# Importance of Nanomedicines for cancer therapy - Review Article

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**Abstract**

Due to the restrictions of present day most cancers treatments, nanotechnology has been used to expand extra powerful and more secure most cancers treatments. The improvement of nanomedicines has made excellent development in overcoming a number of the issues related to conventional most cancers treatments, including negative drug solubility, negative concentrated on, and drug resistance. As a result of nanoparticle modulation, the pharmacokinetics of the drug may be improved, resulting in higher concentrated on and less facet effects. In addition, nanoparticles can bind to ligands that mainly target most cancers cells. Furthermore, techniques to result in drug launch in tumors via way of means of leveraging tumor traits have proven that they beautify the effectiveness of centered drug delivery. Despite a few medical success, maximum nanomedicines do now no longer attain the clinic. Clinical translation is hampered via way of means of many factors, consisting of layout complexity, incomplete expertise of organic mechanisms, and excessive production demands. Clinical translation can be progressed via means of integrating information from exceptional disciplines which includes chemistry and tumor pathophysiology. Understanding how nanoparticle change influences organic structures is crucial for growing greater powerful nanomedicines. This evaluation summarizes the important thing achievements of nanomedicines, consisting of excessive molecular weight nanoparticles to enhance drug shipping and release, and techniques to conquer drug resistance.

**Keywords-** Nanomedicine, cancer therapy, drug delivery, nanoparticles, chemotherapeutic agents

## 1. Introduction

Cancer is a severe human health issue and the world's leading cause of death. In 2020, an estimated 19.3 million new cases of cancer and approximately 10.0 million deaths are expected, with cancer accounting for roughly 70% of mortality in developing nations. In conventional chemotherapy, cancer cells and normal tissues are both killed, resulting in severe side effects in patients and affecting their quality of life[2]. Cancer develops as a result of the deregulated cell division of an abnormal cell or changes that result in normal cells acquiring abnormal functions. The four most common types of cancer are carcinomas, sarcomas, leukaemia and lymphomas. Cancer, which causes considerable morbidity and mortality worldwide, has recently overtaken heart disease as the leading cause of death worldwide. Lack of access to drugs, adverse side effects, and drug resistance prevented conventional chemotherapy from being effective. A review of recent advances in nano-medicine showed that this field has improved cancer treatment considerably in recent years. Nanomedicine has shown promising results

in a few notable cases for cancer treatment. Notwithstanding the advantages of tumor-targeted delivery systems over standard formulations of cancer drugs, some argue that cancer nanomedicines have not fully delivered on their promise, as the number of nanomedicines that have reached the clinic is considered to be rather low[3]. There is a need for improved technologies since the current treatments are inadequate. The fast expansion of nanotechnology and the development of nanomedicine products has enormous potential for improving cancer therapy techniques. Nanomedicine products provide the possibility of developing complex targeting tactics as well as multi-functionality[4]

## 2. Conventional Treatment Methods

### 2.1 Surgery

Solid tumours are removed as the initial line of cancer treatment. In cases of large tumours, close proximity to other essential tissues, and the development of distant metastases that are high grade cancers requiring support treatment, surgical excision is frequently not recommended.[5].

### 2.2 Radiation therapy

Cancer cells are killed or slowed down by radiation, which damages their DNA. Radiation therapy causes cell damage by damaging the genetic information that regulates cell growth and division[5]. While radiation therapy affects both healthy and cancerous cells, the goal of radiation therapy is to harm as few normal, healthy cells as possible. Radiation-damaged cells can often be repaired by normal cells

### 2.3 Chemotherapy

Chemotherapy refers to the use of drugs to kill cancer cells. Chemotherapy is classified as a systemic treatment because the drug travels throughout the body and can kill cancer cells that have spread to areas of the body far from the original tumour. This distinguishes it from treatments such as surgery and radiation[5]. Surgery involves the removal of a tumour from a part of the body where cancer has been discovered, whereas radiation therapy is directed at a specific area of the body in order to kill or damage cancer cells[6].

