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Novel Drug Delivery Approach in Cancer Therapy

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ABSTRACT
Novel Drug Delivery Systems (NDDS), including improved therapy through enhancing the effectiveness and duration of medication use, enhanced patient adherence by decreased frequency of dose. The main disadvantages of chemotherapy include its poor absorption, high dose requirements, negative side effects, low therapeutic indices, development of multiple drug resistance, and non-specific targeting, despite the fact that conventional chemotherapy has been somewhat successful. Developing drug delivery vehicles with the primary goal of effectively addressing these delivery-related issues and transport medications to the intended therapeutic regions while minimising unfavorable side effects. Because it responds less well to anticancer treatments, diffused metastatic breast cancer has a poor prognosis and requires vigorous therapy. Theoretically, combination medication therapy is superior to single-agent therapy; nevertheless, no discernible improvement in survival has been observed; instead, combination treatment is often associated with higher toxicity, particularly in the case of chemotherapy. There are several reasons to be interested in One of the main illnesses that threaten people's health is cancer. However, there are a number of adverse effects associated with the usage of anticancer medications. Appropriate drug delivery methods can lessen the harmful side effects of medications and increase the bioavailability of medications; including targeted medication Anticancer medication delivery systems' primary area of development is delivery systems.

KEYWORD - cancer therapy, bacteria, drug carrier, Novel drug delivery system, Nanoparticles.

I. INTRODUCTION [1, 2, 3]

A variety of illnesses that result from malignant cells growing out of control and having the ability to invade or spread to other bodily parts is collectively referred to as cancer. The World Health Organization estimates that there will be around 13.1 million cancer-related deaths by the year 20301, with over 10 million new cases per year contributing to the expected increase in cancer-related fatalities. But during the last five years, the death rate has dropped as a result of advancements in diagnostic tools and therapeutic approaches, as well as a deeper comprehension of tumour biology. One of the main illnesses that threaten people's lives and health is cancer. In 2023, there were 10 million cancer-related deaths and approximately 19.3 million new cases globally, according to a report published by the International Agency for Research on Cancer. Still, the Modern therapeutic approaches, like radiation and chemotherapy, are accompanied by severe adverse effects, including alopecia, bone marrow suppression, and gastrointestinal toxicity, and so forth. The non-targeted distribution of medications is primarily responsible for the occurrence of these side effects. Thus, the creation of efficient delivery systems that target tumours is a primary area of research and development for anticancer drug delivery systems.In the United States, breast cancer ranks second in terms of causes of death for women and is the most common cancer among females. The most advanced stage of breast cancer, known as metastatic breast cancer, involves the disseminationof malignant cells spreading from the breast to other parts of thebody. When diagnosed, fewer than 10% of womenare exposed to a disease that has spread. But whenRelapse happens following conclusive treatment for early stage orWith locally advanced disease, most patients eventuallywith widespread metastases as opposed to a single, localizedrepetition.

MECHANISMS OF BACTERIA FOR CANCER THERAPY [4,5]

Bacterial Carriers' Targeting of Tumours
Bacteria are a novel class of anticancer drug carrier that will assemble preferentially in after entering

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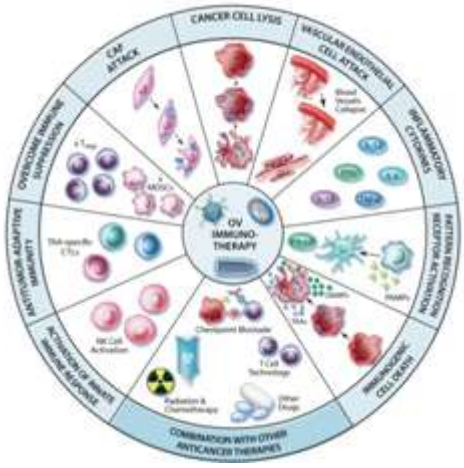
the human body, tumours. In contrast to healthy tissues, the build-up more than a thousand times greater amount of bacteria in tumour tissues



ADVANTAGES [6]

1) Greater patient compliance and convenience as a result of less frequent medication administration 2) Boost safety margin;3) maximum drug utilization;4) lower dosage frequency, etc

2) Negative aspects

3) A reduction in system availability 2) Inadequate in vitro and in vivo correlation 3) The potential for dose dumping, etc.

