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Review

Nanotechnology in Targeted Drug Delivery for Cancer Treatment: A Comprehensive Review of Innovations and Future Applications in Medicine

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Abstract:

This study examines the developments in nanotechnology for targeted drug delivery in cancer therapy, emphasising breakthroughs that maximise therapeutic efficacy and minimise side effects. Conventional treatment approaches for cancer can have severe side effects and low specificity, making it a major worldwide health concern. Through the creation of diverse nanocarriers, such as liposomes, dendrimers, and polymeric nanoparticles, which may precisely target malignant cells while sparing healthy tissues, nanotechnology offers a transformative approach. The processes of both passive and active targeting are covered in the review, along with more recent developments such smart nanocarriers that react to tumour microenvironments. This review intends to provide insights into future possibilities for nanotechnology in medicine by synthesising current research and clinical applications, highlighting its potential to revolutionise cancer therapy and enhance patient outcomes.

Keywords: *Nanotechnology, Nanocarriers, Targeted Drug Delivery, Chemotherapy, Cancer*

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1. INTRODUCTION

One of the worst diseases in the modern world, cancer claims the lives of millions of people annually. It is one of the main health issues of the twenty-first century that knows no geographical bounds and can damage any organ in any person, anywhere. A extremely complicated treatment plan is needed for cancer, which is the unchecked growth of cells in the absence of apoptosis. Clinical variation and resistance to treatment are evident due to the intricacy of both genetic and phenotypic levels. There are numerous methods being used to cure cancer, but they all have some serious drawbacks and adverse consequences. Surgery, chemotherapy, radiation therapy, and hormone therapy are all part of the cancer treatment regimen. Chemotherapy is a highly common treatment that gives patients systemic delivery of anticancer medications to stop the unchecked growth of malignant cells. Unfortunately, numerous adverse effects arise from anticancer medicines' nonspecific targeting, and in most cases, these agents' inadequate drug delivery prevents the desired goal [1-10]. The process of developing new drugs for cancer is extremely intricate and is linked to electronic engineering and sophisticated polymer chemistry. Distinguishing between diseased and normal bodily cells is the primary challenge in cancer therapy. Because of this, the primary goal now is to tailor the medication to recognize cancer cells and inhibit their development and

multiplication. Traditional chemotherapy is unable to specifically target the malignant cells without interfering with the healthy bodily cells. As a result, they have major adverse effects that include organ damage, which makes treatment less effective at a lower dose and ultimately results in low survival rates.

Depending on their intended application, nanotechnology often deals with sizes between a few nanometers (nm) to several hundred nm. Over the past ten years, there has been increased interest in creating precise drug delivery systems since they provide many advantages over traditional formulations, which help them overcome their constraints. Given that it can penetrate tissues at the molecular level, it has great promise for both cancer diagnosis and treatment. A significant advancement in cancer detection, diagnosis, and treatment is indicated by the passionate evaluation and application of cancer nanotechnology. Numerous studies are being conducted to find more precise cancer treatments based on nanotechnology that minimize the negative effects of traditional ones. Therapeutic drugs are presently being developed with the help of nanoparticles to detect molecular changes, facilitate molecular interactions, and help them cross biologic barriers. Compared to macroparticles, they have a higher surface area and adjustable optical, electrical, magnetic, and biologic properties. Presently available drug delivery technologies for cancer treatment based on nanotechnology include liposomes, polymeric micelles, dendrimers, nanospheres, Nano capsules, and nanotubes. These systems are also being researched and evaluated. Two formulations based on nanotechnology that are now on the market are Abraxane (albumin bound paclitaxel) and DOXIL (liposomal doxorubicin).

1.1. Fundamentals of nanotechnology-based drug design techniques

The field of medication known as "nanomedicine" applies the study of nanotechnology to the counteraction and treatment of different illnesses using nanoscale materials, for example, biocompatible nanoparticles and nanorobots, for various purposes, like conveyance, drug conveyance, tangible, or incitation inside something living. Drugs with extremely low solvency have various issues with biopharmaceutical conveyance, for example, unfortunate oral bio-openness, a decreased capacity to diffuse into the external layer, a higher amount required for intravenous mixture, and troublesome secondary effects that happen before the conventional vaccination process. By the by, by using nanotechnology techniques in the medicine conveyance framework, this multitude of limitations may be eliminated [11-17].

