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INNOVATIVE CANCER MANAGMENT STRATEGIES AND DRUG DELIVERY METHODS

***Mane Dhananjay Shivaji, Salunke Sanjana Sunil and Shegade Pooja Rajendra**

B. Pharmacy, in SGMSPM's Sharadchandra Pawar College of Pharmacy, Dumbarwadi (Otur), Tal-Junnar, Pune 410504, Maharashtra, India.

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***Corresponding Author**
Mane Dhananjay Shivaji
B. Pharmacy, in SGMSPM's Sharadchandra Pawar College of Pharmacy, Dumbarwadi (Otur), Tal-Junnar, Pune 410504, Maharashtra, India.

ABSTRACT

Cancer is one of the leading causes of morbidity and mortality globally, and current treatment options, including chemotherapy, radiation, and surgery, confront substantial limitations such as poor selectivity, systemic toxicity, and drug resistance. Novel drug delivery systems (NDDS) have emerged as a promising way to increase cancer therapy efficacy by increasing medication targeting precision, minimising side effects, and overcoming drug resistance. This study focusses on current advances in various NDDS, such as nanoparticles, liposomes, micelles, dendrimers, and exosomes, which have shown considerable promise in cancer therapies. These systems can improve drug solubility, shield therapeutic compounds from early degradation, and enable controlled and long-term drug release at the tumour site. Furthermore, the addition of stimuli-responsive mechanisms and active targeting techniques has increased the therapeutic index of anticancer drugs. The paper also examines the problems of clinical translation, such as scalability, biocompatibility, and regulatory concerns, emphasising the importance of interdisciplinary approaches to overcome these barriers. Overall, NDDS have great potential to revolutionise cancer treatment, paving the way for more effective and less toxic therapies.

KEYWORDS: novel drug delivery systems, cancer treatment, nanoparticles, liposomes, targeted therapy, drug resistance.

INTRODUCTION

Globally, cancer was the second leading cause of death.[1] In the past few decades, considerable attention has been focused on the development of novel drug delivery system

(NDDS) for herbal drugs.[2] Enhancing solubility and bioavailability, protecting against toxicity, enhancing pharmacological activity, enhancing stability, improving tissue macrophage distribution, sustained delivery, and protection against physical and chemical degradation are just a few of the benefits of developing nano dosage forms (polymeric nanoparticles and nano capsules, liposomes, solid lipid nanoparticles, phytosomes, and nano emulsion, etc.) for herbal drugs in phyto-formulation research.[3] The goal of developing targeted medication delivery systems is to improve treatment outcomes while decrease in collateral damage to healthy tissues by delivering therapeutic molecules directly to tumor locations. Depending on the stage of cancer treatment may involve chemotherapy, radiotherapy or surgery followed by chemotherapy and/or radiotherapy. Unfortunately, current therapies are largely inadequate, as they are generally invasive and the cytotoxic drugs used adversely affect the human body in the process.[4] Cancer encompasses a variety of diseases characterized by the uncontrolled prolifeeration and division of abnormal cells that can invade and damage surrounding tissues and organs.[5] An example of a tumor suppressor is p53. The p53 tumor suppressor protein is one of the most important cell cycle controls in normal cells and in human cancer cells too, and is altered in almost every case of the latter. This review will focus on the Novel Drugs in treatment of cancer.[6]

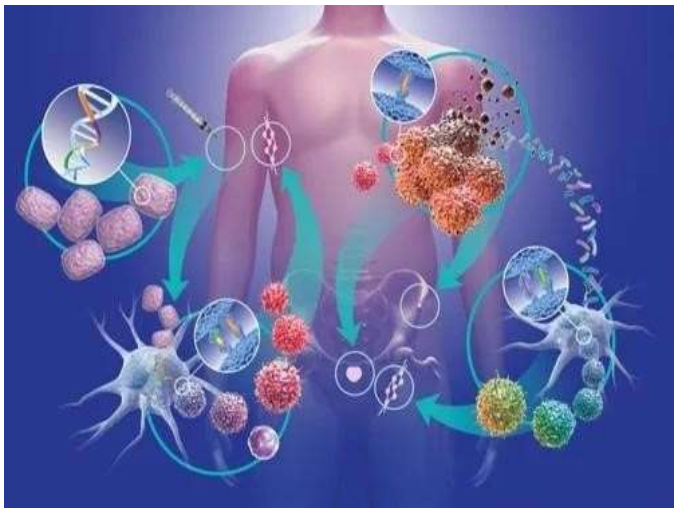

Figure 1: Novel Drug Delivery System.