### 2.4 Bone marrow transplant

Bone marrow is the tissue that lines the inside of bones and produces blood cells from blood stem cells. A bone marrow transplant, also known as a stem cell transplant, can employ either your own or a donor's bone marrow stem cells. A bone marrow transplant allows doctors to use higher chemotherapy doses to treat cancer. It'll also be utilised to keep sick bone marrow up to date[5].

### 2.5 Immunotherapy

Biological therapy is an immunotherapy treatment that employs the body's immune system to fight cancer. Cancer cannot live in the body because it is not recognised as an invading entity by the immune system. Immunotherapy can assist the immune system in detecting and destroying cancer[7].

### 2.6 Hormone therapy

Some cancers are caused by hormones in the body. Hormones in the body have a role in several malignancies. Breast and prostate cancer are two examples. Cancer cells can be stopped from growing if these hormones are removed from the body or their effects are blocked.
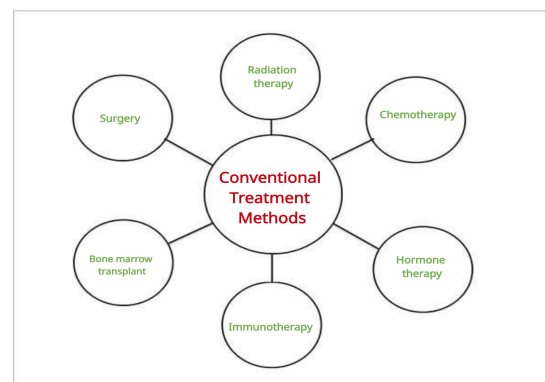


## 3. Limitations of conventional cancer treatment methods

### 3.1 Limitations of chemotherapy

There are disadvantages to chemotherapy, including the toxic side effects, the development of resistance to chemical agents, and the necessity of combining chemotherapy with other treatments to cure an individual. Anemia (low red blood cell count), Fatigue, Hair loss, Skin problems, Boils, Easy bruising, Nausea, vomiting, changes in appetite, constipation, and diarrhea are common side effects caused by chemotherapy[8].

### 3.2 Limitations of radiation therapy

Due to the proximity to the tumor, radiation therapy causes damage to nearby tissues (e.g. lungs, hearts). On 3D models, tumor cells which cannot be seen on imaging scans (e.g. cancer cells near nearby lymph nodes) cannot be treated with radiation therapy.

### 3.3 Limitations of bone marrow transplant

Graft-versus-host disease (allogeneic transplant only), stem cell failure, organ damage, infection, infertility, and new cancers are all possible complications from a bone marrow transplant.

### 3.4 Limitations of hormone therapy

Hot flashes are among the most common complications of hormone therapy, while tamoxifen may cause blood clots, strokes, bone loss, changes in mood, and depression.

### 3.5 Limitations of immunotherapy

The most severe side effects are generally related to inflammation, and can include colitis, hepatitis, pulmonary inflammation, or pneumonitis, kidney failure, a serious infection, serious skin reactions, neuropathy, paralysis, meningitis, or encephalitis[8].



## 4. Nanomedicines For Cancer Therapy

In addition to cancer, other causes of death include stroke and heart disease. While conventional therapies have improved, some limitations remain. In recent years, nanomedicine has rapidly developed into a field that may have the potential to overcome many of the limitations of currently available anti-cancer medications and traditional methods. There is a possibility that nanomedicine will lead to the cure for cancer and could even be the most appropriate way to fight it in the future. New developments in nanomedicine may eventually lead to the development of cancer treatments that are both effective and effective against cancer[9]. Various nanoparticles have been developed in recent years to deliver drugs to tumors, including viruses, lipid-based and polymeric nanoparticles. As a result, there are many variations in shape, size, surface coatings, and material, for example, spherical or rod-like. While most approved nanomedicines rely on passive targeting in order to increase drug specificity, targeted drug delivery has gained attention, and new nanoparticle approaches are developing rapidly. These new approaches have shown promising results. The research program faces a wide array of challenges, ranging from design difficulties to limitations in translation into clinical practice. In numerous therapeutic areas, nanoparticle drug delivery systems are being studied to overcome limitations of conventional oral dosage forms, including cancer chemotherapy, where the majority of anticancer drugs have harmful side effects. In cancer chemotherapy, nanoparticle drug delivery systems such as folate-mediated targeting and transferring targeting are the most studied[10].

