ejpmr, 2023,10(8), 188-195

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

MOLECULAR LEVEL PHYSIOLOGY OF TUMOR AND DIFFERENT STRATEGIES OF TUMOR TARGETING

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Article Received on 10/06/2023 **Article Revised on 30/06/2023** **Article Accepted on 20/07/2023**

ABSTRACT

Tumor targeting strategies aim to combat the complex and heterogeneous nature of cancer by focusing on the molecular level physiology of tumors. Tumor development involves a series of genetic and epigenetic alterations in normal cells, leading to uncontrolled cell proliferation, evasion of cell death, angiogenesis, and invasion. Dysregulation of key signaling pathways involved in cell cycle control, apoptosis, DNA repair, and angiogenesis plays a crucial role in tumor growth and progression. Moreover, the tumor microenvironment, composed of immune cells, stromal cells, and extracellular matrix components, significantly influences tumor behavior. Targeting tumors at the molecular level necessitates the implementation of diverse strategies. One approach focuses on targeting specific molecular alterations within tumor cells. Small molecules and monoclonal antibodies can be utilized to inhibit oncogenic signaling pathways or induce tumor cell death. For example, targeted therapies have emerged as effective options for tumors harboring specific driver mutations, such as the use of tyrosine kinase inhibitors in certain types of lung cancer. Nanotechnology-based approaches have also shown promise in tumor targeting. Nanoparticles can be engineered to deliver therapeutic agents selectively to tumor cells, minimizing off-target effects and enhancing drug efficacy. These nanoparticles can be designed to release drugs in response to specific stimuli present in the tumor microenvironment, further enhancing targeted therapy. Understanding the molecular-level physiology of tumors provides critical insights into the mechanisms underlying tumor development and progression. Various strategies, including targeted therapies, modulation of the tumor microenvironment, and nanotechnology-based approaches, are being investigated for tumor targeting. The development of precise and effective tumor-targeting strategies holds significant potential for improving cancer treatment outcomes and patient survival.

1. INTRODUCTION

A significant global health issue for people is cancer. It is a condition characterized by unchecked growth and proliferation in which cells have developed the capacity to divide endlessly after eluding the body's usual systems for controlling development. Both benign and malignant tumors are collections of cells that are growing improperly. Leukemia, a tumor with fluid qualities, is distinguished from a localized mass of tissue by the phrase solid tumor. Solid tumors make up around 85% of all human malignancies. The proper distribution of the therapeutic substance to tumor cells is essential for the success of cancer therapy in solid tumors. As a result of inadequate drug delivery to the tumor cells, leftover tumor cells could cause tumors to grow again or even generate new cancers.[1,2]

Chemotherapy, radiation therapy, and surgery are the three most often utilized methods for treating cancer. In clinical practice, the three modalities are typically used in combination, taking into account the benefits and drawbacks of each therapy. In particular, traditional surgery is helpful for treating small, localized tumors; nevertheless, it frequently fails to stop tumor metastasis, which can cause the spread of the tumor to healthy organs, increasing the risk of recurrence and mortality.[3] Radiation is an effective adjunctive cancer treatment; however, it is still ineffective in preventing neoplasm metastasis. Due to the distinct advantage that anti-tumor medications have in that, they can reach the entire body through blood circulation, chemotherapy is used as a primary technique for whole-body cancer treatment.[2] Although chemotherapy lacks the ability to target specific cells because isolated drug molecules are unable to differentiate between normal and tumor cells, its clinical application is still limited by the accompanying unfavorable side effects on healthy tissues.[1] Additionally, many anti-tumor medications have serious

limitations that make it difficult to use chemotherapy, like poor water solubility and significant toxicity to normal cells. Additionally, another serious issue for native chemotherapeutic medicines is multiple drug resistance (MDR).[3] Therefore, the creation of novel therapeutic strategies is critical for the treatment of tumors.

