs, liposome-based NPs, and organic NPs are widely employed in cancer therapy.

2. Inorganic NPs:

Because of the nature of their central core, nanoparticles (NPs) made of inorganic materials such as ceramics, carbon, magnetic materials, quantum dots, gold (AuNPs), and have special optical, magnetic, electrical, and fluorescent capabilities [43].

3. Hybrid NPs:

In order to improve the effectiveness of cancer treatments and reduce drug resistance, several types of nanoparticles (NPs) are combined to generate multifunctional features inside single nanoplateforms. To create hybrid NPs, a common method is to combine native biomaterials with either organic or inorganic NPs. For instance, naturally existing cell membranes can be coated on either organic or inorganic NPs to provide hybrid NPs instant biological characteristics and increase the efficacy and security of traditional NPs [44].

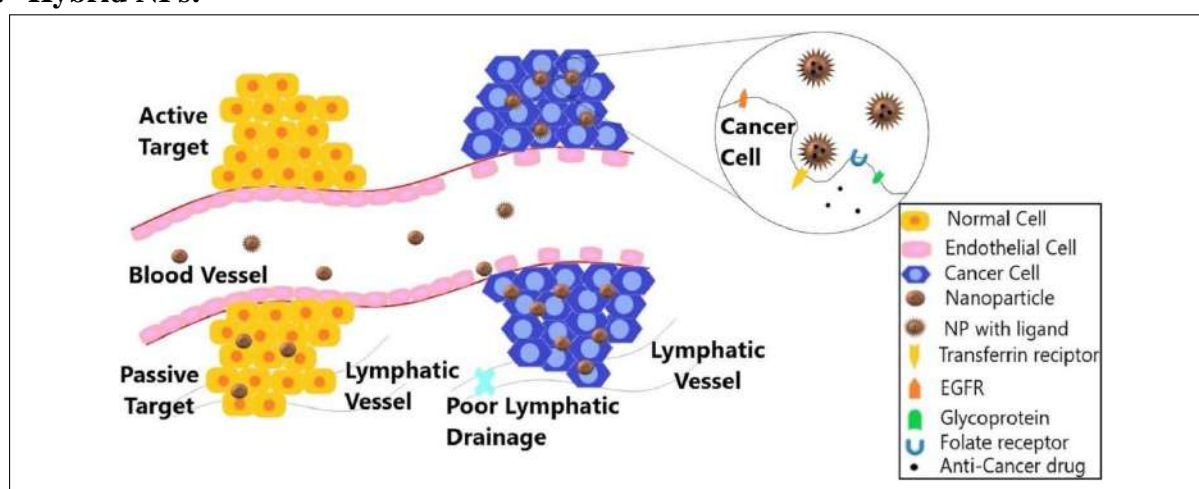


Figure 3. shows how targeting systems are often divided into two categories: active targeting and passive targeting.

TARGETED DRUG DELIVERY (TDD)

Targeted drug delivery, or TDD, is a technique that increases the concentration of therapeutic medications or agents in relation to other regions of the patient's body at specified places, such as illness sites or afflicted areas [45]. The main obstacle to systemic medication delivery is the lack of pharmacological selectivity towards diseased target sites. This causes drugs to spread throughout the body and may cause damage to both healthy and diseased cells. Achieving high local concentrations at low doses is necessary to address these problems, improving therapeutic effectiveness and lowering nonspecific toxicity and other side effects linked to greater drug

dosages [46]. As a result, the four steps of targeted drug delivery (TDD)—retention, evasion, targeting, and release of drug molecules to certain target areas—are essential to complete drug development and delivery techniques. Enhancing the medicinal Index (TI) of medicinal compounds by accurate distribution to specific regions is a challenging aim to achieve. Some of these issues have been handled by recent developments in liposomes, prodrugs, gene expression modulation, external targets, and vaccinations. Methods particular to a certain area are increasingly given priority due to scientific developments and a better comprehension of the complexities of delivery

systems. Frameworks including neutrophils, red blood cells, and secretory granules are a few examples. Because they are tiny enough to pass across the blood-brain barrier (BBB), nanotherapeutics potentially solve the long-standing problem of the BBB. Generally speaking, nanoparticles (NPs) are smaller than commercially available nanomedicines, which are generally