The sizes, shapes, and surface features of nanoparticles employed in medical treatment are generally unique because these three variables have a significant impact on the effectiveness of nano-drug delivery and hence govern therapeutic efficacy. Nanoparticles having a diameter of 10 to 100 nm are commonly used in cancer therapy because of their ability to efficiently carry medicines. Smaller particles (less than 12 nm in diameter) can easily leak from the normal vasculature, causing harm to normal cells, and can be quickly filtered by kidneys (less than 10 nm in diameter), but particles bigger than 100 nm are more likely to be cleaned from circulation by phagocytes. Nanoparticles coated with hydrophilic molecules like polyethylene glycol, for example,
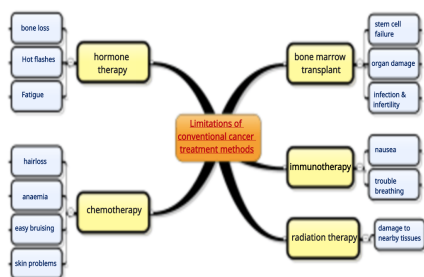
are less likely to be rejected by the immune system. As a result, nanoparticles are frequently changed to become hydrophilic, extending the duration in circulation of medications and improving their penetration and accumulation in tumours. Nanoparticles' therapeutic impact in cancer therapy is determined by their numerous features taken together[5][9].

## 5. Factors Influencing the Targeting of Nanomaterials

Nanoparticles may be changed in quite a few ways, which includes converting their size, shape, chemical and bodily properties, and so on, to programme them to goal precise cells.

### 5.1 Size

Biological behaviour of the nanoparticle is partly dependent upon the size of the nanoparticles. Nanoparticle with size scale 40–60 nm can more readily bind to cells and elicit endocytosis than particles less than 40 nm in diameter. Hence by fine tuning of particle size, it is possible to direct them for accurately inhibiting different pathways and specific targeting to cancer cells without adversely affecting the normal cells[5].

### 5.2 Shape

Several studies based on the shape effect on endocytosis revealed that endocytosis of non-spherical particles are dependent on the local shapes that are made at the interface of the cells with nanomaterials.

### 5.3 Surface charge

Properties of nanomaterials can be further enhanced by conjugating with different moieties on their surface. The biomoieties includes ligands like folic acid, thiamine, antibodies specific to cancer cells, proteins (transferring, lectins, and cytokines), polymers (Poly ethylene glycol), polysaccharides (oligosaccharides), fatty acids (palmitic acid, phospholipids), aptamers (synthetic molecules of DNA or RNA), siRNA, plasmid etc. Increase in

charge of the nanomaterial has an important role in tubular reabsorption by kidney[5][11].

## 6. Nanoparticle uptake and drug delivery

In recent decades, we've seen an enormous increase in the use of nanotechnology in medicine, including applications for diagnostics, treatment, and tumour targeting that are safer and more effective.Drug delivery systems based on nanoparticle technology have shown a number of advantages in cancer treatment therapies, including good pharmacokinetics (the kinetics of drug absorption, metabolism, and elimination), precise targeting of tumour cells, and reduced side effects. Originally developed as nano-carriers, nanoparticles are used for cancer therapy through the carrier effect of the nanoparticle and the positioning effect of the targeting substance after they are absorbed. In order to kill the tumour cells, the nanomedicines are transferred to the target tumour cells and release their drugs there. In addition to traditional chemotherapy agents and nucleic acids, nano-carriers may contain nucleic acids. Both cytotoxic and gene therapy drugs can be derived from these nanoparticles. Nucleic acids and traditional chemotherapy agents are among the drugs that are inside the nano-carriers. They can both be used in cytotoxic and gene therapy. Nanoparticles have been found to serve as drug delivery systems in three different ways: organic nanoparticles, inorganic nanoparticles and hybrid nanoparticles[12].