Significant progress has been made in understanding the molecular causes of cancer during the past 30 years. This foundational understanding has proven that cancer is a spectrum of diverse diseases and that these diseases are caused by faulty genes. Additionally, there are a variety of gene abnormalities, some of which can result in the loss or gain of gene functions. Novel therapies, such as monoclonal antibodies, cytokines, sense or antisense oligonucleotides, viral and non-viral gene vectors, and genetically modified cells, have been discovered as a result of recent developments in molecular targeting technique. Following systemic administration, specific methods for drug distribution to cells in solid tumors are influenced by the physiological characteristics of the tumor.

2. DEFINITION AND DIFFERENT TYPES OF TUMOR

A mass of aberrant tissue that develops from preexisting body cells without apparent origin has no discernible function, and is distinguished by a propensity for autonomous and unregulated growth is referred to as a tumor. Due to the aberrant appearance and other properties of the cells in tumors, they differ significantly from inflammatory or other swellings. Tumor-forming abnormal cells differ from normal cells in that they have experienced one or more of the following changes: (1) Hypertrophy, or an increase in cell size; this characteristic is infrequently seen in tumors but is frequently seen in other situations; (2) hyperplasia, or an increase in the number of cells within a given zone; in some instances, it may constitute the only criterion of tumor formation; (3) anaplasia, or a regression of the physical characteristics of a cell toward a more primitive or undifferentiated type.[8]

Tumors are broadly classified into two types benign tumors and malignant tumors. Benign tumors are not "cancer" and do not spread widely throughout the body, although they can grow substantially and damage surrounding tissues, if not treated. A malignant tumor is a group of cells displaying uncontrolled growth (division beyond the normal limits), invasion (intrusion on and destruction of adjacent tissues), and sometimes metastasis (spread to other locations in the body via lymph or blood). These three malignant properties of cancers differentiate them from benign tumors, which are self-limited, and do not invade or metastasize. Only malignant tumor cells and infections have the established capacity to metastasize.[27]

The biological and medical consequences of a tumor are highly dependent on whether it is benign or malignant.

Listed below is a comparison of the primary differences between benign and malignant tumors:

Table 1: Primary differences between Benign and Malignant tumors.

Features	Benign tumors	Malignant tumors
Cell characteristics	Similar to cell of origin (well differentiated)	Dissimilar from cell of origin (poorly differentiated)
Growth characteristics	Tumor edges move outward in a smooth manner (encapsulated), grows by expansion and compresses and displaces surrounding tissues. Tumor cells stay attached to the clone or mass of cells and do not break away and start new growths elsewhere in the body.	The tumor edges move outward in an irregular fashion (usually no capsule) and can infiltrate, invade, and destroy surrounding tissues. Tumor cells can break away from the cloned mass, live independently, move to other area of the body and start new clones or growths.
Rate of growth	Slow growth rate	Rapid growth rate
Degree of vascularity	Slight vascularity	Moderate-marked vascularity
Recurrence after surgical removal	Seldom recurs after removal	Frequently recurs after removal
Degree of necrosis and ulceration	Necrosis and ulceration unusual	Necrosis and ulceration common
Likelihood of causing systemic effects	Systemic effects are unusual unless the tumor is a secreting endocrine neoplasm	systemic effects are common and usually life- threatening.

3. Molecular level physiology of tumor

3.1 Cell cycle Regulation and The importance of apoptosis

In healthy cells, protein-protein interactions in a predetermined pattern tightly control cell growth and progression through the cell cycle. Checkpoints make ensuring that each stage of the cell cycle is successfully completed and prevent DNA that has not been fully copied from being passed on to daughter cells. Cyclin-dependent kinases (CDKs) are at the center of this

regulatory mechanism. The'master protein kinases', or CDKs, are responsible for promoting progression through the various cell cycle stages by phosphorylating and activating other downstream kinases. Cyclins, which are activating components that are generated and destroyed in a cell cycle-dependent manner, are required for CDK function. CDK inhibitors further tighten the control over cyclin-CDK complexes.[30]