BACKGROUND OF CANCER THERAPY

Over the past two decades, elucidation of the genetic defects that underlie cancer has resulted in a plethora of novel targeted cancer drug.[7] According to the World Health Organisation (WHO), cancer claims the lives of around 10 million people worldwide, making it a serious public health concern. Deaths each year, placing it behind cardiovascular illnesses as the

second greatest cause of death globally.[3] Various drug resistance mechanisms have been discovered over time, allowing tumour to withstand the harm caused by a particular medicine or class of anti-tumor agents.[8] Cancer is a multifactorial disease and is one of the leading causes of death worldwide. The contributing factors include specific genetic background, chronic exposure to various environmental stresses and improper diet.[9] There are several aspects of extreme importance such as the tumor microenvironment and vasculature, the reticuloendothelial system, the blood– brain barrier, the blood–tumor barrier, and the renal system. In order to achieve an effective system for cancer therapy, several characteristics of the nanoparticles have been outlined.[10] In the mid-20th century, Burnet and Thomas developed the immune surveillance hypothesis which postulated that the immune system very efficiently destroys malignant cells, and experimental results showing strong immunemediated rejection of transplanted tumors in mice supported this idea.[11] At the same time, treatment-associated changes such as tumor necrosis, vasculopath, inflammation, and cytologic atypia can pose significant diagnostic pitfalls, particularly if the pathologist is not provided a detailed therapeutic history. Therefore, it is critical to recognize the full spectrum of cancer therapy-associated neuropathology, the topic of the current review.[12] For over 30 years, stem cells have been used in the replenishment of blood and immune systems damaged by the cancer cells or during treatment of cancer by chemotherapy or radiotherapy.[13] Timely diagnosis and appropriate antitumoral treatments remain of utmost importance, since cancer remains a leading cause of death worldwide.[14] Cancer remains a significant cause of morbidity and mortality across the globe.[15] A recent report suggests around 14.1 million new cases and 8.2 million cancerrelated deaths, which are expected to reach 21.7 million and 13 million by 2030 worldwide, respectively.[15] Modern cancer treatments focus on precise drug delivery to the cancer tissues and minimize adverse effects on healthy cells.[16]

PATHOPHYSIOLOGY

There are several important elements that affect and modify cancer-related fatigue (CRF), and it is yet unknown what mechanism is required and sufficient to cause cancer patients to experience severe fatigue.[17]

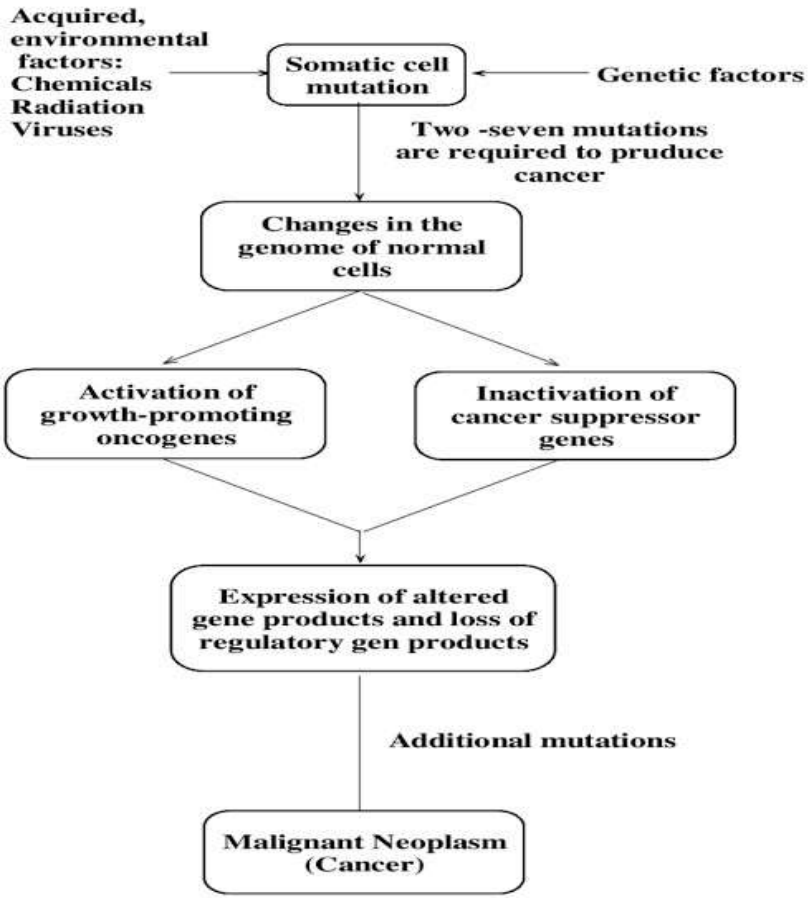

Figure 2: Pathophysiology of cancer.