### 6.1 Organic Nanoparticles

Polymer-based nanoparticles, liposome-based nanoparticles, and dendrimers are all examples of organic nanoparticles. Organic nanoparticles include polymer-based nanoparticles, liposome-based nanoparticles, and dendrimers. Liposomes, the first nanoscale medicine, entered clinical trials in 2004. Liposomes are the first nanoscale medicine to receive Food and Drug Administration approval for use in humans. Inside a lipid core, liposomes hold either hydrophobic or hydrophilic medicines. Liposomes conduct a range of activities by modifying the outer lipid layer. Anticancer treatments such as doxorubicin and paclitaxel (anticancer chemotherapeutic agents) as well as nucleic acids can be delivered in vivo using liposomes. Liposomes are in vivo delivery vehicles for chemotherapeutic medicines and nucleic acids, such as doxorubicin and paclitaxel, rather than

causing toxicity (anticancer chemotherapeutic drugs).

Dendrimers are another type of polymer that has been employed in nanomedicine. They are biocompatible macromolecules with a three-dimensional branch structure that makes them adaptable. Dendrimers are employed as dendritic boxes and unimolecular micelles (dendrimer-drug networks) primarily for the inclusion of hydrophobic/hydrophilic molecules into their empty cavities (nanoscale containers) existing surrounding the core through host guest interactions[12][13]

### 6.2 Inorganic Nanoparticles

Gold, carbon nanotubes, silica, magnetic, and quantum dots are examples of inorganic nanoparticles that have been synthesised for medication delivery. The surface area to volume ratio of inorganic nanoparticles is greater. Gold nanoparticles are the most commonly researched inorganic Nanoparticles because they are nontoxic and inert. The gold cores have been shown to increase drug accumulation and overcome treatment resistance in tumours. Carbon nanotubes are biologically, physically, and chemically distinct. They've been found to have a lot of promise in the medication delivery sector because of their qualities. They're employed to deliver doxorubicin, paclitaxel, and methotrexate siRNA, among other medications. Silica nanoparticles have completely changed the way drugs are delivered. These nanoparticles are regarded as one of the most effective medication delivery vehicles due to better pharmacokinetics and treatment efficacy. Metal and metal oxide nanoparticles are magnetic nanoparticles utilised in medication delivery systems. Organic compounds, such as polymers and fatty acids, are used to coat them[12][13].

### 6.3 Hybrid Nanoparticles

Organic and inorganic nanoparticles are combined to create hybrid nanoparticles. Because of their superior biological features, they are known as multifunctional carriers. Lipid-polymer nanoparticles combine the properties of liposomes and polymer nanoparticles. An inner polymeric core and a lipid shell make up these. A frequent way of Nanoparticle design is to combine organic and inorganic hybrid nanomaterials. The invention of dual-membrane coated nanoparticles might help

Nanoparticles perform even better. Erythrocyte-platelet hybrid and erythrocyte-cancer hybrid membrane-coated nanoparticles, for example, have been shown to have greater stability and circulation life[12][14].
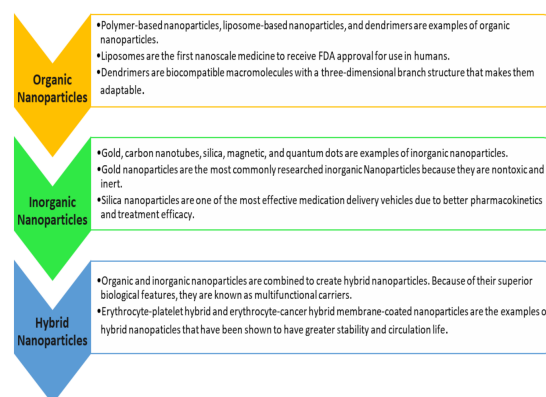