Nanoscale drug configuration has been the subject of much examination and is at present the most complex innovation that anyone could hope to find for use in nanoparticle applications because of its possible advantages, which incorporate the capacity to modify properties like diffusivity, immunogenicity, dissolvability, drug discharge profiles, and bioavailability. Thus, there might be upgrades made to the formation of more viable conveyance strategies, decreased poisonousness, less unfriendly impacts, improved biodistribution, and a delayed medication life cycle. The fitted medication conveyance frameworks are intended to deliver remedial mixtures at a particular put under managed conditions, or they are coordinated towards a specific district. They make through a cycle called self-gathering, in which foreordained structures or examples arise naturally from constituent parts. They likewise need to defeat deterrents including the mononuclear phagocyte framework's opsonization/sequestration [18-20].

Medications can be conveyed by nanostructures in two unique ways: latently and precipitously. In the previous, the hydrophobic impact is principally used to integrate drugs into the inside hole of the design. Since the medication is contained in a hydrophobic climate, possibly a little measure of the medication is delivered when the nanostructure parts are focused on to a particular spot. Then again, in the last option case, the meds that are intended to be delivered are formed straightforwardly to the substance of the transporter nanostructure for helpful dissemination. The medicine won't arrive at the objective site in this strategy since it quickly isolates from the transporter; then again, on the off chance that the medication is let out of its nanocarrier framework at the proper time, its bioactivity and adequacy will be diminished. One more significant part of medicine conveyance that utilizes nanomaterials or Nano definitions as dynamic or inactive medication conveyance strategies is focusing of drugs. In dynamic focusing on, drug conveyance frameworks are joined with moieties, including peptides and antibodies, to tie the medications to the receptor structures communicated at the objective district. The created drug transporter complex is headed to the objective site by liking or restricting in uninvolved focusing on, which is directed by variables like pH, temperature, sub-atomic site, and shape. The medication transporter complex courses through the circulatory system. The body's essential targets remember proteins or antigens for cell surfaces, lipid parts of the cell layer, and receptors on cell films. Most of medication conveyance frameworks

intervened by nanotechnology are right now centered around treating disease and tracking down a remedy for it [21-28].

1.2. Cancer Chemotherapy

It is simple to eradicate biological pathogens. How to eliminate them without endangering the host is the key. This is particularly clear when addressing cancer. Although there have been advancements in lung cancer diagnosis and treatment recently, lung cancer is still the most common cause of tumor-related death globally. Globally, gastric cancer ranks second in terms of cancer-related mortality and is the fourth most frequent malignant disease. Chemotherapy frequently fails for numerous unknown causes, making it difficult to objectively assess treatment, wait periods in patients with colon cancer (CRC), and discover clinical and systemic hurdles to treatment, let alone the intricacies of cancer. Anti-mitotic medications and single-cell genomic technologies are examples of recent technical advancements that target the reorganisation of microtubules, which is necessary for healthy cell division and proliferation. Numerous cancer types have demonstrated roles for the epigenetic machinery. Numerous cancer types have demonstrated roles for the epigenetic machinery. The research suggests that chemotherapy can help people with metastatic or recurrent GC live longer and have better quality of life. Ovarian cancer management as a chronic condition is becoming more and more important due to advancements in ovarian cancer treatment over the last ten years.

Figure 1: Chemotherapy:

In the event that a cell is subjected to an external electric field, the extremely resistant membrane will amass charges akin to that of a capacitor. More recently, significant new clinical studies have been initiated by NEK1, the first cloned mammalian NIMA related protein kinase therapeutic discovery in the field of ovarian cancer. Phase II and phase III clinical trials are investigating numerous biologic treatments for recurrent illness. A broad-spectrum anticancer triterpene that demonstrated antiproliferative activities against nearly all of the NCI-60 cell lines at the nanomolar range could be a promising lead molecule for the creation of novel anticancer medications. Anti-angiogenesis is a highly investigated area of cancer care because it plays a crucial role in the survival and invasion of cancer cells. It was anticipated that antiangiogenesis therapy would reduce interstitial fluid pressure, improve drug administration, and normalise tumour vasculature in addition to pruning immature ones. Monotherapy with oxygen is advised for the treatment of advanced colorectal cancer that advances rather slowly. In addition to being the second most common cancer form, breast cancer also accounts for the majority of cancer-related fatalities among women [29-37].