Passive targeting

By taking advantage of leaky vasculature and inadequate lymphatic fluid, passive targeting exploits the enhanced permeability and retention (EPR) effect to create nanoparticles (NPs) in tissue. The mononuclear phagocyte system (MPS), which is part of the reticuloendothelial system, is capable of recognizing and eliminating certain microorganisms (drugs) from the bloodstream with ease. One potential long-term delivery mechanism for precisely crafted nanocarriers is the endothelium system's conditioning process and subsequent absorption. Stealthy particles coated with polyethylene glycol (PEG) are widely used to improve the efficacy of medication delivery to specific areas. Different PEGs are used to adjust the thickness of the PEG coating and the efficacy of grafting, with differences in numbers of chains and molecular weights. Longer-chain PEGs interact with the nanocarrier surface more

Active targeting

Because of the shortcomings of passive targeting tactics, efforts are being made to improve NP accumulation using alternate ways. In particular, overexpressed tumor cell surface receptors provide chances for precise targeting and internalization into tumor cells, in conjunction with phagocytosis and endocytosis processes. For instance, active drug delivery systems target the transferrin and folic acid receptors, which are frequently overexpressed in different forms of cancer (DDS). The glycoprotein transferrin, which is connected to cell membranes, is essential for

between 100 and 1000 nm in size. Because of their greater surface area and quantum effects, NPs have special characteristics not seen in bulk materials. These characteristics ultimately impact how NPs behave in vivo. Optimizing the size and structure of nanoparticles enables extended residence times and ideal release schedules [47].

sterically. Another way to modify the surfaces of nanocarriers is by employing various PEG derivatives, such as block copolymers. Furthermore, block copolymers of the poloxamer type are used to modify the surface of nanocarriers. Genexol-PM is a commercially available medication that is a micellar formulation made of a block copolymer based on PEG [46]. Represents the interaction between targeting ligands and receptors, as well as Because of the increased permeability and retention (EPR) effect, both passive and active targets can be reached. Cancer cells have a variety of receptor types, such as transferrin, glycoproteins, folate receptors, and EGFR (epidermal growth factor receptor). Targeting anticancer drug-loaded nanoparticles decreases systemic toxicity and increases the effectiveness of cancer treatment.

controlling cellular development and iron absorption. To promote iron absorption, the transferrin receptor helps internalize transferrin that is linked to iron. Similarly, the folic acid receptor permits the administration of medications that are specific to malignancies. Studies show that when cancer progresses, the density of folic acid receptors rises. In addition to tumor-specific indicators, active targeting can take advantage of mechanisms involved in the formation of tumors, such as neoangiogenesis [46].