Cancer patients often struggle with malnutrition, which is a major issue. The incidence varies between 30 and 87% of the various populations analysed, with patients with certain malignancies, such as head and neck, stomach, lung, and prostate cancers, being more commonly impacted. Cachexia from cancer refers to the advanced condition of famine brought on by reduced food intake and the hormonal/metabolic abnormalities typical of the tumor-host relationship.[18] Cancer patients' metabolic response is mostly caused by mediators secreted by the tumour or the host; cytokines including interleukin-1 (IL-1) and -6 (IL-6), interferon γ (INFγ), and tumour necrosis factor α (TNFα) have been highlighted recently. Additionally implicated are catabolic chemicals like adrenaline and glucocorticoids. The clinical symptom of cancer cachexia can be experimentally reproduced by cytokines. The clinical symptom of cancer cachexia can be experimentally reproduced by cytokines.[19] Because it promotes tumour growth in far-off, hematogenously seeded areas and makes the vascular space accessible, tumour angiogenesis is crucial to tumour metastases. Angiogenesis is also central to a number of other nonneoplastic disorders, including retinopathies, hemangiomas of childhood, and autoimmune disorders.[20] Whether these observed protective

effects are caused by the presence of dietary phyto-oestrogens, or whether they are merely indicators of a healthy diet in general, has not been established.[21] The full understanding of the immunobiology of cancer immunosurveillance and immunoediting will hopefully stimulate development of more effective immunotherapeutic approaches to control and/or eliminate human cancers.[22] Glutamine is an abundant and versatile nutrient that participates in energy formation, redox homeostasis, macromolecular synthesis, and signaling in cancer cells.[23]

DIOGNOSIS

Cancer is one of the leading cause of death in the world with the prevalence of> 10 million mortalities annually.[24] If a kid exhibits concerning or persistent signs and symptoms, primary care physicians should investigate the possibility of cancer. Red flag symptoms for lymphoma or leukaemia include hepatosplenomegaly, fever, anorexia, weight loss, lymphadenopathy, hemorrhagic diathesis, and prolonged, unexplained pallor. Concern for central nervous system tumours should be expressed if recent or ongoing morning headaches are accompanied by nausea, neurological symptoms, or back pain.[25] Two different patient behaviours may be useful in the early detection of cancer. These include going to cancer screenings, such as mammograms for breast cancer, which are intended to find the disease before it manifests symptoms, and promptly bringing possible cancer symptoms to primary care. The increasing fervour for public awareness programs aimed at raising awareness of early cancer indications underscores the significance of symptomatic presentation.[26] The symptoms cover a period of up to 11 months preceding the diagnoses, although most recorded symptoms occurred during the last three to four months before diagnosis.[27] Cancer related stroke has a distinct phenotype in terms of infarction pattern and laboratory findings.[28] Cachexia affects nearly half of cancer patients, causing the clinical manifestations of anorexia, muscle wasting, weight loss, early satiety, fatigue, and impaired immune response.[29] Lung cancer can present with a variety of early clinical signs, some of which may be present in addition to symptoms. Malignant lesions in the lungs can manifest as localised growth or invasion, metastatic illness, or paraneoplastic processes.[30]

TREATMENT

CHEMOTHERAPY

Solid lipid nanoparticles (SLN) offer a promising medication delivery technology for enhanced cancer treatment. By employing SLN to deliver anticancer drugs, a number of

common challenges are at least partially addressed, including normal tissue toxicity, poor selectivity and stability, and a high rate of drug-resistant tumour cells. The development of more recent SLN forms, including long-circulating SLN, nanostructured lipid carriers, and polymer–lipid hybrid nanoparticles, may increase the application of this adaptable drug carrier in the treatment of cancer.[31] As an alternative to traditional treatment, regional chemotherapy increases the anticancer medications' therapeutic efficacy while at the same time reducing their adverse effects on healthy tissues.[32] A new class of medications that identify particular targets on the outside or inside cancer cells is increasingly replacing cytotoxic chemotherapy, and research on resistance to antitumor medicines is still ongoing.[33] Enhancing the therapeutic efficiency of anticancer medications in cancer treatment may be achieved by the regulation of signal transduction pathways, targeting the proteins implicated in these pathways using antisense IAPs and growth factor antibodies.[34] The idea of combination chemotherapy has made the co-delivery of anticancer medications via nanotechnology a desirable tactic and a current area of research in drug delivery.[35] Determining an anticancer chemotherapeutic agent's cell-autonomous effects, or its ability to inhibit tumour cell growth (cytostasis) and cause tumour cell death (cytotoxicity), both in vitro and in vivo (often in immunocompromised mice that have been xenotransplanted with human tumours), is the primary motivation for developing new and evaluating existing ones. In addition to devising plans to effectively eliminate all cancer (stem) cells through the appropriate dosing and sequencing of chemotherapeutic agents, winning the battle against cancer requires striving to elicit an immune response, which will enable the immune system to suppress any remaining tumour cells.[36] The successful management of choriocarcinoma and leukemias with methotrexate led to further investigations in cancer chemotherapy. And drugs like thiopurines (e.g., 6mercaptopurine), 5-fluorouracil came into the forefront of cancer treatment.[37] Curability of cancer by chemotherapy generally is inversely related to age, i.e., the above tumors are most common in children and young adults. There are new and promising treatment strategies, such as neoadjuvant chemotherapy and autologous bone marrow transplantation. The revolution in molecular and cellular biology is providing an increase in targets, rationale, and opportunity for more effective and novel chemotherapeutic approaches.[38]