The re-entry of cells into the cell cycle is decided at the restriction point (R point). This decision is influenced by extracellular mitogenic signals which are transmitted via signaling pathways to key regulatory proteins, such as transcription factors (e.g. E2F) in the nucleus. These regulatory proteins ultimately activate the S-phase CDKs, which trigger the start of DNA synthesis. the cell cycle is catalyzed primarily by complexes containing cyclin-dependent kinases (ckds) and cyclins.[31]

In normal cells, activation of another transcription factor, p53, often referred to as the 'guardian of the genome', can impose cell cycle arrest and induce apoptosis (programmed cell death) through its ability to:

- Induce the expression of cell cycle inhibitors to prevent the proliferation of a cell until any damage has been repaired or
- Initiate apoptosis, if the genomic damage is too great and cannot be repaired.

In >50% of all human tumors, the p53 pathway is aberrant. Inactivation of the p53 protein renders it unable to signal and activate the cell's apoptotic machinery resulting in increased survival of cancer cells.[30]

3.2 Cell immortalisation and Tumorigenesis

The gaining of an infinite lifespan is known as immortality. Normal mammalian somatic cells can divide only so many times before going through senescence. Even though senescent cells no longer proliferate, they may still be metabolically active. Telomerase, the enzyme responsible for preserving telomeres at the ends of chromosomes, is present in immortalized cells, which is a necessary step in the malignant transformation of normal cells. Telomerase prevents the progressive telomere shortening that would otherwise result in cell death by lengthening telomeric DNA. About 90% of human cancers are composed of cells that have measurable quantities of active telomerase, in contrast to normal cells that do not.[26]

3.3 Surface markers

Anything present in or produced by cancer cells, other cells of the body, or certain benign (noncancerous) conditions is referred to as a tumor marker. Tumor markers can reveal details about a cancer, including its aggressiveness, its ability to be treated with targeted therapies, and its response to therapy.

Proteins or other chemicals that are produced by both normal and cancer cells, however more abundantly by cancer cells, have traditionally been used as tumor markers. Some cancer patients' blood, urine, stool, or other body fluids may include circulating tumor markers. Circulating tumor markers are used to:

- Determine prognosis;
- Identify cancer that has returned or is still present after therapy (residual disease);
- Evaluate the effectiveness of the remedy
- Keep track of any malignancy that has developed therapy resistance.

Tumors are not collections of a single cell type or a monoculture. Even a cultivated cell line exhibits heterogeneity in its cell population, including cancer stem-like cells that have a different set of surface markers from other bulk cells and are able to withstand conventional cytotoxic therapies. The surface markers distinguishing a cancer stem-like cell population can differ from isolated cell lines from that tumor, indicating that the origin of cancer stem cells may not be the same.[28]

3.4 Biological unique characteristics of tumor

3.4.1 Tumor vasculature

The following characteristics distinguish the tumor vasculature from the normal vasculature:

- The tumor vessels' permselectivity is lower than that of normal vessels, likely as a result of the numerous pores in the vessel wall. The absence of basement membrane next to endothelial cells could be explained by this.
- Inhibited and changed tumor vasculature endothelium expression of adhesion molecules.
- The average lifespan of normal endothelium cells is thought to be 1,000 days or longer, but malignant endothelial cells have a lifespan of about 4-5 days.
- A heterogenic endothelial cell population is produced by heterogenicity in angiogenic peptide expression.
- Modified vascular permeability across the tumor mass, with the tumor's center being denser and less permeable than the surrounding areas.[13]

3.4.2 Lymphatic drainage

The body's lymphatic tubes are widely distributed and more permeable to liquids and solutes than blood capillaries. Solid tumors have a compromised lymphatic system as a defining feature. Larger particles, such tumor cells removed from a primary tumor, can infiltrate the lymph by slipping through the lymphatic capillaries' endothelial cells.[14]