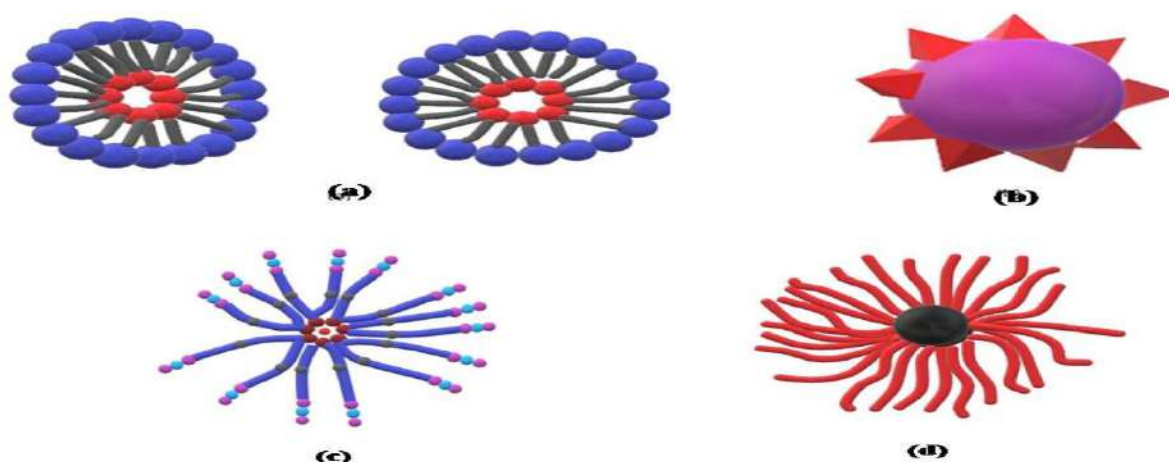
The characteristics of nanocarriers and NPS

Generally speaking, nanoparticles (NPs) are tiny enough to be injected intravenously or locally (mucosally) and diffuse into cancer cells. They have the ability to transport medicines and exhibit cytotoxic characteristics [47]. The size, shape, hydrophobicity, surface charge, and biological interactions of CTX nanoparticles (NPs) can all have a major impact on their characteristics, including how they affect intravascular flow and organ accumulation. Nanoparticles used in imaging, diagnostics, and therapy that are smaller than 200 nm, the diameter of microcapillaries, are used. The ideal particle size for cancer therapy is usually in the region of 20 to 50 nm. These particles exhibit enhanced tissue dispersion, wide effective surface areas, compatibility with many delivery methods, longer circulation durations, and excellent efficiency in integrating both hydrophilic and hydrophobic compounds [48, 49]. A number of variables, including size, shape, zeta potential, drug loading capacity, and surface activity with ligands, influence the characteristics of nanoparticles (NPs) [50]. The distribution and absorption of NPs are influenced by their zeta potential. Negatively charged plasma proteins interact with cationic particles to produce reduced circulation times and insufficient accumulation

within tumors [51]. Nanoparticles (NPs) have the capacity to target cancer cells directly, eliminating tumor cells with precision while causing the least amount of harm to healthy organs. They are useful delivery vehicles for drug-loaded ligand-conjugated nanocarriers because of their variable efficiency in targeting tumor cells based on their type and the formulation additives used [52, 53].

POLYMERIC MICELLES

In aqueous medium, Self-assembling amphiphilic di- or tri-block copolymers can form nanoscale spherical cores or shells. structures, generating polymeric micelles. Anticancer medications can be encapsulated in the copolymer's hydrophobic core, while the micellar system's hydrophilic exterior gives it stealth characteristics. This stealth characteristic lengthens the bloodstream's circulation duration by preventing absorption by the reticuloendothelial system. Compared to surfactant-based micelles, polymer-based micelles are more stable and have reduce the crucial micellar concentration values (usually in the range of 10^{-6} M) [54, 55]. Current clinical research has demonstrated the effectiveness of micellar-based anticancer medication formulations as possible carriers in oncology therapy [56].



Dia 1 .Polymer micelle

ADVANTAGE OF NPS

Properties including form, size, particle material, surface charge, surface coating (such PEGylation), and targeted ligands are what define nanoparticles (NPs) employed in chemotherapy [57,58]. Using NPs instead of conventional chemotherapeutic methods has the following benefits:

- A. Because of their huge surface area to mass ratio and ability to elude macrophage absorption, nanoparticles with unique surface coatings have longer half-lives (59,60).
- B. The greater surface area of small-sized NPs increases their efficiency. Their little stature contributes to their effortless passage through the cardiovascular system (59, 61).
- C. Smaller particles are more effective because they can more readily pass through targeted organelles' cell membranes (59, 61).
- D. By improving brain transport across the blood-brain barrier (BBB) for the treatment of brain cancer, nanocarriers may be able to increase the therapeutic benefits and decrease the negative effects of medication (62).
- E. Following intratumoral injection, drug oligonucleotides are severely degraded by enzymes such as endonucleases and exonucleases, which results in decreased bioavailability. This problem is solved by encapsulation in NPs, which increases their stability until they reach their destination (63).
- F. NPs may be made to target certain cells by adding particular ligands to their surface, which reduces the amount of off-target effects on nearby normal cells (63).
- G. Drug resistance may result from P-glycoprotein (P-gp) overexpression on cell membranes. To solve this problem, new polymers can be applied to NPs (64, 65).

Drug resistance in cancer cells might build over time, requiring greater dosages to get the best possible outcomes.

BACKGROUND OF NANOTECHNOLOGY AND NANOMEDICINE

In 1990, the development of sophisticated instruments led to the growing popularity of nanoscience, a relatively new area, in the medical profession. Prior to these discoveries, theoretical evidence for the existence of incredibly tiny particles that obeyed unique physical rules was put out by Albert Einstein and Max Planck in the early 1900s. Structures as tiny as 4 nm were first found in ruby glass in 1902, thanks to the ultra-microscope Henry Siedentopf and Richard Zsigmondy created. This discovery sparked more scientific curiosity. Ernst Ruska and Max Knoll went on to create the transmission electron microscope (TEM) in 1931, which opened up new avenues for the visualization of nanoscale events. The ability to analyze and work with nanoparticles was expanded with the development of new tools over time, including atomic force microscopes (AFM), field ion microscopes (FIM), instruments such as scanning tunneling microscopes (STM), scanning electron microscopes (SEM), and others. Orio Taniguchi first used the word "nanotechnology" in 1974, which served as an official acknowledgement of this rapidly developing sector. The first lipid-based nanotechnology medication delivery system—later known as a liposome—was created in 1960. This discovery led to a great deal of study into the identification of appropriate nanoparticles for medication delivery systems. When the controlled drug delivery system—often dubbed the "magic bullet"—was first presented in 1976, it caught the interest of academics. Peter Paul Speiser created the first nanoparticle for targeted medication administration in the late 1960s. Since the introduction of polymer nanoparticles in 1994, scientists have investigated several polymers for their synthesis and evaluated the benefits and limitations of each. Due to their many advantages, biodegradable polymer nanoparticles gained



attention fast. These advantages include safety benefits including decreased toxicity, non-allergenicity, and immunogenicity, as well as the ability to break down spontaneously in the body without the need for removal [66, 67].

MERITS AND DEMERITS OF POLYMERIC NANOPARTICLES

Compared to regular nanoparticles, polymeric nanoparticles were created to simplify the production processes. Because of their many benefits, they are the subject of intensive investigation. Because of their greater surface area, these nanoparticles may display more surface functional groups, such ligands. Because of their tiny size, they can easily enter smaller capillaries, which helps with efficient cellular targeting. Furthermore, polymeric nanoparticles provide exact control over their size distribution and size [67]. Compared to ordinary nanoparticles, polymeric nanoparticles have longer clearance periods, which enables lower dosages to produce improved therapeutic effectiveness with less toxicity. They provide high drug loading capacity, easy loading procedures that don't require chemical reactions, and simplicity of modification and control. Furthermore, there are several ways to give polymeric nanoparticles, including oral, intraocular, parenteral, nasal, etc. [68–71]. Although polymeric nanoparticles have many benefits, they also have certain drawbacks. These include possible toxicity from using PVA or other detergents during preparation. It might also be difficult to cease therapy in an emergency. The manufacture of these nanoparticles must be scaled up, which is expensive, challenging, and equipment-intensive.