4) Controlled drug delivery is the process of administering a medication locally or systemically at a predetermined rate. Drug release with controlled release is excellent zero order.

5) Lower dosage concentration and frequency of administration 3) Lessened GI poisoning 4) Improved reception by patients.

DISADVANTAGES [7]

1) Dumping doses

2) Diminish the possibility of exact dosage measurement

3) Additional patient education is required

4) Issue with stability.

DIAGNOSIS OF CANCER [8, 9, 10]

Suitable TME for Bacterial Survival The external reasons for the tumour targeting of bacteria can be roughly divided into three points. Firstly, the hypoxia TME attracts obligate and facultative anaerobic bacteria to tumour tissue. Due to the rapid proliferation of tumour cells and incomplete vascular development, the supply of oxygen in solid tumours is insufficient, which eventually leads to the existence of hypoxic areas in tumours. This is a necessary condition for the survival and reproduction of obligate and facultative anaerobic bacteria in tumours. Moreover, with further penetration of the tumour tissue, hypoxia tends to be more severe. This is very unfavorable for conventional treatment but is more conducive for bacterial tropism and depth of penetration

The Chemotaxis Properties of Bacteria Some of the properties of bacteria can also help them to colonize tumours. It has been proposed that some chemical-specific receptors on the bacteria may sense chemicals secreted by cancer cells. Kasinskas et al. proved that chemical receptors have an important effect on the tumour tropism of bacteria by knocking out different chemical receptors on the surface of Salmonella. More interestingly, the accumulation of bacteria in different parts of the tumour can be controlled by selectively eliminating chemical receptor genes. In addition, some bacteria have special tendency properties. For example, magnetotactic bacteria have a tendency to a specific magnetic field Tumour-Targeting Modifications of Bacterial Carriers Gene editing and surface modification can further improve bacteria's tumour-targeting ability. With the use of gene editing technology, it is possible to design modified auxotrophic bacteria corresponding to some specific purines, amino acids, and other nutrients within the tumour. Zhao et al. designed a leucine–arginine auxotroph S. typhimurium. The engineered bacteria can only survive in tumours but not in normal tissues. In terms of surface modification, modifying tumour-homing peptides or tumour antibodies on the surface of bacteria can lead to better tumour-targeting ability. Park et al. improved the tumour tropism of bacteria by modifying an arginine–glycine–aspartate peptide on the outer membrane protein of S. typhimurium Immunomodulatory Effects of Bacterial Carriers Cancer patients cannot clear cancer cells through their immune system, because cancer cells can develop multiple pathways to avoid being cleared by the immune system. It has been found that bacteria inside the tumour can alter the immunosuppressive TME and stimulate the host immune system, thus enhancing the body's immune system to clear the cancer cells (Figure 1). 2.2.1. Weak Antitumour Immunity The reasons for the inability of the anticancer immune response to eliminate tumours can be broadly classified as follows: 1. Tumour cells themselves have developed specialized mechanisms to suppress immune responses, including downregulation of tumour antigen and major histocompatibility

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complex (MHC) class I expression [39,40], high expression of programmed death receptor-ligand 1 (PD-L1) to prevent the Bacteria Activate the Immune System Bacteria at the tumour site can stimulate the immune system to produce a series of anticancer immune responses is another advantage of bacterial carriers in cancer therapy. This is because bacteria carry a large number of antigens such as lipopolysaccharide and flagellin, which can bind to toll-like receptors and, thus, trigger a series of cellular signaling events. The mechanisms by which bacteria activate anticancer immunity in the body are complex and interact with each other. For the sake of description, we roughly divide these mechanisms into two parts: promotion of anticancer immune response and reduction of tumour immune escape. In enhancing the anticancer immune response, the recruitment of immune cells to reach the tumour site Oncolysis of Bacterial Carriers In addition to activating the immune system to kill cancer cells, bacteria colonizing tumours also have a certain anticancer effect, which can help drugs better play their anticancer role. This oncolytic activity can be achieved through a variety of pathways, including the induction of tumour cell death, inhibition of tumour angiogenesis, inhibition of tumour metastasis, and reduction of tumour drug resistance.