IMMUNOTHERAPY

Cancer immunotherapy has advanced significantly in recent years as a result of a better knowledge of the fundamental principles of tumour biology and immunology. These ideas

have proven crucial in the development of immunotherapy in the laboratory as well as its clinical deployment. The identification and further elucidation of immunotherapy's role in various tumour types, as well as the development of strategies for combining immunotherapy with cytotoxic and molecularly targeted agents for future multimodal cancer therapy, will allow for even greater progress and, ultimately, better outcomes for patients receiving cancer immunotherapy.[39] A better understanding of the molecular and cellular mechanisms controlling the immune system has opened the door to many innovative and promising new cancer therapies that manipulate the immune response.[40] Immune-based cancer treatments are already transforming the treatment of a number of previously incurable cancer types and provide great hope that over the next several decades, the toll that cancer takes on both individual suffering and societal expenses will decrease significantly. As they are developed and their combinations with currently available conventional therapies and one another are learnt to employ, at least two immunotherapeutic strategies—checkpoint inhibition and cellular therapy using autologous ('self') chimeric antigen receptor T cells (CAR T cells)—show unquestionable evidence of efficacy in a number of cancer types and promise even faster advancements.[41] Clinical support for the idea that the immune system might restrain the development of cancer emerged in the 1800s, when physicians noticed that tumors sometimes regressed in cancer patients who contracted bacterial infections.[42] Immune responses are regulated by a number of immunological checkpoints that promote protective immunity and maintain tolerance.[43] In some instances, under the pressure of the immune system, both the tumor and its microenvironment are shaped and immune-resistant tumor variants are selected initiating the process of cancer immunoediting[44] A subgroup of patients had a pre-existing T cell-inflamed tumour microenvironment, according to transcriptional profiling and immunohistochemical investigations. This characteristic makes a predictive biomarker potentially possible and may be indicative of the clinical response to immunotherapies.[45] With the goal of developing an effective therapeutic technique to increase the immune system's specificity and capacity to fight tumours, cancer immunotherapy has developed.[46] An significant development in cancer immunotherapy is adoptive cell transfer following host preconditioning via lymphodepletion. Here we demonstrate how adoptively transferred T cells' differentiation state can impact treatment outcome, and how a lymphopaenic environment allows cancer-reactive T cells to kill enormous loads of metastatic tumour.[47]

RADIOTHERAPY

The promise of completely eliminating tumour cells with the least amount of damage to healthy cells has been the foundation of successful cancer radiation treatment. Modern equipment made possible by technological advancements allows radiation to be precisely delivered to tumour lesions with significantly less damage to surrounding healthy tissues. Furthermore, a deeper comprehension of radiobiology, namely the mechanisms behind radiation toxicity in normal tissues and sensitivity and resistance in tumour lesions, has increased the effectiveness of radiotherapy as a treatment.[48] The rates at which cancer patients worldwide utilise radiation therapy vary greatly. It has been proposed in the past that 50% of cancer patients ought to receive radiation treatment. The Tree Age software (Tree Age Software, Williamstown, MA) was then used to determine the ideal percentage of cancer patients who should receive radiation therapy. Out of all cancer patients, 52% are recommended to get external beam radiation based on the best available data. The 95% confidence limits ranged from 51.7% to 53.1%, according to Monte Carlo analysis.[49] The impact of radiation therapy on cancer patients' longevity is typically understood to result from better local control of the tumour, which directly reduces systemic dissemination.[50] Up to 25% of newly diagnosed cancer cases in high-income nations should undergo a second round of radiation therapy, with 52% of cases requiring treatment at least once. Patients with cancer in low- and middle-income countries may require more radiation treatment than those in high-income nations due to the divergent distribution of tumour types worldwide and the advanced stage at presentation. Cost-effectiveness of radiotherapy for palliation or cure has been demonstrated.[51] Damage to cancer cells caused by radiation reveals antigens unique to tumours, making them apparent to immune surveillance and encouraging the priming and activation of deadly T cells. The tumour microenvironment's modification by radiation may also make it easier for immune cells to invade and recruit new members.[52] In animal models, a number of radiolabeled multifunctional nanocarriers have shown useful for both cancer detection and treatment. However, more preclinical, clinical, and long-term toxicity research will be needed before this technique can be used to treat cancer patients.[53] How to best take advantage of the differences between the features of the tumour and the host tissue has been a fundamental consideration in the use of radiotherapy; in the past, this has been accomplished empirically by radiation-dose fractionation.[54] One breakthrough has been the creation of a method known as "tomotherapy." A fan beam of radiation with intensity modulation is used to administer computer-controlled rotational radiotherapy, which is known as tomotherapy.[55]

Even the oldest old can take radiation therapy rather well. Aggressive radiation is not contraindicated by age.[56]