3.4.3 Extracellular matrix composition

Macromolecules such fibrous proteins (like collagen and elastin) and polysaccharides (like hyaluronan and proteoglycan) make up the extracellular matrix of solid tumors. These macromolecules are made by the host cells, but tumor cells control how much of them are made. The extracellular matrix proteins in a tumor are a source of physical medication transport resistance. The

extracellular matrix of the tumor contains collagen, which makes the interstitium more resistant to medication delivery.[26]

3.4.4 Tumor cell density

Diffusion through the tumor interstitial space is a major mode of drug transport in solid tumors. A larger fraction of interstitial space or a decrease in tortuosity would result in more rapid drug diffusion. Tumor histocultures have been used to study the spatial relationships between interstitial space, tumor cell density, and drug penetration in solid tumors. Stromal tissues and interstitial space in tumors are important determinants of drug delivery and transport.[25]

4. DIFFERENT STRATEGIES OF TUMOR TARGETING

The development of tumor-targeted delivery of the therapeutic molecules of interest to the tumor site(s) in the body (both primary and metastatic), passage of the molecular therapeutic through the cell membrane, and targeting specifically a growth or apoptotic pathway are the three main prerequisites for the development of effective targeting therapeutic modalities for the treatment of cancer (1). In order for anticancer medications to be effective in the treatment of cancer, they must first be able to penetrate bodily barriers and reach the targeted tumor tissues with the least amount of volume or activity loss. Second, medications should be able to selectively destroy tumor cells without harming normal cells once they have entered the tumor tissue by using a controlled release mechanism of the active form (2). By concurrently boosting the intracellular concentration of medications and lowering dose-limiting toxicities, these two fundamental techniques are also linked to increases in patient survival and quality of life. The three main methods of targeting are physical, functional modification of the particle's surface to improve therapeutic delivery, and passive targeting of large areas of cancerous tissue where the body concentrates inert nanoparticles. Active targeting of particular tumor cells results in specific tissue targeting (1).

4.1 Passive targeting

Utilizing the architectural and functional distinctions between the normal and tumor vasculature, passive targeting strategies enable the selective accumulation of medications at the tumor location. Utilizing the tumor tissue's permeability is passive targeting. Rapid vascularization to support rapidly expanding malignant tissue favors a leaky and faulty design, which can make hazardous chemotherapy medicines easily accessible. Some medications can be supplied as prodrugs, or inactive medications, which, when they come into contact with the tumor environment, turn on and become highly active. Additionally, drug delivery to the tumor bed through a variety of invasive techniques is a component of passive targeting.[10]

4.1.1 Leaky vasculature

The improved permeability and retention effect is present in the majority of polymer nanoparticles. Two variables account for the increased permeability and retention phenomenon: (a) the capillary endothelium in malignant tissue is more disorganized and, as a result, more permeable to macromolecules than the capillary endothelium in normal tissues. This enables extravasation of circulating polymeric nanoparticles into the tumor interstitium, and (b) drug accumulation is caused by a lack of tumor lymphatic outflow in the tumor bed. When a chemotherapeutic agent is linked to an appropriate polymer or other molecular carrier by a degradable linker, the concentration of the chemotherapeutic agent in the tumor tissue may be increased. As a result of these characteristics, concentrations of polymer-drug conjugates in tumor tissue can reach levels 10 to 100 times higher than that resulting from the administration of the free drug.[13]