The quality of life of breast cancer patients is impacted by psychological issues such as anxiety, sadness, low self-esteem, and the employment of improper coping mechanisms. Double-Strand Breaks (DSBs) in modern therapies

can be quickly identified by the MRE11-RAD50-NBS1 (MRN) complex or the Ku70/Ku80 heterodimer. The MRN complex facilitates ATM recruitment and activation. Chemotherapy has emerged as a primary therapeutic strategy in recent decades for a number of fatal illnesses that affect humans, including microbial infections. In the adjuvant and relapse settings, dose-dense carboplatin and paclitaxel regimens are being utilised more frequently to treat advanced serous gynaecological cancers (ovary and uterine). In recent times, drug resistance has emerged as a grave concern in cancer chemotherapy, as drug-resistant cancer cells are more difficult to eradicate with the same treatment.

2. NANOTECHNOLOGY

The area of science and designing known as "nanotechnology" is worried about making, fabricating, and applying structures, devices, and situation by the control of particles and atoms at the nanoscale, or with at least one aspects on the request for 100 nanometres (100 millionth of a millimeter) or less.

In spite of the fact that there are a few instances of designs with at least one nanometre aspects in the regular world, and albeit numerous innovations have long utilized such nanostructures coincidentally, it has just had the option to as of late do as such deliberately.

In contrast with similar materials made at greater sizes, a considerable lot of the uses of nanotechnology incorporate new materials with totally various properties and novel results. This is on the grounds that, in contrast with greater particles, nanoparticles have an exceptionally high surface to volume proportion. Furthermore, peculiarities that are apparent at small scopes however not at bigger ones are likewise answerable for this.

Uses of nanotechnology can possibly fundamentally influence society and can be exceptionally gainful. Aside from the industrial sectors that have already embraced it, including the information and communications industry, food, energy, and several pharmaceutical and medical items also use nanotechnology. Additionally, nanomaterials might present fresh possibilities for lowering pollution levels in the environment [37-40].

2.1. Nanocarriers

A nanomaterial that serves as a model for the transport of any material, including peptides, proteins, RNA, medicines, enzymes, immune complexes, and genes, is called a nanocarrier. The adequacy of nano drug delivery systems (DDSs) is confined by extracellular and intracellular hindrances, like mucosal boundaries, cell layers, platelet hindrances, and vague take-up, which impede the way from the delivery framework to the objective cells. For DDSs, a variety of nanocarriers were commonly employed, such as liposomes, niosomes, carbon-based materials, micelles, nanoparticles, and other carriers. As a prospective DDS for Alzheimer's illness, cancer, TB, and antibiotic therapy, nanocarriers have garnered a lot of interest.

Table 1: Physical Properties of Different Nanocarriers

Nanocarrier Type	Average Size (nm)	Drug Loading Capacity (%)	Surface Charge (mV)	Biodegradability (Yes/No)
Liposomes	100-200	5 – 20	-10 to +10	Yes
Polymeric Nanoparticles	50-300	10 – 30	-20 to +5	Yes
Dendrimers	1 - 10	20-50	+10 to +50	Yes
Metallic Nanoparticles	1-100	1 - 5	Neutral	No

A comparison of the physical characteristics of several nanocarriers employed in drug delivery systems is shown in Table 1. Liposomes, which have an average size of 100–200 nm, are biodegradable due to their neutral to slightly positive surface charge and moderate drug loading capability of 5–20%. With a larger surface charge range and a higher drug loading capacity of 10–30%, polymeric nanoparticles, which have a size range of 50–300 nm, are adaptable for a variety of uses. Dendrimers are biodegradable because of their larger size (1-10 nm) and high drug loading capacity (20–50%). They also have a mostly positive surface charge, which improves their interaction with negatively charged biological membranes. Then again, metallic nanoparticles, which range in size from 1 to 100 nm, are frequently less biodegradable and possibly unsafe because of their unbiased charge and lower drug stacking limits (1-5%).

2.2. Types of nanocarriers

- **Liposome**

Liposomes, which range in size from 80 to 300 nm, were the first kind of nanocarriers. They are made of steroids and phospholipids and are spherical in shape. Lipids can be dispersed in aqueous solutions to spontaneously prepare them.

- **Dendrimer nanocarriers**

The components of dendrimer nanocarriers are surface-active groups, dendrons, and a core. The dendrons are joined to the core, and the kind of surface-active groups dictates the characteristics of the nanocarriers.
Dendrimers can bind to a variety of ligands, including PEG, folic acid, antibodies, peptides, and antimicrobial compounds. The chemical and physical characteristics of dendrimers are altered by these additions.