## 7. Overcoming drug resistance

Cancer cells can develop the ability to reprogram to become resistant to treatments that were previously effective. Drug resistance is responsible for many cancer recurrences and deaths. There has been progress in understanding drug resistance from the last ten years. Still there is a knowledge gap in understanding biological causes of drug resistance and the design of cancer treatments to overcome it. Drug resistance can be categorized in two forms, intrinsic or acquired resistance based on the time when it is developed. Intrinsic resistance exists before drug treatment while the acquired resistance is induced after therapy. Nanoparticles can prevent drug resistance by delivery of multiple drugs or siRNAs. The co-delivery of doxorubicin and siRNA to silence B-cell lymphoma 2 drug resistance genes was successfully achieved by targeting the epidermal growth factor receptor on cancer cells. Compared to mice that were treated by doxorubicin alone or with siRNA alone, lung tumors treated with co-delivery were twice as small, suggesting more effective suppression[12]. Drug efflux or reduced uptake caused by overexpressed transmembrane transporters is a common cause of multidrug resistance. It has been suggested that nanomedicines' increased efficacy in multidrug resistance is due to their different uptake mechanisms. Unlike free drugs, targeted nanoparticles are taken up by endocytosis, which improves cellular uptake and circumvents drug efflux mechanisms. In order to develop the best nanoparticle design to treat chemo-resistant tumors, we must be familiar with each patient's specific

multidrug resistance mechanism. It will be very challenging to identify the best strategy to overcome drug resistance due to the high heterogeneity of tumors in patients and the high complexity of tumor progression. For treating the problem of drug resistance, current strategies involve continuous monitoring of patients and the use of chemotherapeutics target drugs, each of which targets a protein encoded by a driver gene responsible for drug resistance pathways.It is possible to overcome resistance by cutting off the supply of energy to tumour cells. Tumors may avoid mechanisms, but they cannot avoid the need for energy for growth, proliferation, drug resistance, cell migration, and other processes. The tumor microenvironment is shown to play a very important role in tumorigenesis and drug resistance in new cancer research. It has been suggested that the tumor microenvironment factors contribute to intrinsic resistance to anticancer therapies. One of these factors is pH. In normal tissues and cells, the extracellular pH is usually slightly higher than the intracellular pH. Furthermore, the earlier a tumor is detected, the lower the heterogeneity of tumor cells, as well as the lower the drug resistance and the higher the likelihood of treatment success. Preventing cancer and detecting it early should be considered at least as important as treating it at an advanced stage[12][15][16].

## 8. Generation progress of nanomedicines
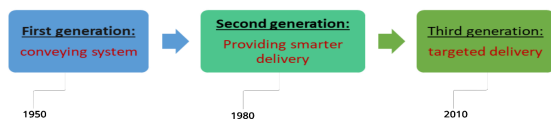


## 9.  First Generation Cancer Nanomedicine

Nanomedicines developed in the first generation consist of improving the function of certain organs. Some commonly used, highly hydrophobic chemotherapy drugs such as paclitaxel, doxorubicin, and others can be made more bioavailable and more toxic by using this technique.

### 9.1 Polymers:

Polymers offer increased shelf life in addition to superior drug release qualities, making them suitable for nanoparticle manufacturing. Polymeric nanoparticles are divided into two categories: natural and synthetic polymers. Polylactic acid, polyglycolic acid, polylactic glycolic acid, and polycaprolactone are among the polymeric compounds accessible. Polyethylene glycol, a polymer, has also been widely researched for drug delivery applications. In phase III clinical studies for the treatment of lung cancer, Xyotax demonstrated promising results[17][5].

### 9.2 Liposomes:

A liposome is a colloidal nanostructure made up of lipid bilayers that surround a core aqueous region that is encircled by the outer lipid bilayers. The anti-cancer drug cisplatin showed better effectiveness in liposomes coupled with antibodies. Liposome-mediated siRNA is also being used to treat juvenile cancers such as neuroblastoma and chronic myeloid leukaemia. In addition, liposome-mediated RNA delivery has been shown to be successful in treating melanoma, lung cancer, breast cancer, and ovarian cancer in adult patients[5][8].

### 9.3 Dendrimers:

Widely studied dendrimers are complex molecules with branched structures that are evenly distributed over the surface. Dendrimers have a variety of sizes, shapes, and pharmacokinetics based on the number of generations, core and branch chemistry, and surface functional groups. The dendrimer has many uses, increased solubility, photodynamic therapy, drug delivery, bioimaging, and cancer treatment. Dendrimers combined with gold nanoparticles have been used to fight cancer cells in various molecules such as folic acid[5][18].