Anti-Cancer Drugs

Any efficient treatment used to treat malignant or cancerous disorders is referred to as an anticancer drug (sometimes called an antineoplastic agent). These medications fall under a number of general groups, Including herbal remedies, hormones,

antagonists, alkylating agents, antimetabolites, and more medications. Other factors that can be used to categorize them include the type of cancer they treat, cytotoxicity, chemical structure (such as alkylating drugs, purine or pyrimidine analogs, platinum coordination complexes, folate analogs, or protein kinase inhibitors), mode of action (such as alkylating drugs, antibiotics, or chemicals. field modifiers), or other values. Drugs used to treat cancer can have harmful side effects that harm the liver. Anticancer medications can cause liver damage in a variety of ways, depending on the substance being used. Medications such as melphalan, azathioprine, cyclophosphamide, mercaptopurine, and temozolomide, for example, might occasionally result in drug-induced cholestasis. However, it is known that thalidomide, flutamide, and bicalutamide might result in acute hepatocellular injury. Steatohepatitis can be caused by medications including tamoxifen, methotrexate, and L-asparaginase, however Rather than being the product of unique damage, this pattern may be the outcome of direct poisoning. Antibiotics have also been linked to autoimmune damage that resembles hepatitis or liver disease. Different autoimmune patterns have also been shown by protein kinase inhibitors and monoclonal antibody therapies. Nevertheless, little is known about the fundamental reasons behind these immunological reactions. Furthermore, several anticancer drugs have the potential to exacerbate chronic hepatitis C, reactivate hepatitis B, or accelerate the decompensation of pre-existing cirrhosis.

Alkylating agents: Alkylating drugs, including bendamustine, are used to treat white blood cell malignancies such as chronic lymphocytic leukemia. Trabect is another medication in this class that is administered for different forms of cancer and stops the proliferation of cancer cells.

Antimetabolites: Methotrexate is an antimetabolite used to treat rheumatoid arthritis



that has not improved with conventional therapy, severe psoriasis, and some forms of cancer. Additionally, it is used to treat juvenile rheumatoid arthritis.

Natural products: Dabrafenib, which comes from natural sources, is used to treat some melanomas that are incurable or have spread to other regions of the body. It can be taken alone or in conjunction with trametinib (Mekinist). **Reference: MedlinePlus** After menopause, medications

called hormones and antagonists, such as raloxifene, are used to lower the risk of invasive breast cancer.

Other agents: drugs such as Venetoclax work by assisting in the inhibition or inhibition of the development of cancer cells. Chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), and acute myeloid leukemia (AML) are among the cancer types it is used to treat.