- **Silica materials**

Mesoporous silica nanoparticles and xerogels are two types of silica materials that are utilised as nanocarriers. One well-known silica nanomaterial is MCM-41. Diffusion controls medication release whereas adsorption handles drug loading in these materials.
Recent research has also revealed certain dangerous side effects, such as oxidative stress and the generation of reactive oxygen species in cells, when silica nanoparticles are present. Therefore, more research into the impacts of these silica nanocarriers is necessary.

- **Polymeric nanoparticles**

They range in size from 10−100 nm and are made of synthetic polymers. They can be separated into biodegradable and non-biodegradable categories. Drugs can be conjugated via polymerisation on the surface of these nanocarriers, and they can be released in the target tissue by diffusion or desorption.
The body can hydrolyse biodegradable nanocarriers to produce lactic and glycollic acid. They are also non-toxic, non-thrombogenic, and stable in blood.

3. MECHANISMS OF TARGETED DRUG DELIVERY

Designated drug organization, otherwise called shrewd drug delivery, is a method for directing prescription to a patient such that makes specific region of their body more thought with the drug than others. This delivery strategy is basically founded on nanomedicine, which plans to defeat the weaknesses of conventional prescription organization by utilizing nanoparticle-intervened drug delivery. The reason for these drug-stacked nanoparticles is to target just the region of the body with ailing tissue, staying away from contact with sound tissue. To expand, restrict, target, and have a safeguarded remedial contact with the debilitated tissue is the point of a designated drug delivery framework. Though the designated discharge framework conveys the medication in a portion structure, the customary drug delivery framework includes the drug being retained across an organic layer. The benefits of the targeted release system include a decrease in the patient's dosage frequency, a more consistent drug impact, a decrease in adverse effects, and less variation in the levels of the drug in circulation. The system's expensive cost, which hinders production, and its limited capacity to modify dosages are its drawbacks [41-45].