Induction of Tumour Cell Death Bacteria induces cancer cell death through multiple pathways, including the induction of apoptosis, the release of bacterial toxins, and competition for nutrients. For example, Listeria can induce tumour cell apoptosis by activating nicotinamide adenine dinucleotide phosphate (NADPH) oxidase and increasing intracellular calcium levels to increase ROS levels in tumours [73]. Salmonella induces autophagy and caspase-mediated apoptosis in tumour cells by downregulating the AKT/mTOR pathway [74], and metabolizes nitrate to nitrite via nitrate reductase and further converts it to nitric oxide in tumours to induce tumour cell apoptosis [75]. Secondly, bacteria can release toxins to kill tumour cells. For example, Colicins have anticancer activity against breast cancer, colon cancer, bone cancer, and other human tumour cell lines. However, bacterial. Bacterial Carriers' Strategies for Drug Loading

Drug Loading on Bacterial Surfaces

There are two types of drug-loading tactics on the surface of bacteria: chemical Physical adsorption, linker grafting, and bonding. The purpose of chemical bonding is to use the Bacteria's surface groups to create covalent connections with medications to establish a connection.

The goal of linker grafting is to achieve the noncovalent force between the ligand and the receptor.

Loading of merchandise. The Coulomb force acts primarily to realize physical adsorption between The surface of medications and bacteria. In contrast to various surface drug loading techniques, Chemical bonding and linker grafting have relatively stable connection structures, and Modifying the structure and active function in vivo is a challenging task. Adsorption through physical means Possesses.

Chemical Interactions

Since peptidoglycan, lipopolysaccharide, and polypeptide make up the majority of the surface of bacteria, a variety of chemical groups, including amine, sulfhydryl, andsurface hydroxyl groups. Groups can react with the cargo to create covalent bonds. binds to the bacteria's surface, and the amidation reaction is the most common reactionamid carboxyl and amino groups. Furthermore, in situ polymerization predicated onAnother technique for covalent binding is oxidative self-polymerization and biomineralization. Frequently employed to modify the surface of bacteria.The Most Recent Innovative Methods for Overcoming the Obstacles: Drug Delivery Through Carrier-Mediated CombinationThe aforementioned difficulties have prompted scientists to look into cutting-edge methods that combine nanotechnology and combination anticancer therapy. The promising theory is that a comination system can produce synergistic anticancer effects and lessen toxicity associated with individual drugs by simultaneously delivering two or more drugs via a carrier-mediated drug delivery system.However, because single agent delivery systems are the main focus of most research efforts, this area of delivering multiple drugs with a single vehicle remains largely unexplored. Consequently, we will discuss carrier-mediated drug delivery systems with several anticancer agents here for the treatment of cancer in general, not just metastatic breast cancer. Compared to the physical combination of multiple drug delivery methods, carrier-mediated drug delivery systems have numerous advantages.

Liposome-Based Combination Drug Delivery Systems. Spherical vesicles made up of one or more as many lipid bilayers with an aqueous

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core drug (Figure 2(a)). Liposomes are among the most frequently utilizedpharmaceutical carriers with a number of distinctive qualities For example, the capacity to encapsulate hydrophilic andhydrophobic medications and safeguarding the enclosedmedications derived from outside sources [64]. Not changedPhagocytic cells rapidly remove liposomes from the bloodreticuloendothelial system (RES) cells, leading toearly deterioration and elimination from the system. Toconquer this obstacle long-lasting covert liposomeshave been created by applying an inert surface coating.and polymers that are biocompatible, like polyethylene glycolThe layer of polymer offers a shielding layer over

The surface of the liposome and inhibitsA polymer-caged liposomal system is another unusual type.

Lee et al. developed nanobin (PCN, Figure 2(b)), which shows the various ways to incorporate multiple drugs.in the same liposome, such as when one medication is encapsulatedand the other's covalent conjugation. PCN made up of aLiposomal core loaded with doxorubicin (Dox-) and encircled By a pH-responsive polymer cage conjugated with cisplatin (Pt).was created using surface-tunable drug ratios (Pt/Dox).potentials for charging. This combination of two agents significantly Increased each drug's overall effectiveness against breast andovarian cancer cells in smaller quantities. Index of Combinationsand isobologram research verified more potent synergistic medicationeffects at a greater range of concentrations than when single drugs are nanopackaged or when drugs are combined. The significance of single carrier-mediated combination drug delivery platforms that enable such tunable drug loading is highlighted by the fact that the degree of synergism was further dependent on the individual drug ratios. Further in vitro research using the PCN system showed that the original drug-combination ratio in the liposome was maintained during cellular uptake through endocytosis.It is common practice to attach targeting ligands, such as antibodies and peptides, to a drug carrier in order to significantly increase carrier accumulation in the targeted cells, tissues, and organs. Such targeted liposomes have been developed in several instances for applications involving combination drug delivery.