The development of new blood vessels is an important event in tumor progression since it supports tumor growth and allows the dissemination of cancer cells throughout the body, leading to metastasis.[14] Further approaches for passive targeting involve size of the nanocarriers and surface charge modulation. The optimum size of nanoparticles that can be accumulated in a tumor by the EPR effect is not yet precisely known. Although direct examination of the tumor vasculature has shown a tumor dependant pore cutoff size ranging from 200 nm to 2 mm, research using liposomes and nanoparticles have suggested that the cutoff size of the pores in tumor arteries is as large as 200 nm to 1.2 mm. These size ranges appear to suggest that drug-loaded nanoparticle accumulation in malignant tumor cells may be caused by these nanoparticles. The EPR effect was used to determine that polymer-based nanoparticles containing DOX circulated in the blood for longer than three days and eventually accumulated in tumors.[16]

4.1.2 Tumor microenvironment

The pathogenic status of tumors is tightly correlated with the tumor microenvironment. The extracellular matrix (ECM), fibroblasts, lymphocytes, immunological cells, and the blood arteries in the vicinity make up the majority of it. It has a significant role in the development, spread, invasion, and metastasis of tumors. Due to the significant differences between the tumor microenvironment and the nearby normal tissues, including pH value, vascular anomalies, and ECM composition, the tumor microenvironment sensitivity is another heavily researched subject in the realm of tumor-targeted DDS.[4]

The drug is conjugated to a tumor-specific molecule and is administered in an active state, and once it reaches its destination, the tumor environment is able to convert it to an active and volatile substance, so-called tumor activated prodrug therapy. Fast-growing, hyperproliferative cancer cells show a high metabolic

rate, and the supply of oxygen and nutrients is usually not sufficient for them to maintain this. Therefore, tumor cells use glycolysis to obtain extra energy, resulting in an acidic environment. The pH-sensitive liposomes are designed to be stable at a physiologic pH of 7.4 but degraded to release the active drug in target tissues in which the pH is less than physiological values, such as in the acidic environment of tumor cells. Additionally, cancer cells express and release unique enzymes such as matrix metalloproteinases, which are implicated in their movement and survival mechanisms.[8]

4.2 Active targeting

Another viable technique for drug targeting is active targeting, which is mostly used to treat tumors. In order to establish passive targeting coupling of a particular ligand on the surface that will be recognized by the cells present at the illness site, addition of PEG modification of nanocarriers is required for active targeting to the disease site. Therapeutic agent or carrier system conjugation to a tissue- or cell-specific ligand is required for active targeting to occur. To deliver drugs to the target place, various forms of nanoparticles are being produced. These ligands are extraordinary in that they can recognize and bind to complementary molecules, or receptors, found on the surface of tumor cells. When such targeting molecules are added to drug delivery nanoparticles, more of the anticancer drug finds and enters the tumor cell, increasing the efficiency of the treatment and reducing toxic effects on surrounding normal tissue.[4]

4.2.1 Ligand-based targeting

4.2.1.1 Monoclonal antibodies

The first macromolecular ligands employed for targeted administration are antibodies. After the development of hybridoma technology, monoclonal antibodies (mAb) were widely used. Murine monoclonal antibodies were unsuitable for therapeutic uses because of their innate immunogenicity. Chimeric and fully humanized antibodies were created as a result of engineering antibody technology. Transgenic mice can now manufacture human immunoglobulins thanks to techniques that have just been discovered. Additionally, combinatorial phage display libraries have become an effective technique for choosing new protein ligands. The latter strategy depends on numerous screening criteria and selection criteria to choose human antibodies against particular cell types or antigens. The selection procedure can be planned to enhance the ligand's internalization, stability, affinity, and selectivity. Most recently, this approach was used to isolate cancer-targeting antibodies using live cancer patients in the selection process.[1]

4.2.1.2 Aptamer based targeting molecule

Aptamers are a class of macromolecules that are isolated from combinatorial libraries of synthetic nucleic acids by an iterative process of adsorption, recovery, and reamplification and can be produced against amino acids, drugs, proteins, and other molecules.[4] Aptamers are analogs of antibodies and can bind with high affinity and specificity to a wide range of targets, such as small molecules, proteins, viruses, or cells. RNA aptamers are single-stranded RNA molecules that can recognize target molecules by folding into particular three-dimensional shapes. Single-stranded DNA, RNA, or synthetic oligonucleotides that fold into distinctive shapes and can attach to particular targets with great affinity and specificity are known as nucleic acid aptamers.[2] As small molecules, with a half-life of minutes to hours due to nuclease degradation, aptamers can be rapidly cleared from the bloodstream by the kidneys. The combination of aptamers with novel nanomaterials, including nanomaterial-based aptamer bioconjugates has attracted considerable interest and has led to a wide variety of applications.