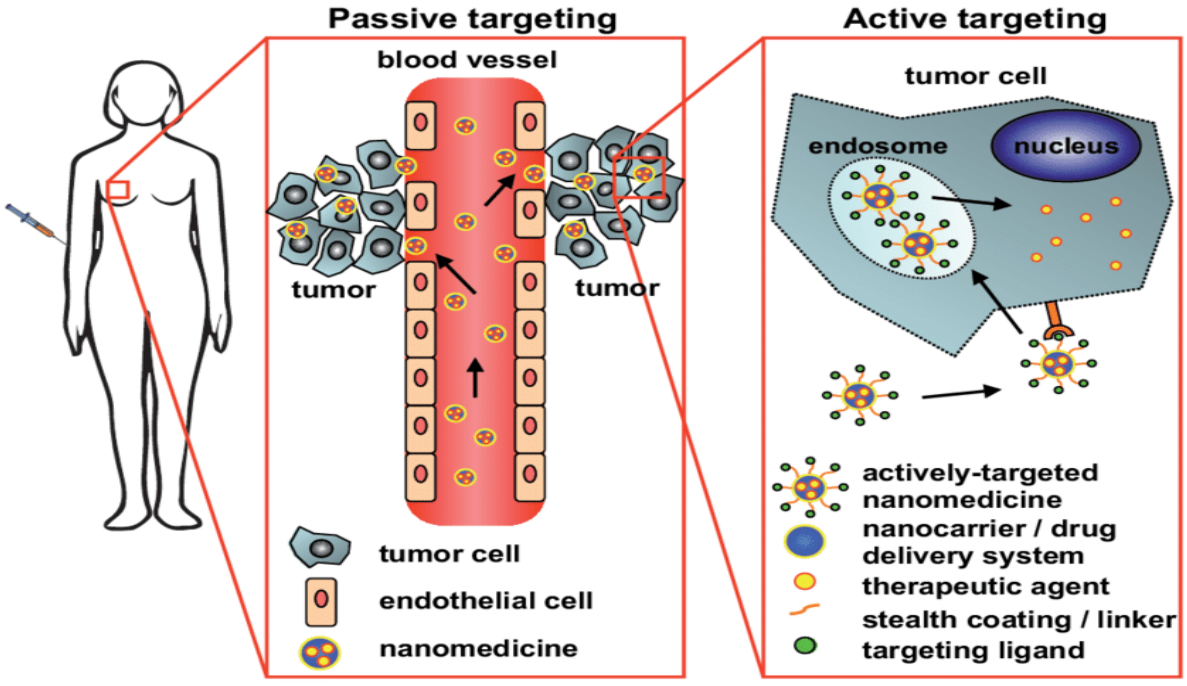

Figure 2: Active and Passive Targeting Targeted Drug Delivery

Systems for the targeted delivery of drugs have been created to enhance regeneration methods. The system is based on a technique that targets a sick location within the body and delivers a specific amount of a therapeutic drug there for an extended length of time. This aids in preserving the body's necessary levels of tissue and plasma drugs, avoiding any potential drug-induced harm to healthy tissue. Because of the high level of integration in the drug delivery system, experts from many fields, including chemists, biologists, and engineers, must collaborate to maximise system performance.

3.1. Passive Targeting Targeted of Drug Delivery

The course of inactive focusing on includes the delivery of prescriptions by nanocarriers by detached dispersion or convection into the growth mesenchyme or cells through the interstices of cancer slender openings. The development of particles inside a liquid is known as convection. Convection takes over as the primary technique for moving most macromolecules through the vascular pore spaces when the net filtration rate drops to nothing. Low-atomic weight substances, then again, similar to oxygen, are generally moved by dispersion.

3.2. Active Targeting of Drug Delivery

To give more exact prescription delivery, dynamic focusing on involves changing specific ligands, antibodies, or different particles on the outer layer of nanoparticles to perceive and stick to specific cells or tissues at the designated locale. For example, antibody-adorned nanoparticles can recognise and bind to particular antigens on the outside of tumour cells, allowing for more targeted drug administration. The four essential classes of dynamic focusing on are aptamer-based focusing on, little atom based focusing on, peptide-based focusing on, and immunizer based focusing on. Through a detour component, the dynamic focusing of nanoparticles in vivo first focuses on the EPR impact prior to showing up at the designated cancer site with surface changes [46-49].

Table 2: Efficacy of Targeting Mechanisms in Clinical Studies

Targeting Mechanism	Number of Studies	Average Tumor Reduction (%)	Adverse Effects (%)	Patient Response Rate (%)
Passive Targeting	15	30	20	50
Active Targeting	20	60	10	70

The effectiveness of the various targeting methods used in clinical trials for cancer treatment is compiled in Table 2. Fifteen trials examining passive targeting produced an average tumour reduction of thirty percent, with side effects occurring in twenty percent of cases and a fifty percent patient response rate. Active targeting, on the other hand, proved to be more effective; according to 20 trials, the average tumour reduction was 60%, the side effects were 10%, and the patient response rate was 70%.

4. INNOVATIONS IN NANOTECHNOLOGY FOR CANCER TREATMENT

Improved medication delivery systems are one of the many novel ways that nanotechnology has brought to cancer therapy.

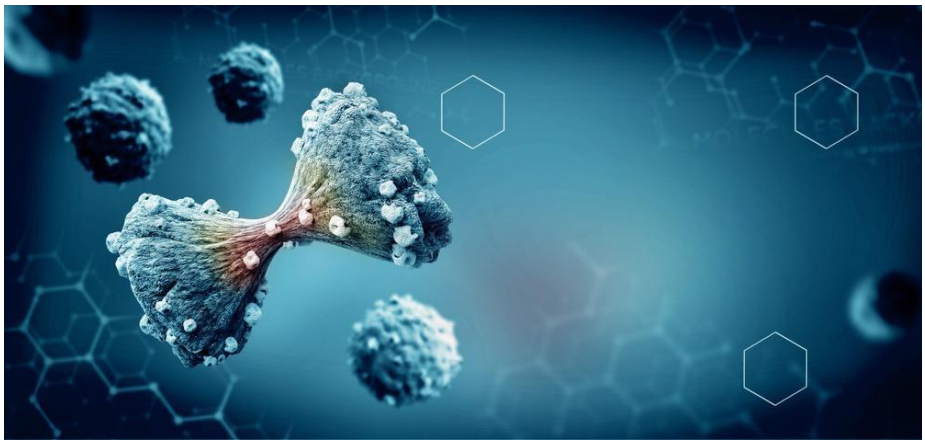

Figure 3: Nanotechnology in Cancer Treatment

Here are some key innovations:

- **Smart Nanocarriers**

Responsive Nanoparticles: These are made to release their payload in reaction to particular stimuli, including light, temperature, or pH, in the tumour microenvironment. This minimises negative effects by enabling focused and regulated medication release.