MATERIALS AND STRATEGIES USED IN CANCER THERAPY [11,12]

Several innovative methods of drug delivery are being used in cancer treatment. A wide range of nanoscale compounds baseFor the creation of cancer treatments, artificial polymers, proteins, lipids, and organic and inorganic particles have been used. Drug encapsulation in a carrier provides a number of benefits over administering bare chemotherapy drugs directly, including protection from bloodstream degradation, improved drug solubility, increased drug stability, targeted drug delivery, a reduction in toxic side effects, and improved pharmacokinetic and pharmacodynamic drug properties. With targeting strategies, an amazing library of different drug delivery vehicles with different sizes, architectures, and surface physicochemical properties has been developed to date A few examples of drug delivery systems that are either in the clinical or preclinical development stages or have received approval are included in Using nanocarriers to deliver drugs Cancer treatment and diagnosis are being revolutionized by the quickly emerging field of nanomedicine. Because of their small size (diameter of 1–100 nm) and large surface area to volume ratio, which enable them to bind, absorb, and carry anticancer agents, such as drugs, DNA, RNA, and proteins, along with imaging agents with high efficiency, nanoparticles have special biological properties. Chemotherapy-related nanocarriers fall into two main categories: those with an inorganic core (often metals) and those that use organic molecules as a primary building block for targeted or non-targeted drug delivery. Liposomes, lipids, dendrimers, carbon nanotubes, emulsions, and synthetic polymers are examples of organic nanocarriers.

DISTINCTIVE MEDICATION DELIVERY SYSTEM LIPOPROTEIN [13]

An appropriate quantity of an active therapeutic drug must be absorbed and delivered to the site of activity at the optimal time and rate in any optimal drug delivery system.

As a targeted drug delivery system, lipoprotein can be used in cancer treatment to improve the therapeutic index of anticancer agents. This can be achieved by either increasing the concentration of medication in tumour cells or reducing its interaction with normal host tissues.

One possible transporter for chemotherapeutic mediators is low density lipoprotein. Because certain types of cancerous cells exhibit increased receptor-mediated uptake of lowdensity lipoprotein, they are used for targeted delivery of anticancer drugs [8]. Liposomes for clinical cancer therapy

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A NANOPARTICLE

Nanoparticles range in size from 10 to 200 nm and exist in the solid state as either amorphous or crystalline particles. It protects medication from enzymatic and chemical deterioration. Biodegradable polymeric Few applications exist for nanoparticles in the controlled release of therapeutic drugs to target particular organs or tissue as transporters for gene therapy Gold nanoparticles, nanotubes, nanowires, nanoshells, quantum dots, and nanopores are among the different types of nanomaterials nanoemulsion Oil-in-water (o/w) emulsions, which have an average droplet size ranging from 50 to 200 nm, are known as nano emulsions. The particles in these emulsions can be either water-in-oil or oil-in-water, with the water or oil serving as the particle's core Similar to microemulsions, nano-emulsions can exhibit high kinetic constancy and optical transparency.

MICROCAPSULES

Many anticancer drugs with stumpy aqueous solubility affect their application and complicate direct parenteral administration, including paclitaxel (PCT), camptothecin (CPT), and some porphyrins, like meso tetraphenylporphine (TPP), which is used in photodynamic therapy (PDT) [45–47]. It has been suggested that novel drug delivery techniques based on drug carrier systems approaches be used to address the less stable, harmful side effects, and decreased solubility of these drugs. Due to their excellent pharmacological characteristics and easily controlled properties, PEG diacyllipid conjugates have garnered a lot of attention.

TINY-EMULSIONS

Microemulsions are described as liquid scatterings of oil and water that are created by adding a relatively high concentration of a surfactant to a thermodynamically stable formulation that is homogenous, transparent, or translucent in nature. Microemulsion droplets, which range in diameter from 10 to 100 nm, have been thoroughly investigated as a targeted drug delivery method for the brain . It improves the bioavailability of the poorly soluble drugs and is a financially sensible tactic.

