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CHEMOTHERAPEUTIC DRUG DELIVERY SYSTEMS: NEW IDEAS AND PERSPECTIVES

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ABSTRACT

Targeted medication delivery to the organ, tissue, or cells currently offers great opportunities in the field of drug therapy. Drug delivery systems (DDS) are essential for improving the efficacy of chemotherapy in cancer treatment. Chemotherapy is a subject of great interest since new drug delivery techniques are constantly being created. The ability of therapeutic agents to reach their intended sites and their low accumulation in non-specific sites (healthy organs and tissues) are both crucial components of anti-tumor chemotherapy success. As a result, the targeted distribution of medications to the organs, tissues, or cells is currently thought to provide wonderful prospective in the field of chemotherapy. The fundamental idea behind targeted delivery is that molecules that can be recognised by a specific receptor on cells or target sites can be used to modify delivery systems (such as the vector, containers, and others) rather than just the medication itself.

These are therefore referred to as "targeted drug delivery systems." Yet, the development of multifunctional nanocarriers, such as nanoparticles, liposomes, micelles, dendrimers, and others, can greatly improve the effectiveness of numerous therapeutic and diagnostic procedures.

I. INTRODUCTION

Before reaching their target areas, all administering medications (molecules or particles) must go past a number of biological obstacles. What obstacles are influenced by drug delivery methods, modes of action, and pharmaceutical formulations? The intersection of a subcellular cell membrane and an organelle is one of these barriers, as are the reticuloendothelial system (RECs), gastrointestinal epithelial lining, vascular endothelium, and stroma (interstitial tissue) barriers (transport across the cell). As a result, the ability of medications to effectively reach their targets directly affects the therapeutic impact of those therapies. Every therapeutic treatment's effectiveness is greatly influenced by the therapeutic agent's bioavailability at the site of action in the human body, in addition to its pharmacokinetic/pharmacodynamic activity. The importance of dose forms was first made public by biopharmacy fifty years ago, which also identified drug formulation as the primary pharmaceutical factor affecting the therapeutic efficacy of medicines. Parallel to this path, scientists made early attempts to develop pharmacological formulations with specific pharmacokinetic properties. These pharmaceutical drug forms—also known as therapeutic systems or drug delivery systems—have a structure and technology that are significantly more complex than those of conventional drug forms (DDS).

II. DRUG DELIVERY SYSTEM (DDS)

A formulation or piece of machinery known as a drug delivery system (DDS) enables a therapeutic substance to target its site of action while avoiding nontarget cells, organs, or tissues. The main goals of constructing such systems were to increase the lifespan of pharmaceuticals in biological fluids, the direction of their actions, the enhancement of their solubility and bioavailability, shield drugs from early biodegradation before they reached problematic areas, decrease undesirable drug reactions in healthy tissues, organs, or cells, and minimise the emergence of side effects. It was necessary for the drug to be distributed relatively uniformly throughout the organism after conventional administration in order for targeted drug transport to appear. Drugs must also penetrate not only the target sites where they must have a therapeutic effect but also other organs, tissues, or cells where their action may have negative effects. When medications are distributed uniformly, their concentration in problematic locations might be reduced below the therapeutic level, which results in a weak drug therapeutic effect. Higher dosages of the medication are prescribed for better outcomes, but this

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increases the chance of unintended side effects (this is the main problem for most antineoplastic drugs). Drug adverse drug reactions, therapeutic drug doses, and frequency of administration can all be significantly reduced by transporting the drug solely or at least predominately in the region affected by the pathological process. Currently, researchers are concentrating on nanotechnological ways to achieve these goals.