- **pH-Responsive Nanoparticles:** A lot of tumours have an acidic surrounding. It is possible to modify these nanoparticles such that they release medication when exposed to lower pH values, so assuring that the therapeutic agents are preferentially activated in tumour tissues.
- **Thermo-Responsive Systems:** Certain nanoparticles react to heat, and when exposed to localised hyperthermia (higher temperature), they release their pharmacological payload. With the preservation of healthy tissues, this approach can assist in precisely targeting tumour cells.
- **Light-Triggered Nanocarriers:** Exogenous light sources, such near-infrared light, can trigger these systems, providing accurate spatial regulation of medication release.

➢ **Combination Therapy**

Combination therapies are made possible by nanotechnology, which makes it easier to co-deliver several therapeutic agents and overcome drug resistance. Synergistic effects can be obtained by encapsulating many medications into a single nanocarrier, thereby targeting multiple pathways implicated in the growth of cancer.

➢ **Targeted Delivery Systems**

Active Targeting Mechanisms: One innovation is the attachment of ligands (such as peptides or antibodies) to nanocarriers that bind to cancer cells' overexpressed receptors. This improves medicinal efficacy by increasing cellular absorption.

- **Antibody-Drug Conjugates (ADCs):** These are specific nanocarriers that mix cytotoxic medications with antibodies. By delivering the medication straight to the tumour while protecting healthy cells, the antibody selectively targets cancer cells.

➢ **Improved Imaging Techniques**

Through the creation of multifunctional nanoparticles that can act as both medication delivery systems and imaging agents, nanotechnology has also improved cancer imaging. The simultaneous monitoring of medication distribution and therapeutic efficacy is made possible by this dual functionality.

➢ **Enhanced Biocompatibility and Stability**

Advances in nanocarrier stability and biocompatibility have been the focus of recent developments. For instance, surface modification approaches can decrease immunogenicity and lengthen the period that nanoparticles circulate in the bloodstream, enabling longer drug delivery.

➢ **Personalized Nanomedicine**

Drug delivery systems can now be customised based on the unique characteristics of each patient thanks to nanotechnology. Tailored nanocarriers that optimise therapeutic outcomes and minimise side effects can be designed by analysing unique characteristics of tumours and patient responses.

➢ **Nanotechnology in Immunotherapy**

The delivery of immunotherapeutic drugs via nanoparticles is being investigated as a means of boosting immune responses against tumours. This involves delivering checkpoint inhibitors or cancer vaccines via nanoparticles, which may increase the effectiveness of immunotherapy.

Table 3: Comparison of Responsive Nanocarrier Systems

Responsive System	Trigger Type	Drug Release Rate (mg/h)	Targeted Release (Yes/No)	Clinical Trials (Yes/No)
pH-Responsive	pH Level	1.5	Yes	Yes
Thermo-Responsive	Temperature	2	Yes	No
Light-Triggered	Light Exposure	1	Yes	Yes

Table 3 presents a comparison of different responsive nanocarrier systems that are used for drug administration, emphasising the types and functions of their triggers. Clinical trials have previously shown that the pH-responsive systems, which are intended for targeted release, are successful in releasing medications at a rate of 1.5 mg/h. Thermoresponsive systems—which react to temperature fluctuations—have not yet advanced to clinical trials, but they do have a somewhat faster drug release rate of 2 mg/h and allow for targeted release. On the other hand,

clinical trials have been conducted on light-triggered devices, which have a lower drug release rate of 1 mg/h but allow for precise control over drug administration.

CONCLUSION

In this study, the field of nanotechnology has great promise for the development of more precise and potent cancer treatments. By increasing specificity and lowering systemic toxicity, developments in nanocarrier design and functionality have the potential to greatly improve drug delivery systems. Through the utilisation of both passive and active targeting mechanisms and the creation of intelligent nanocarriers that adapt to the distinct features of tumour microenvironments, scientists are laying the groundwork for novel approaches to treatment. It is possible that further research and practical application of these technologies could change the paradigms surrounding cancer therapy, ultimately improving patient outcomes and quality of life. To fully realise the potential of nanotechnology in oncology, future research should concentrate on overcoming current obstacles like scalability and regulatory barriers.

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