### 9.4 Micelle:

In micellar spheres, amphipathic diblock or triblock copolymers self-assemble into small spherical particles with a size of 1-100 nm. The size of micelles is determined by the chemical nature of the drug and its micelle nuclei. Most anticancer drugs have low bioavailability after oral administration due to poor absorption, and most of these drugs should be prescribed for intravenous administration. Micelles can attach to tumour cell membrane receptor-specific ligands to induce internalisation. Polymer micelles provide a number of benefits over conventional drug delivery technologies. Micelles are utilised to transfer medications across the lymph veins of the skin by easy extravasation from blood arteries to tumour tissue due to their tiny size[5].

### 9.5 Virus:

Viruses are considered natural nanoparticles and have been extensively studied for use in the treatment of cancer. The main advantages of viral nanoparticles over synthetic nanoparticles include accurate dimensions, potential immune system bypass, biocompatibility, and biodegradability.

### 9.6 Carbon nanostructures:

Carbon nanotubes (CNTs) are nanomaterials made of ordered carbon graphite. Therapeutic agents can bind to CNTs via non-covalent and shared interactions. CNTs are also used to kill cancer cells by combining thermal ablation with high frequency and laser treatment.
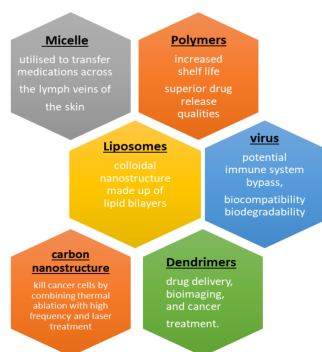


## 10. Second Generation Nanomedicines

Nanocarriers were created as a second-generation nanomedicine approach to selectively target cancer cells while causing no damage to healthy cells. When nanoparticles are created right, it is feasible to amass them within tumour tissues. Targeting the primary mechanism of medication resistance has been demonstrated to be useful in cancer therapy. Chemosensitizers, active targeting components like folate receptors, and nanocarriers holding cancer treatments are all part of the future generation of nanomedicine. This section examines the many cancer treatment options[5][18].

### 10.1 Targeting aberrant cancer kinome

New generation cancer nanomedicines target an aberrant cancer kinome. Nanomedicine is an advanced therapeutic approach for inhibiting deregulated cancer kinomes simultaneously.We created a polymer protein core shell nanomedicine that suppresses Adult acute myeloid leukemia - related prosurvival kinases like mitogen-activated protein kinase , and Signal transducer and activator of transcription 5. The construct's shell is around 25 nm thick and contains a mitogen-activated protein kinase inhibitor similar to sorafenib. To surface coat the whole complex and the nanomedicine with the antibody, monoclonal antibodies targeting the CD33 that is sialic acid binding Ig-like lectin 3 receptor were utilised. Immunoblotting, cytotoxicity, and apoptosis experiments have all shown that inhibiting many key kinases at the same time causes synergistic lethality in leukemic cells. This multi-kinase targeted nanomedicine was proven to be more selective and tolerated than the present clinical regime of cytarabine and daunorubicin[19].

### 10.2 Nanoparticle mediated gene silencing

A key focus of research is developing new therapies to more effectively halt tumor growth and prevent recurrence of tumors as well as combining them with conventional therapies. Genetic regulation holds promise in achieving these objectives. Double-stranded RNAs cause RNA interference RNAi, a powerful gene-silencing phenomenon. The RNA-induced silencing complex binds to siRNA once it has been introduced into a cell, which then aligns the siRNA with perfectly complementary transcribed mRNA to facilitate its degradation and prevent protein translation. As a quality guideline system, the RNAi pathway enjoys a few benefits. Generally, siRNA-intervened quality guidelines hold extraordinary guarantees as

a therapy for an assortment of diseases[20]. Despite the fact that there are still some unsettled difficulties to viable siRNA conveyance, ongoing exploration with nanoscale transporters has shown the capacity to conquer these difficulties, and we have featured a couple of these transporters here. While some siRNA nanocarriers are presently entering clinical preliminaries, continuous exploration will keep on advancing material plans to further develop siRNA conveyance to growths for powerful quality quieting. These siRNA nanocarriers could be utilized to further develop cancer annihilation and patient endurance later on.