4.2.1.3 Folate-Based targeting molecules

Folic acid (folate) is one of the small molecules targeting moieties for drug delivery that has been the subject of the most research. Due to the fact that a variety of tumor cells usually overexpress the folate receptor (FR), the high-affinity vitamin is a widely employed ligand for cancer targeting.[10] A number of folate derivatives and conjugates can deliver molecular complexes to cancer cells without harming healthy cells since folate preferentially binds to FRs with a high affinity (KD = 10-9 M). It has been employed as a targeting moiety in combination with a variety of drug delivery systems, such as dendrimers, liposomes, protein toxins, polymeric NPs, and linear polymers, to deliver medicines specifically into cancer cells by FR-mediated endocytosis.[18]

4.3 Stimulus responsive targeting

It is also called as physical targeting. It is a new targeting strategy which makes use of an external stimulus to target the release of drug at a specific site in the body. The physical properties, such as swelling/deswelling, particle disruption, and aggregation of stimuli-responsive nanocarriers change with respect to changes in environmental conditions.[2]

In turn, these properties alter the interactions of the nanocarriers with the cells and trigger the drug release from slow to fast at the tumor site. Various physical targeting strategies are as follows:-

4.3.1 pH-Sensitive targeting

Based on inherent variations in the relative acidity of various solid tumors and the surrounding normal tissues, pH-sensitive polymeric carriers have been employed in targeted anticancer medication delivery. Most cancers have extracellular pH that is more acidic than normal tissues (pH 5.7–7.4). Because tumor tissues have an environment that is more acidic due to lactic acid created by hypoxia and by acidic intracellular organelles, a change in the pH there is beneficial. For quick anticancer medication release at tumor locations, different pH-

responsive polymeric nanoparticles have been employed.[32]

To take advantage of the tumor's acidic environment, anticancer medications can be attached to pH-sensitive polymers. The medicine can be released either in somewhat acidic extracellular fluids or after endocytosis in endosomes or lysosomes of tumor cells.[2]

4.3.2 Temperature sensitive targeting

Due to their extreme sensitivity to heat, cancer cells shrink and die when exposed to temperatures between 40 and 46°C for extended periods of time. Hyperthermia is the term for sustained heating of tissue between 40 and 46°C, which has been utilized to treat a number of malignant conditions.[1] Hyperthermia may cause cancer-killing cells to proliferate through a variety of mechanisms, including protein coagulation, membrane fluidity, and nucleic acid changes. Potential candidates for triggering medication release in conjunction with hyperthermia therapy include temperature-sensitive nanoparticles.[4] These particles can be directed at the malignant tissue after intravenous administration. The heat generated during hyperthermia therapy would then stimulate the medication release from the particles into the surrounding tissue. Hyperthermia is reported to increase tumor blood flow and tumor vascular permeability compared to normal vasculature. PNIPA particles would release anticancer drugs at these temperatures causing a significant reduction in the tumor size due to the combination of hyperthermia and drug activity.[32]