MICROSPHERES: The most recent advancement in cancer chemotherapy is microsphere technology. Particles with diameters ranging from 1 to 100 µm are known as microspheres. By physically trapping medication in blood veins—a process known as chemotherapy embolization—it can target their dosage and maintain the therapeutic agent's action through controlled release. By placing a therapeutic drug in the end organ vessels, biodegradable microspheres are used to directly deliver drugs to the organ or organs. The size and method of administering the microsphere—intravenous or intra-arterial—determine its impact.

DENDRIMERS

Monodisperse, highly branched, three-dimensional molecules with tightly controlled structures are called dendrimers. The large number of peripheral functional groups, water solubility, encapsulation ability, and monodispersed nature of these materials make them excellent candidates for evaluation as drug delivery systems. Dendrimers have been utilized recently in a number of cancer therapies as a drug delivery system for anticancer medications.The three main ways that drugs are delivered through dendrimers are as follows: (a) the drug attaches itself to the periphery of the dendrimers via a covalent bond to form dendrimers pro-drugs; (b) ionic interactions synchronize the drug to the outer functional groups; or (c) host-guest supramolecular assembly.

Final Thoughts and Prospective Routes

In addition to creating new therapeutic opportunities, the co-administration of two or more therapeutic agents on a single carrier platform also presents a number of novel challenges. Comprehensive biological evaluation, underpinned by a deep comprehension of the molecular mechanisms involved, is required to determine the right drug combination. Determining the ideal mass ratio of each component in a combination drug delivery system is another crucial step. This necessitates methodical study examining how various drug ratios affect the combination delivery systems' biological activity. A Canadian pharmaceutical company called Celator has created a systematic method for evaluating various drug ratios in their liposomal technology, which has led to the development Not only do live bacteria work well as drug carriers, but there are otheris also the delivery of antitumour drugs via bacterial outer membrane vesicles,bacterial-derived microcells, and bacterial ghosts. These carriers derived from bacteriapossess bacterial surface characteristics, allowing for the tumour-targeted delivery ofmedicines. These substances are safer because they don't have any bacterial biological activity.however, they also lose the ability to move

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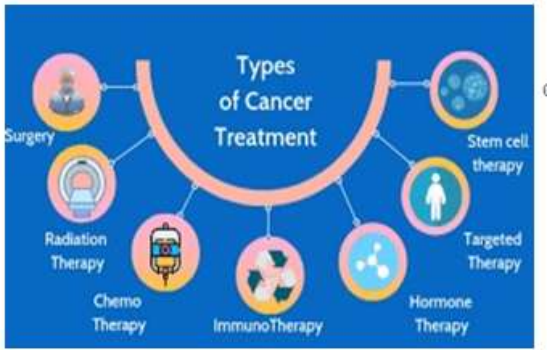
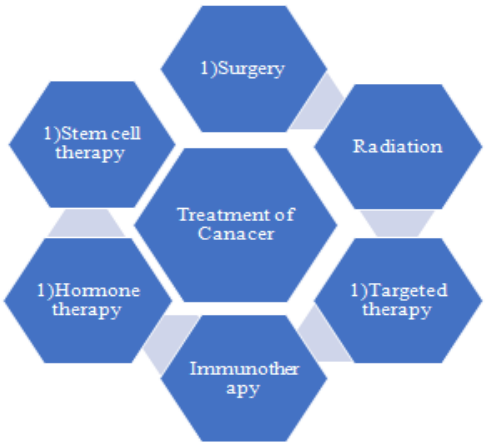
autonomously and penetrate tissue.Ability is significantly diminished.A range of materials that are currently being used or may be used as drug delivery vehicles for the treatment of cancer have been summarized in this review. Because of their special qualities, medical professionals can now use them as either standalone treatments (monotherapy) or as supplements to other therapies combined therapy to increase therapeutic efficacy. While some of these materials have not been successful in their clinical translation, there is hope for new treatment options in the near future due to the great promise of several new and promising materials that are currently under development.