### 10.3 Targeting tumor angiogenesis

We created a polymer protein core shell nanomedicine that suppresses Adult acute myeloid leukemia - related prosurvival kinases like mitogen-activated protein kinase, and Signal transducer and activator of transcription 5. Everolimus, a mTOR inhibitor, is placed into a poly lactide co glycolide core in nanomedicine. To surface coat the whole complex and the nanomedicine with the antibody, monoclonal antibodies targeting the Siglec-3 is a transmembrane receptor were utilised. Immunoblotting, cytotoxicity, and apoptosis experiments have all shown that inhibiting many key kinases at the same time causes synergistic lethality in leukemic cells. There are multiple redundant pathways involved in angiogenesis that offer investigators new therapeutic strategies [21].This multi-kinase targeted nanomedicine was proven to be more selective and tolerated than the present clinical regime of cytarabine and daunorubicin.

### 10.4 Brain targeting

Only a few substances can flow past the blood-brain barrier and into the brain's cerebrospinal fluid. Even though the integrity of the blood-brain barrier is disturbed during tumour growth, nanoparticles smaller than 15 nm have been shown to penetrate the brain. The uptake efficiency of nanoparticles is found to decrease exponentially. The use of nanoparticles conjugated with lipophilic moieties such as Apolipoprotein E may be a successful way to mediate the clotting process brain barrier passage as well as liver hepatocytes trafficking[22].

### 10.5 Lymphatic system

Metastatic spread can also occur through lymphatic vessels, and in such cases the patient's survival rate is poor. As a result, a number of researchers have focused on lymphatic dispersed cancer cells. In recent investigations, dextran-coated iron oxide nanoparticles accumulated in lymph nodes. The particle size has an impact on lymph node targeting as well. When injected subcutaneously, particles having a diameter of less than 80 nm can migrate to lymph nodes.

## 11. Targeted Delivery of Nano-Drug Carriers

Traditional chemotherapy drugs can kill tumor cells with high efficiency, but they also cause toxic side effects on normal tissues as a result of their lack of specificity, while nanotechnology provides a new opportunity for tumor-targeted therapy. In the near future, it is possible to identify cancerous tissues more accurately in complex organisms and release anti-tumor drugs to cancerous tissues without causing toxic side effects on normal tissues by using nanoparticles. All three methods can transport anti-tumor drugs through the body: passively, actively, and physically and chemically[23].

### 11.1 Passive Targeted Transport

As a result of passive targeting, also known as permeation and retention effect(EPR), the drug is swallowed by macrophages as a foreign body immediately upon entering the body, reducing the chance of non-specific binding to non-target sites and allowing selective binding at the targeted sites. It was found that liposomes transported drugs via passive targeting embedded in long-circulating nanoparticles and enriched drug targeting to mice tumor sites by the EPR effect, thereby achieving slow targeting, high efficiency, and low toxicity.Clinical trials involving passive targeting nanoparticles, such as Marqibo, Myocet, and lysosomes, have shown promising therapeutic effects at this time[24][25].

### 11.2 Active Targeted Transport

Passive targeting has the disadvantage of having a lower specificity to tumor site, whereas active targeting has a higher level of specificity.Antigens or receptors overexpressed on tumor cells are found to be overexpressed on normal cells and normal cells express the antigens normally, such as folate receptors, prostate-specific membrane antigen, biotin receptors, transferrin receptors, peptide, and carbonic anhydrase IX.Active targeting is achieved by the specific recognition between receptor and

ligand, or by the covalent modification of targeting groups on multifunctional poly(ethylene glycol)-block-poly(lactic acid)) nanoparticles modified by folic acid and fluorescent probes, which can serve both purposes of cell imaging and targeting the delivery of anti-tumor drugs[24][25]

### 11.3 Physical and Chemical Targeted Transport

Cancer cells inhabit a different microenvironment from normal cells. In response to the unique physical and chemical environments of tumor sites, researchers developed nano-drug carriers with stimulus response, which can achieve targeted drug release by controlling either exogenous stimulus (change in temperature, magnetic field, light, or pulse frequency) or endogenous stimulus (change in PH value or redox), thus improving drug efficacy and reducing side effects. The development of nanocarriers that can be used to deliver anti-tumor drugs[25][26][27]