SURGERY

Surgery is an important step that gives cancer patients a shot at a cure. The perioperative phase is associated with an elevated risk of micrometastatic disease progression and the creation of new metastatic foci. In order to improve migration and invasion to the target site, surgery can cause changes in the target tissue and cancer cells themselves. It can also upregulate adhesion molecules in target organs, recruit immune cells capable of entrapping tumour cells, and increase the shedding of cancer cells into the bloodstream.[57] Surgery is necessary for cancer care in all resource settings. Over 80% of the 15·2 million new cancer cases in 2015 will require surgery, maybe multiple times. By 2030, we estimate that 45 million surgical procedures will be required worldwide. However, fewer than 25% of cancer patients globally receive safe, inexpensive, or timely surgery. Many of the most important adjunct treatment modalities for cancer surgery, such as pathology and imaging, are similarly inadequate.[58] Excisional surgery is a key therapeutic option for cancer.[59] Aggressive Musculoskeletal Cancer Surgery: Treatment of Sarcomas and Resection of Metastatic Deposits has been the volume of care now provided for musculoskeletal cancers.[60] Resection is the cornerstone of treatment for localised oesophageal cancer when there are no medical reasons why surgery cannot be performed.[61]

TARGETED THERAPY

Around 1600 BC, a papyrus discovered in Egypt contains the earliest known account of cancer. The development of antineoplastic chemotherapy, which targets all tumour cells, may be traced back to the 1940s with the introduction of nitrogen mustard. Numerous direct and indirect methods are included in targeted therapy.[62] The basic dependence of tumour cells on biological pathways, to which medications blocking those processes can be applied, is the basis for targeted therapy in oncology.[63] Because targeted therapy selectively targets cancer cells while sparing off-target cells from damage, it is becoming increasingly important. This review covers the range of targeted therapeutic techniques, including prodrugs, nanoparticulate antibody conjugates, small molecule inhibitors, and monoclonal antibodies.[64] Molecular targeted therapies are cutting-edge treatments that obstruct particular molecules to stop the spread, growth, and metastasis of cancer.[65] The Food and Drug Administration (FDA) has approved a number of molecular targeted medicines that have

shown exceptional clinical success in treating a wide range of cancer types, including lung, ovarian, colorectal, breast, and leukemia.[65] Many FDA-approved molecular targeted medicines have shown exceptional clinical success in the treatment of a wide range of cancer types, including breast, leukaemia, colorectal, lung, and ovarian cancer.[65] A major therapeutic advance, targeted therapy in the form of selective tyrosine kinase inhibitors (TKIs) has revolutionised the way cancer is managed. One of the first cancer medications to show promise for this kind of targeted activity was imatinib. BCR-ABL, c-KIT, and PDGFRA are among the tyrosine kinases that are inhibited by imatinib, an oral targeted medication.[66] The identification of ligands that target cancer cells, as well as the development of ligand-targeted therapies, will aid in improving treatment efficacy and reducing adverse effects. Unlike current forms of therapy, it will allow us to retain patients' quality of life while effectively treating the cancer tissue. It shows that ligands play a critical role in cancer cell targeting.[67]

HORMONE THERAPY

For prostate and breast cancers that are oestrogen and progesterone receptor-positive, hormone therapy is a successful and non-toxic treatment.[68] To evaluate postmenopausal and perimenopausal women using various hormone therapy for their risk of ovarian cancer.[69] Even some malignancies may be prevented by estrogen.[70] After the diagnosis of certain cancer types, but not others, menopausal hormone therapy is linked to an increased risk of recurrence and mortality. Millions of women continue to treat their menopausal symptoms with hormone therapy. In clinical settings, women on hormone therapy get mammograms more frequently than women who do not, which results in the diagnosis of cancer at an earlier stage.[71] Hormonal therapy has advanced iteratively, from gonadal testosterone deprivation to methods that prevent the production of adrenal and other extragonadal androgens, to those that directly bind to and inhibit the androgen receptor (AR).[72] Determine whether there is a major cognitive impairment in women receiving hormone therapy for breast cancer, and create a cognitive package that is sensitive to the possible effects of oestrogen insufficiency on cognition. As more hormone drugs are utilised in clinical trials for both adjuvant and preventive purposes, it is critical that any potentially harmful effects on cognitive function be thoroughly measured.[73]