TYPES OF CANCER [14,15]



The most common type Trusted Source of cancer in the U.S. is breast cancer, followed by lung and prostate cancers, according to the National Cancer Institute, which excluded nonmelanoma skin cancers from these findings. Each year, more than 40,000 people in the country receive a diagnosis of one of the following types of cancer:

TREATMENT OF CANCER THERAPY [16,17]



Surgery

When it's possible the goal of cancer surgery is to remove all of the cancer from the body. to do this, the surgeon uses cutting tools to remove the cancer and some healthy tissue around it. The surgeon may also remove some lymph nodes in the area. The lymph nodes are tested to see if they contain cancer cells. Surgery removes cancer that is contained in one area. Surgery removes some, but not all, of a cancer tumour. Debulking is used when removing an entire tumour might damage an organ or the body. Removing part of a tumour can help other treatments work better.

Radiation Therapy

Radiation Therapy is the term for treatment types that use radiation to destroy or shrink cancer cells and tumours. The two main types of radiation therapy for treating cancer are external beam radiation and internal radiation therapy. The type of radiation that a doctor recommends will depend on the type of cancer, the size and location of the tumour, and the person's general health. Radiation therapy may help meet different treatment goals. For instance, it may enhance the effectiveness of surgery, help prevent the spread of cancer, or relieve symptoms of advanced cancer. This article discusses the different types of radiation therapy, including how they work and the side effects and risks. It also explains what a person can expect from radiation therapy and the likely outcome. Radiation therapy is a type of cancer treatment that uses high energy beams to destroy cancer cells and shrink tumours. Radiation damages genetic material called DNA inside of cancer cells. If the cancer cell cannot repair the DNA, the cell will not be able to produce new cells and may die.

Chemotherapy

Chemotherapy can be used in metastatic, combined, adjuvant, and neoadjuvant settings. An adjuvant treatment is one that is administered prior to the primary treatment. Adjuvant therapy is a kind of treatment that can be used in conjunction with initial therapy to inhibit or stop the growth of cancer cells that are hidden from view. Chemotherapy is a pharmaceutical treatment that employs potent chemicals to destroy your body's rapidly proliferating cells. Since cancer cells proliferate and grow far more quickly than most other cells in the body, chemotherapy is the

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treatment of choice for cancer. There are numerous chemotherapy medications available.

Targeted therapy

Targeted therapy is a kind of cancer treatment in which specific cancer cell types are identified and targeted with drugs or other substances. A targeted therapy may be used as a stand-alone treatment or in conjunction with other medical interventions like radiation therapy, conventional chemotherapy, or surgery.

Immunotherapy

One kind of treatment for cancer is immunotherapy. It uses materials produced in a lab or by the body to strengthen the immune system and assist the body in locating and eliminating cancer cells. Cancer of many different kinds can be treated with immunotherapy. It can be taken either on its own or in conjunction with other cancer treatments, such as chemotherapy.

Hormone therapy

Cancers that rely on hormones to spread, like certain prostate and breast cancers, are treated with hormone therapy. One type of cancer treatment called hormone therapy slows or even reverses the growth of cancers that use hormones to spread. Other names for hormone therapy include endocrine therapy, hormonal therapy, and hormone treatment.

Stem cell therapy

The body uses stem cells as its basic building blocks, from which all other cells with specialized roles are derived. In the right circumstances, stem cells can divide in the body or in a lab to produce additional cells known as daughter cells. These daughter cells differentiate into new stem cells or become specialized cells with a more narrowly focused purpose, like bone, brain, heart, muscle, or blood cells. No other bodily cell possesses the innate capacity to differentiate into new cell types.

IN FUTURE SCOPE

In addition to creating new therapeutic opportunities, the co-administration of two or more therapeutic agents on a single carrier platform also presents a number of novel challenges. In To determine a suitable medication combination, it is required to carry out an exhaustive biological assessment which needs to be backed by a thorough comprehension of the underlying molecular processes. One more crucial Identifying the ideal mass ratio is one aspect of every element in a combination medication delivery system framework.

II. CONCLUSION

Globally, cancer has become one of the leading causes of death. Conventional chemotherapy has been the mainstay in the fight against cancer, but it comes with normal cell toxicity. Conventional cancer treatments frequently cause severe side effects because they lack specificity. consequences and toxicity. The severity of cancer necessitates the development of innovative methods to Control Discharge. Author manuscript; accessible through PMC. One author, one manuscript, one manuscript, one manuscript handle these illnesses. The location of current obstacles in the development of anticancer drugs targeted administration with minimal systemic toxicity. A tumour that is ebbing symbolizes a dynamic environment with modifications to its extracellular matrix, cell mass, and angiogenic state composition, in addition to other elements. Given recent developments and improvements in medication delivery

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