III. NANOTECHNOLOGY

New opportunities are made possible by nanotechnology that are not possible through conventional means. Because of its distinctive size and high surface-to-volume ratios, nanotechnology has the potential to provide solutions to the present problems in cancer therapy. Because of the makeup of their materials, nanotechnologies have characteristics such as self-assembly, stability, specificity, drug encapsulation, and biocompatibility. Due primarily to the improved half time and targeted drug delivery, DDS at the nanoscale (10–1000 nm) or on multifunctional carriers were capable of altering the therapy for a number of diseases. Targeted drug delivery is currently carried out using a variety of nanotechnological platforms, each with unique physical and chemical properties, including polymersomes, nanoparticles, nanoshells, quantum dots, nanotubes, nanoemulsions, nanoerythrosomes, dendrimers, polymeric micelles, and polymer-drug conjugates. Moreover, nanomaterials are now used by pharmaceutical companies for packaging as well as drug delivery. Hence, it is possible to retain medicine consumer attributes while increasing productivity. The distribution of anticancer medications can be accomplished using liposomes, which are uni- (mono), bi-, or multi-laminar vesicular structures having a range of desired features. Liposomes are biocompatible from a biomedical perspective, cause little to no antigenic, pyrogenic, allergic, or toxic reactions, and easily degrade in the body. They can transfer encapsulated substances to intracellular space in various cells and shield the host from any negative side effects of the entrapped medicine while also shielding it from the physiological medium's inactivating effects. From a clinical perspective, liposome biodistribution is a crucial factor. The stability and inactivity of these standard liposomes in the treatment of cancer and cancer tissue led to a severe issue with their ability to supply sufficient concentration at the site of tumour tissue. One of the key drawbacks for the potential use of liposomes as DDSs is their excellent absorption by macrophages and subsequent elimination from circulation when the diseased target location is outside the mononuclear phagocyte system. In this situation, new technological approaches like nanotechnology, biotechnology, and others can be used to solve some difficulties. Ordinary liposomes can be altered using a variety of techniques to create distinct kinds of liposomes with unique qualities, including those that are pH-sensitive, thermosensitive, stealthy, targeted, and others. If we take a look at "stealth liposomes," they are hypothetically covered with a highly hydrating polymer, covalently attached antibodies, and other protective surface proteins (serum proteins), preventing macrophages from recognising them as foreign objects that need to be cleared away. Animal experiments have demonstrated that the therapeutic effects of anticancer medications were exceptionally amplified when utilised in "stealth liposomes," and in some cases, led to a complete remission of malignancies. A significant reduction in the size of the metastasis was seen in cancerous tumours. Doxorubicin (DOXIL®) in the form of liposomes (stealth liposomes) significantly improves the effectiveness of treatment against Kaposi sarcoma, and Lipoplatin TM (liposomal cisplatin) significantly lessens the neurotoxicity of cisplatin in phase III human clinical trials with patients with pancreatic, head, neck, and non-small-cell lung (NSCL) cancer. Moreover, the biopharmaceutical qualities of vincristine (VCR) and vinblastine (VLB) sulphate can be enhanced by using well-known liposome technology. For instance, Jeffrey A. Silverman et al. demonstrated that the pharmacokinetic limitations and dose-limiting adverse effects of vincristine might be overcome by the liposomal version of vincristine sulphate (Marqibo®). Also, there is scientific proof that the circulation half-life of liposomes is increased when polyethylene glycol (PEG) is connected to their surface.

IV. RESEARCH PERSPECTIVE

Researchers concentrate on a number of elements when creating new chemotherapeutic DDSs. These variables may have an impact on the carrier's therapeutic options, as well as the enhanced permeability and retention (EPR) effect of some tumours, extravasation potential, intratumoral distribution, tumour heterogeneity, and overexpression of particular cell markers on the target, among other things. For the development of novel anticancer DDS, researchers now use research data and evidence of the histological and physiological characteristics of the majority of cancer types (including the overexpression of cell markers, the EPR effect, the pH of tumour tissues, hypoxia in tumour tissues, and others) (pH-sensitive, redox sensitive, targeted and others DDS). To improve the effectiveness of the main cancer treatment, targeted drug delivery systems (TDDS) or drug formulations with tailored action are more crucial. "Active targeting" and "passive targeting" systems are the two categories into which targeted drug delivery can be divided. The idea of passive drug targeting was first put forth by Prof. Hiroshi Maeda in 1985 and was based on the EPR-effect of tumours and the potential use of nanocarriers for target anticancer medication delivery by the EPR. However, certain instances demonstrate that the passive targeting strategy can be restricted to particular types of tumours, as they merely lack the expression of the EPR effect and may not all have the same shape of tumour blood vessels. Programmed nanoccarries, which can actively and selectively interact with particular target cells after extravasation, can get beyond these restrictions. It can be done by adding targeting molecules, such as

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ligands, to the surface of nanocarriers, which can then bind to particular cell surface receptors through various chemical conjugations (polymer conjugates, linkers, and others). A unique contact between the drug carrier and the target cells via ligand-receptor interactions was thought to be the definition of active direction. The drug carrier needs to be very close to the target cells (less than 0.5 nm). Nevertheless, these DDSs lack the capacity to navigate themselves to the target site. These systems also penetrate the target by extravasation and blood flow. Targeted medication delivery can also be divided into two categories: intracellular direction and system locations (systemic targeting) (intracellular targeting).

V. CONSCLUSION

Chemotherapeutic drugs are currently delivered through a variety of techniques, each of which has advantages and downsides. The majority of DDS are synthetic in nature and can produce hazardous chemicals during metabolic processes in the human body, which can lead to problems and harmful effects on elimination, among other things. Hence, developing a more natural mechanism for the delivery of medicinal drugs is important. At the moment, targeted administration of chemotherapeutic agents, and drug delivery systems can fundamentally transform strategies and approaches to the treatment of cancer therapy, decrease adverse effects of the medications, and boost overall effectiveness of therapy. As we will see in this article, the majority of these techniques, platforms, and medication formulations are still under investigation, however some of the discovered ways are slowly finding practical use in medicine and other fields. The ultimate objective of all these initiatives is to enhance chemotherapeutic efficacy while also enhancing living conditions and convenience for cancer patients. We may infer from the analysis of available data that the theoretical foundation of these methods will hold up in the event that chemotherapy quality needs to be improved in the future. We still have a lot of questions to address about the current issues with medicine distribution, but researchers are moving forward in the correct direction and will eventually uncover the solution that Paul Ehrlich predicted would be the magic bullet.

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