## 12. Strategies of controlled drug release

Nanoparticles must release their drug upon taking up the drug in the cell for therapeutic effects.The nanoparticles must release the drug in the cell to be effective. The design of effective release strategies is one of the main challenges encountered in nanomedicine. Nanoparticle internalisation occurs mainly via cargo release, but cargo release is a rate-limiting step and may affect a nanoparticle's bioavailability. Nanoparticle internalisation occurs via the release of cargo, which is a rate-limiting step[28][29].

### 12.1 Sustained drug release

Sustained drug release is possible with biodegradable polymers. Despite the advantages of prolonged and controlled release of synthetic polymers, they are less expensive to produce. A synthetic polymer is advantageous because it offers a more gradual and controlled release. The most widely used non toxic polymers are poly (D, L-lactide-co-glycolide) (PLGA) and polylactides (PLA). One may vary the pace of hydrolysis by changing the size and form of these particles, allowing you to release the medicine over several days to weeks. As a result, particle size may be readily adjusted to regulate the rate of hydrolysis, allowing for long-term drug release ranging from a few hours to many weeks. PLA and PLGA nanoparticles are excellent for drug delivery, however they are not compatible with biological

systems. Several biodegradable materials are being investigated to address the wide range of current drugs. Polymers such modified poly(glycerol-adipate) (PGAS), PEGylated poly(-caprolactone) (PEG-PCL), and calcium-based biomaterials are promising materials for drug release systems because of their high tunability and low toxicity[29].

### 12.2 Stimuli-responsive drug delivery

Several nanoparticles have been developed to release their contents following tumor-specific stimuli for localised drug release in cancer cells. Considering cyclodextrin-based nanoplatforms can have numerous functionalities to make them sensitive to stimuli including pH, temperature, redox, enzymes, light, and magnetic fields, they have a wide range of medicinal applications for cancer therapy and theranostics. Furthermore, polymers and liposomes can be functionalized with groups that cause disruption and subsequent drug release when the pH of the environment changes. Nanoparticles that release their cargo when exposed to endogenous enzymes have also been built using polymers and liposomes as building blocks. Furthermore, because of its potential to improve standard nanomedicine procedures, the usage of glucose oxidase is gaining popularity. By raising the acidity of the tumour microenvironment, glucose oxidase efficiently catalyses the oxidation of glucose into hydrogen peroxide and gluconic acid, which can cause pH-responsive medication release[30]. Photosensitive and magnetic release systems are common examples of exogenous stimuli used to control drug release because they are easy to activate localised release by exposing them to light or a magnetic field. When compared to light in the visible spectrum, near-infrared (NIR) light has a greater tissue penetration. The release of doxorubicin from poly (ether amine) nanoparticles containing the dye cyanine was triggered by near-infrared light.

## 13. Challenges and Conclusion

Biological problems, biocompatibility and safety, large-scale production, intellectual property, and overall cost-effectiveness are some of the most prominent issues in nanomedicine. Development of superior diagnostic and therapeutic tools for cancer is crucial. As the conventional methods have low efficiency and more side effects, developing new approaches to improve treatment of cancer is an area of intensive research. But as the advancement

is done in medication the cost of treatment has also gone high.To justify this increased cost,treatment should have more efficiency, decreased invasiveness and fewer side effects than current treatment methods. Nanotechnology has immense potential to satisfy the above subjects[31]. Different types like Protein and liposomes based nanomedicine formulation are already in clinical use and many new formulations are in stages of evolution. Like most other scientific advances that have revolutionised medicine over the past decades, cancer nanomedicine must also mature before its full impact can be realised. Improving our understanding of tumour heterogeneity will enable selection of patients maximally responsive to nanotherapies. Hyperthermia is also an attractive concept to address the issues related to providing more localised affect and enable a non -invasive approach. Meticulous evaluation is still confirmed regarding the short and long term toxicity effects by nanoparticles, targeting efficiency, off- target effects of radio and magneto-thermal therapies,clearance of nanoparticles from the body[11].

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