DIAGRAM

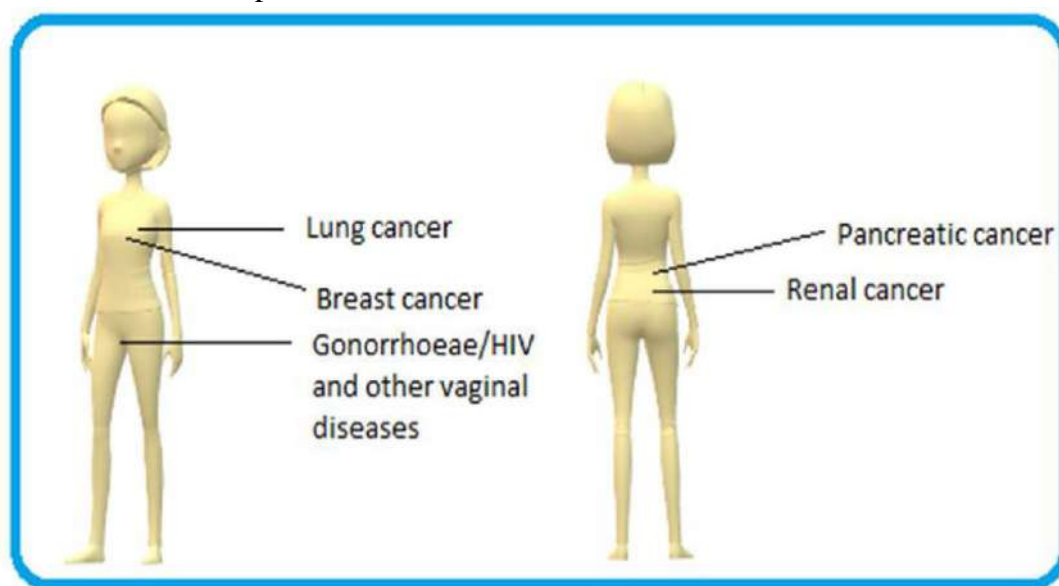


Fig 4. Polymeric nanoparticles are used to treat various tumors and illnesses

PROSPECTS AND DIFFICULTIES FOR THE FUTURE

Polymeric nanoparticles are effective in delivering drugs because of their increased extravasation into tumor tissues. Their adaptability makes it possible to alter them using different ligands and targeting agents, which improves their capacity to bind to certain locations. Polymers are exceptionally excellent medication delivery solutions because of their potential. Technological developments now underway seek to convert polymeric nanocarriers into dual-purpose platforms for therapeutic diagnostics and bio-imaging. In the future, polymers may be developed to evaluate the genotypic phenotypes of patients, allowing for

individualized treatment plans depending on patient traits. Significant obstacles for polymeric nanoparticles include the possibility of hazardous breakdown from leftover ingredients and the danger of excessive buildup that may become poisonous. Polymeric nanostructures are essential in four important pharmacological and therapeutic fields, despite these difficulties. They are crucial in tissue engineering, theranostics, targeted drug delivery systems, and as analytical and imaging instruments. The potential of polymeric nanocarriers in medicine and biological applications is highlighted by their flexibility. Functionalized polymeric nanoparticles could be used in stem cell technologies in the future.

Nowadays, in medication delivery methods, polymeric nanoparticles are often utilized. intended for nucleic acid therapies as well as gene therapy. However, problems with biocompatibility and biodegradability might make creating these polymeric drug delivery systems difficult. Notwithstanding these difficulties, it is anticipated that the broad use of polymers will transform the domains of research, health, and biological applications.

CONCLUSION

A clever drug delivery method is the functionalized polymeric nanoparticle. Numerous polymer variants have been investigated for their safety and efficacious medication delivery to a particular location. The uses of functionalized polymeric nanoparticles are numerous and include gene therapy, cancer treatment, vaginal medication administration, and many more. Functionalized nanoparticles have come a long way in the previous few decades. Some of these developments include magnetic nanocarriers, ligand-based polymeric nanoparticles, target-specific drug release, nanogels, and many more. Notwithstanding the fact that many functionalized polymeric nanoparticles are in various stages of clinical trials, many have reached the market. Therapeutic oncology has found nanocarriers to be a significant new treatment modality. From preclinical to clinical development, polymer-based nanocarriers have proven to have excellent therapeutic promise. The utilisation of polymer-based nanosystems in clinical settings serves as more evidence of the effectiveness of polymeric platforms in delivering anticancer medicines. The polymeric platform's broad capability for functionalization with targeting ligands has to be verified before it can be successfully implemented in clinical settings, even though preclinical testing has demonstrated the effectiveness of these targeted systems. The security of polymers Drug concentrations at the cancer target areas were

ineffectively reached by conventional means. Nematic particles (NPs) have demonstrated the ability to control drug release, target cancerous regions, alter particles, and reduce drug uptake by healthy cells. Not only that, but they might lessen the harmful effects of chemotherapy medications while also improving their effectiveness.

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HOW TO CITE: Rajashree G. Jagtap, Mrunal S. Pagare, Novel Functionalised Polymer Based Nanoparticle Formulation With Anti Cancer Drug, *Int. J. of Pharm. Sci.*, 2024, Vol 2, Issue 8, 2452-2469.
<https://doi.org/10.5281/zenodo.13173238>