4.3.3 Ultrasound sensitive targeting

To cause the release of anti-cancer medicines from polymeric micelles and enable an efficient intracellular uptake of the drug contained, ultrasonic waves can be directed at the tumor tissue. Polymeric micelles can also make multidrug-resistant (MDR) cells more susceptible to the effects of medications.[10] The precise targeting mechanism is still being worked out, but options include ultrasound-promoted micelle extravasation into tumor tissue and a medication release from the micelles that is only initiated at the ultrasound-irradiated tumor location. For the delivery of anthracycline medicines to drug-sensitive as well as MDR ovarian A2780 cancer cells, this targeted method has been investigated in vitro.[25] Either drug diffusion out of the micelles or micelle breakdown can be induced by ultrasound. The fact that this method is non-invasive, enters the body deeply, and can be precisely directed and focused at particular target regions is a significant advantage. However, questions have been raised regarding the impact of ultrasonic radiation's energy on cell plasma membranes. The intracellular uptake of drugs is increased by the low ultrasound energy needed for this type of targeting strategy, but energies above the cavitation threshold can severely damage cell membranes.[32]

4.3.4 Magnetically sensitive targeting

When a localized external magnetic field is applied, a therapeutic substance that has been attached to or enclosed in a magnetic drug carrier is injected intravenously and can then be targeted and preferentially localized in the tumor tissue. Materials like magnetite, iron, nickel, cobalt, etc. are frequently used as magnetic responsive medicine carriers. Magnetic liposomes, microspheres, nanospheres, and colloidal iron oxide solution (magnetic ferrofluids) are a few examples of such drug carriers.[15] Using strategically placed external magnets, magnetic ferrofluid (100 nm particle size) coated with a unique carbohydrate that may reversibly bind pharmaceuticals was investigated for the purpose of targeting tumor tissues. They were made to desorb the medicine they carry when particular physiological parameters (such as pH or osmolality) were present. Magnetic targeting of the drug-epirubicin was attempted in the first-ever Phase 1 clinical trials using the abovementioned targeting system in patients with advanced sarcomas.[32] Although this new approach of drug targeting was found to be clinically well-tolerated and safe, more than 50% of the carriers ended up in liver due to low magnetic susceptibility. Thus, the trials concluded that the targeting system needs improvements to make it more effective and independent of patient or disease-related problems. Magnetic drug carriers are under active preclinical investigation for various chemotherapeutic agents – mitoxantrone, etoposide, and paclitaxel. The use of magnetic carriers should address some other issues like the drug-carrying capacity, aqueous dispersion stability, and biocompatibility with the tissues.[16]

Without harming the nearby normal cells, radioisotopes enclosed in these magnetic drug carriers can be employed to deliver a targeted high dose of radiation to the tumor cells. Instead of releasing radioactive isotopes, the complete magnetic carrier is brought to and kept near the area that has to be irradiated. In order to externally direct these magnetic drug carriers to the tumor site, efforts are focused on creating targeted carriers with high magnetic moments or constructing magnets that can deliver greater magnetic field gradients.[15]

5. CONCLUSION AND FUTURE SCOPE

The prospects for the creation of an effective targeted drug delivery method for tumor therapy have been boosted by developments in the discovery of tumor-specific targets and the development of several drug delivery systems for tumor targeting. Although the ultimate goal is to completely remove cancer from the patient, more pragmatic aims aimed at enhancing the patients' quality of life are near to being realized. In the next years, there will be a focus on creating systems that can effectively internalize into cells while also being able to detect specific targets on tumor cells. Some of these issues could be solved through the combination of targeted strategies. Other developing ideas that offer great promise for medication targeting in tumor therapy

include employing unique molecular addresses on the vascular endothelium, targeting with magnetic fields, and ultrasound. Better disease understanding, the discovery of tumor-specific indicators, and the concurrent creation of novel, more effective yet less harmful treatments are all necessary for all of these. To ensure that novel medications do not suffer from adverse pharmacokinetics and are rejected in the development pipeline itself, novel drug delivery system development should be carried out concurrently with the drug discovery project. It is more likely that new medications that will reach patients can be improved by targeting tactics utilizing nanotechnology and bioconjugation chemistry, which can change a drug's biodistribution to minimize toxicity and boost its efficacy.

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