BONE MARROW TRANSPLANT

A bone marrow transplant subscale (BMTS) consisting of 12 items was developed for the overall Functional Assessment of Cancer Therapy (FACT) evaluation. The subscale, when paired with the FACT (FACT-BMT), provides a 47-item, valid, and reliable measure of five dimensions of quality of life in bone marrow transplant patients. The validation procedure consisted of three steps: creating and selecting BMT-specific questions, as well as assessing the overall measurel.[74] The chance of developing a radiation-associated solid tumour following BMT is anticipated to increase with prolonged follow-up. This emphasises the significance of close monitoring of patients undergoing BMT.[75] Individuals who get bone marrow transplants are more likely to later in life acquire new solid cancers. The pattern of increasing risk over time following transplantation, as well as the higher risk among younger patients, highlight the importance of lifelong surveillance.[76] In areas where hepatitis B virus (HBV) infection is prevalent, cancer patients who are also chronic HBV carriers are frequently treated with chemotherapy or undergo bone marrow transplantation.[77] Despite a lack of clinical evidence of efficacy, over 41,000 patients had high-dose chemotherapy plus autologous bone marrow transplant (HDC-ABMT) for breast cancer in the 1990s.[78] Transplanting bone marrow with haematopoietic stem cells (BMT) can mitigate myelotoxicity and bypass treatment resistance by boosting the dosage of accessible cytotoxic drugs and radiation. If a dosage response to therapy is real, then one would anticipate that this medication will work for certain patients. Thankfully, it seems that this applies to aggressive NHL, Hodgkin disease, and possibly even some indolent NHL patients.[79]

PHOTODYNAMIC THERAPY

A minimally invasive treatment technique with clinical approval, photodynamic therapy (PDT) can specifically kill cancerous cells.[80] Although light has been used for medicinal purposes for thousands of years, photodynamic therapy (PDT) was not created until the previous century. PDT is currently being investigated in oncology clinics to treat tumours of the skin, brain, lung, pancreatic, intraperitoneal cavity, intramuscular cavity, breast, prostate, and head and neck.[81] Despite all of the recent advances in technology, metastasis and recurrence remain the leading causes of death. Photodynamic therapy (PDT) looks to be a potential alternative treatment for treating malignant diseases because it does not interfere with other treatment options and has a lower long-term morbidity when compared to chemotherapy or radiotherapy.[82] Using medications (photosensitisers) that are activated by light to become cytotoxic, photodynamic treatment (PDT) provides the foundation for

understanding current and future clinical uses in general cancer, gastroenterology, and other specialties.[83] A new cancer treatment called photodynamic therapy (PDT) creates reactive oxygen species and kills tumours by combining non-toxic dyes, sometimes known as photosensitisers (PS), with safe visible light.[84]

NOVEL DRUG DELIVERY SYSTEM

LIPOPROTEIN

The field of drug delivery has improved as a result of advances in pharmaceutical research and pharmaceutical biotechnology, which have coincided with developments in the drug discovery and development process over the past ten years. A suitable quantity of active medication must be absorbed and delivered to the site of action at the proper time and input rate for any optimal drug delivery system. Additionally, it suggests a selective distribution with little uptake elsewhere other than the site of action, which is crucial when the difference between the hazardous and effective concentrations is narrow. Two specific areas of need for better medication delivery have been identified: DNA-based vaccines and cancer treatment. In an effort to get around the drawbacks of traditional medication delivery methods, researchers have been looking into more sophisticated systems for the past few years. Using plasma's red blood cells, albumin, and lipoprotein as medication delivery vehicles is one of the most effective methods. Research on lipoproteins as drug delivery systems is gaining traction, and they are thought to be great options for precisely delivering medications to different tissues.[85]

Lipoprotein as drug delivery system for cancer Therapy

a. Targeted drug delivery system in cancer Treatment

Oncology researchers face a difficulty in developing innovative drug delivery methods for cancer therapy that deliver anticancer drugs to tumour cells selectively while limiting harm to other tissues.[86] By boosting the drug concentration in tumour cells and/or lowering the exposure in normal host tissues, a targeted drug delivery system may improve the therapeutic index of anticancer drugs. The ability to deliver anticancer medicines to tumour cells specifically by taking advantage of the biological differences between malignant and normal cells is often critical to the effectiveness of cancer therapy. Physical and biological targeting strategies are the two methods that can be used to deliver the anticancer medication to tumour tissue in a selective manner.[87] The development of novel drug delivery systems for cancer therapies that selectively deliver anticancer agents to tumor cells with limited toxicity to

normal tissues is a challenge for oncology researchers.[86] Through the increase of drug concentration in tumour cells and/or the reduction of drug exposure in normal host tissues, a targeted drug delivery system presents a promising means of improving the therapeutic index of anticancer medicines. The ability to target tumour cells with anticancer medicines specifically based on the biological distinctions between malignant and normal cells is often critical to the efficacy of cancer therapy. There are two methods for selectively delivering the anticancer treatment to tumour tissue: physical targeting strategies and biological targeting strategies.[87] The foundation of physical targeting is the exact injection or physical implantation of anticancer agents at the tumour site, thereby delivering the agents to the tumour tissue. Examples include the implantation of anticancer agent-loaded wafers, intracerebral delivery of anticancer drugs to brain tumours, and intra-arterial medication delivery to liver cancer.[88] The following strategies can be the foundation of biological targeting. First, some carriers such liposomes, polymer conjugates, bacterial, and viral vectors can convey an anticancer moiety. Second, the distinction in substrate uptake between cancerous and normal cells may serve as the foundation for the creation of tailored drug delivery systems for cancer. The rapid proliferation of malignant cells necessitates increased dietary requirements and overexpression of several receptors, including low-density lipoprotein receptors, growth factor receptors, folate receptors, and transferrin receptors.[89]

b. Low density lipoprotein for targeted delivery of Anticancers

To build their cell membranes, growing cells require cholesterol. They obtain cholesterol by the uptake of low density lipoprotein (LDL) by high affinity receptors and de novo production. In comparison to matching normal tissues, a multitude of tumour cell types exhibit elevated levels of receptor-mediated lipophilic acid absorption. It is proposed that high cholesterol requirements for cell development and/or a process directly related to cell transformation are the causes of the increased LDL receptor activity in cancer cells. For this reason, LDL has been suggested as a possible transporter of chemotherapeutic drugs.[90]

c. Liposomes

It has been acknowledged for thirty years that liposomes, also known as phospholipid vesicles, are a possible medication delivery system. Liposomes can be used to solubilise poorly soluble compounds in a biocompatible manner or as a controlled release carrier, depending on the substance of interest. Liposomes have certain special pharmacokinetic properties because of their size, which normally varies in mean diameter for the systemically

injected vesicles from 50 to 250 nm.[91] Therefore, one way to alter the pharmacokinetic and pharmacodynamic characteristics of medicinal medicines is by liposomal administration. In certain circumstances, these adjustments may lessen or alter the toxicity profile of anticancer medications while also increasing their therapeutic efficacy. For example, it has been shown that the long-circulating liposomal formulation of doxorubicin coated in polyethylene glycol exhibits increased solid tumour accumulation due to its enhanced permeability and retention effect, and lower dose-limiting cardiac toxicity when compared to the free drug.[92] Numerous significant advancements have distinguished liposomes as a medication delivery system. The creation of pH-sensitive liposomes for cytosolic drug delivery, temperature-sensitive liposomes for burst release in response to hyperthermia, cationic liposomes for nucleic acid delivery, pH-or ionic gradient polyethylene glycol-coated long circulating liposomes, and targeted liposomes for targeted delivery to tumour cells or endothelium are a few examples of these remote drug loading methodologies.[93]

MICROCAPSULES

Numerous anticancer drugs, including paclitaxel (PCT), camptothecin (CPT), and some porphyrins (such meso tetraphenylporphine, TPP, used in photodynamic therapy, PDT), have poor water solubility, which makes it difficult to apply and more difficult to provide directly by parenteral means. To address their limited stability, hazardous side effects, and poor solubility, a number of formulation techniques based on the utilisation of drug carrier systems have been proposed. Because of their easily manipulated qualities and strong pharmacological features, polymeric micelles have garnered a lot of interest among these systems.[94] Because of their easily manipulated qualities and strong pharmacological features, polymeric micelles have garnered a lot of interest among these systems.[95]

MICROSPHERES

As a temporary solution before surgery or transplantation, microspheres are used in radiation therapy for liver cancer. The prognosis is bad when liver metastases from any solid tumour occur unless the sickness can be surgically removed. Patients who die from colorectal cancer mainly die from hepatic metastases.[96] Cytotoxin-loaded microspheres are delivered to the breast via surgical implantation into the subclavian artery or one of its branches, typically the thyrocervical trunk. On the other hand, more selective perfusion can be obtained by directly introducing catheters via angiography into the internal mammary artery. Blood carries these intraarterially injected microspheres to the capillary bed, where they embolise and release

their therapeutic payload into the intended organ. A single pulse of adriamycin-loaded albumin microspheres was administered to breast cancer cells via an internal radiologically positioned mammary artery catheter. Research conducted on animals has indicated that albumin microspheres containing adriamycin are a more effective way to decrease cancer growth than free medications in a solution.[97] In vivo lung cancer growth in Lewis lung carcinoma cells is significantly inhibited by paclitaxel-loaded PLGA microspheres, which also exhibit no appreciable toxicity.[98] The intraperitoneal administration of cisplatin in the form of L-lactic acid and glycollic acid copolymer microspheres improves the survival rate of ovarian cancer-affected rats without increasing the systemic toxicity of the drug. The monoclonal antibody MJ01, enclosed in PLGA microspheres, is able to identify the human ovarian cancer antigen CA125 and stimulate T3, as evidenced by the in vitro proliferation of T cells upon encountering the antigen. In preclinical rat models, ovarian cancer immunotherapy using the anti-CA125 antibody has shown an encouraging response.[99]

Dendrimers

The capacity to synthesise dendrimers with particular properties based on the intended use is one of its advantages. Getting dendrimers that can be delivered to tumour areas and carry anticancer medications for treatment is very crucial. Medicines can be stored inside dendrimers or on their surface functional groups, and dendrimers can target anticancer medicines by encapsulation, covalent bonding, or electrostatic interactions.[100] When it comes to cancer, focused dendrimer distribution is essential to minimise adverse effects on good tissues like bone marrow and internal organs, which can happen when chemotherapy medications are given carelessly. To attain more precise targeting, dendrimers can be coupled with pharmaceuticals as well as targeting molecules like folic acid, other peptides, or monoclonal antibodies. Moreover, employing poly (ether hydroxylamine) dendrimers has been shown to improve the water solubility of anticancer drugs that are poorly soluble.[101] Dendrimers can be delivered to specific targets through either passive or active channel. Because of erratic vascularization brought on by tumour angiogenesis and ineffective lymphatic drainage, dendrimer macromolecules are retained in the tumour microenvironment. Dendrimers loaded with pharmaceuticals and various particular targeting compounds that facilitate interactions with specific cell receptors are conjugated to accomplish active targeting.[102] Targeted anticancer chemical administration is crucial in oncological diseases. Dendrimers can be used in cancer treatment through additional processes, such as the use of polyphenol dendrimers with antioxidant effect, in addition to their precise targeting of

anticancer chemicals, their delayed release, and their long-term retention in tumours. To lessen oxidative stress, which is a step in the apoptotic process, these can be directed towards tumours. The application of dendrimers in the treatment of cancer can also be based on neutron capture. It has been noted that the administration of these complexes to laboratory animals bearing tumours produced effective anticancer activity.[103] In addition, certain compounds that absorb light radiation and have an effect that is poisonous to tumour cells may be directed towards tumours when using dendrimers in the treatment of cancer. This kind of dendrimer application is relevant to photodynamic or photothermal therapy.

HYDROGEL

In addition to being able to withstand intravenous injection, in situ injection, in situ implantation, transdermal administration, oral distribution, pulmonary delivery, and transarterial chemoembolization, hydrogels come in a variety of sizes, including macrogels, microgels (0.5–10 μm), and nanogels (<200 nm). As a result, doctors can use customized medication to target various cancer types and places, which significantly enhances drug targeting, lowers dosages, and increases treatment effectiveness. Hydrogels are often generated through cross-linking polymerization in aqueous solution, which significantly reduces the danger of denaturation and aggregation of anti-cancer medications when exposed to organic solvents. Hydrogels' superior biocompatibility and biodegradability can lessen chemotherapy's adverse effects.[104]

Nanoemulsions

The administration of active pharmacological substances is facilitated by nanoemulsion dosage forms, which have garnered significant interest in pharmacotherapy and drug delivery.[105] They have the ability to encapsulate pharmaceuticals that are poorly water soluble due to their hydrophobic core structure. They are also made up of safe gradient excipients, making them a reliable and safe way to administer medications. Cancer therapy has been a problem for many decades. Drugs produced to treat this condition are not always successful and often fail, owing to limited solubility, multidrug resistance (MDR), and unspecific toxicity. Nanoemulsions could be the solution for effective and safe tumor treatment. These formulations not only address water solubility issues, but they also provide particular targeting of cancer cells and may even be engineered to circumvent MDR.[106] Recently, nanoemulsions have been widely used in cancer diagnostics, imaging, and therapy, owing to their ability to efficiently solubilize poorly aqueous soluble drugs, biocompatibility,

Nanoemulsions' multifunctionality has been expanded to include targeting, imaging, medication and oligonucleotide delivery.[107] Oil-in-water (o/w) or water-in-oil droplets that are transparent or translucent and have a mean droplet diameter of 100–500 nm are known as nanoemulsions, mini-emulsions, ultrafine emulsions, or submicron emulsions. In a number of ways, the delivery mechanism based on nanoemulsions is better than traditional topical dose forms like gels and ointments. Stable emulsions are produced by combining safe, well-characterized components in a proprietary way to create nanoemulsions.[108] As a tocopherol-based paclitaxel (PTX) nanoemulsion, TocosolTM uses α-tocopherol (α-T) as a solubilizer and vitamin E TPGS as the main emulsifier.[109] Depending on the lipid composition, surfactant ratio, and other surface modifiers ratio, varied drug loadings can be created and used for drug delivery in cancer chemotherapy.[110]

CONCLUSION

Novel drug delivery systems (DDS) in cancer treatment demonstrate their transformational potential for improving therapeutic efficacy while minimising side effects. These sophisticated methods, such as nanoparticles, liposomes, and targeted therapies, allow for precision administration of chemotherapeutics directly to tumour locations, enhancing drug absorption and lowering systemic toxicity. Emerging technologies, such as nanotechnology and smart drug delivery systems, have the potential to transform personalised medicine by enabling tailored therapies based on specific patient profiles. Several challenges remain, including guaranteeing safety, overcoming biological obstacles, and addressing regulatory issues. However, continuing research and clinical trials are paving the way for novel DDS to play an important role in improving cancer patient outcomes, eventually leading to more effective and less invasive treatment alternatives.

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