REVIEW ARTICLE

Recent Advancements in Drug Delivery System in Lung Cancer

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ABSTRACT

Eliminating the fact that the use of free pharmaceuticals in conventional dosage forms usually involves difficulties in hitting the target site at the appropriate dose after or during a correct time period, medication targeting specific organs and tissues became one of the century's most important initiatives. Thus, finding new drug delivery strategies and modes of action are lines of battle. Difficulties are still encountered with radiation therapy to accurately track the movements of lung tumors while treatments are being admitted. The development of MRI-linac hybrid system prototypes offers the possibility of real-time, ionization-free tumor imaging. This study assesses how well lung tumor tracking algorithms function on five healthy participants' cine-MRI sagittal images. The targets were vascular structures that could be seen. Lung cancer is the leading cause of mortality in the world. This is one of the heterogeneous diseases that include, at the basic level, two main subtypes: small cell lung cancer and non-small cell lung cancer. Less than 20% of patients with LC survive for 5 years on average despite recent improvements in treatment. The effectiveness of existing therapeutic techniques is impaired because of severe off-target effects and innate or acquired medication resistance. The two major types of lung cancers are SCLC and NSCLC; among these, the former is the most frequently diagnosed. Lung cancers account for the highest mortality rate due to cancer. The application of nanomedicines can partially overcome the failures that are associated with the anticancer therapies against NSCLC. One of the nanoparticle subfields that hold out much promise for better delivery while ensuring stability and sufficient bioavailability of administered anticancer medications is nanomedicine.

Keywords: Drug Delivery Strategies, MRI-Linac Hybrid System, Lung Cancer Subtypes, Nanomedicines, Tumor Tracking Algorithms.

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INTRODUCTION

Lung cancer is the most commonly diagnosed cancer, accounting for about 11.6% of all cases, while all over the world, it is responsible for about 18.4% of all cancer deaths. The disease is highly heterogeneous and results from genetic and epigenetic changes in the lung epithelium. Although most cases of lung cancer can be explained by tobacco smoke, an estimated 10 to 25% of cases occurring in non-smokers are due to exogenous carcinogens, including diesel exhaust, radon, fumes, and ionizing radiation from both domestic and occupational sources.[1] Lung cancer is one of the leading causes of cancer-related death all over the world, mostly due to the fact that diagnosis often takes place at an advanced stage and thus the treatment outcomes are poor. One of the major trends in drug discovery is specific medications aimed at the unique nature of lung cancer cells. The nanoparticle-based delivery systems have gained ground because they can house the drugs and send them straight to the tumors. Nanoparticles can be tailored to attach themselves specifically to the cancer cells, reducing their off-target impacts and maximizing drug loading at tumor locations. Among strategies used to increase their selectivity and penetration into tumors include surface coating, functionalization as well as polymerization techniques (where a polymer is added) that are applied on these materials. Inhalable drug release systems represent another interesting direction. In lung malignancy, for instance, drugs are administrated locally thus ensuring the greatest concentration near the target site and minimal exposure throughout the body. New formulations are being designed like dry powder inhalers or nebulizers to allow direct administration of anticancer agents, gene therapies, and targeted drugs solely into the lung tissue. This offers multiple advantages such as minimizing adverse effects on other organs; making it an excellent option for dealing with lung neoplasms. The traditional modalities of treatment, such as surgery, radiotherapy, and chemotherapy, have disadvantageous side effects that include systemic toxicity

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and low therapeutic effectiveness. In the recent development in drug delivery systems, some promising strategies are proposed to improve therapeutic outcomes of drugs by improving drug targeting, reducing side effects, and reverting drug resistance. It covers recent progress in the field of DDS for lung cancer, ranging from novel formulations to targeted delivery mechanisms through emerging technologies. Lung cancer is classified mainly into non-small cell lung cancer and small cell lung cancer and represents one of the prime challenges of clinical management being associated more with its high mortality rate and complex biology. Standard treatments include chemotherapy, radiation therapy, and targeted therapies. However, in most cases, these strategies often come with some drawbacks, such as poor bioavailability, off-target toxicity, and the development of resistance. The recent technological developments in DDS can help deal with these issues by increasing drug delivery precision and, hence, efficacy while reducing possible side effects. Drug delivery systems (DDS) have recently become a promising solution to these challenges by enhancing the targeted delivery of therapeutic agents to reduce off-target effects and improve treatment outcomes. Advanced DDS formulations have recently taken the forms of liposomal, nanoparticle-based systems, inhalable delivery methods, and gene or RNA-based modalities with new opportunities for treatment that are more effective and personalized to each patient's lung cancer condition. The promise of these technology advances holds promise for revolution in the scenario of lung cancer therapy; improved patient outcomes and better survival rates will be realized. Cancer is the reason behind one in every six deaths worldwide. In 2020, records for close to 10 million reports were noted in relation to mortality that was responsible for cancer. Prostate and lung cancers are the leading two cancers (at 1.41 million and 2.21 million cases, respectively), followed by colon and rectal cancers at 1.93 million cases and 2.26 million cases of breast cancer. More than 30% of cancer cases, including those being caused by hepatitis and HPV or human papillomaviruses, occur in countries with low and lower middle incomes. Early detection can lead to the cure of many cancers and efficient medical care. Because of the asymptomatic nature of lung cancer, the diagnosis is usually made after the disease is advanced.[2,3]

Nanoparticles-Based Drug Delivery for Therapy of Lung Cancer

Lung cancer has only a 15% five-year survival rate, making it the leader in cancer-related mortality worldwide. In the US alone, estimates show that nearly 220,000 new cases are diagnosed every year, with 85% being non-small-cell lung carcinoma and the rest as SCLC. This is suggestive of the fact that the type and stage of the cancer are major influencing factors on the current treatment methods generally a combination of radiation, chemotherapy, and/or surgery. For patients who are suffering from late-stage lung cancer, the application of chemotherapy through the vein is a common practice that makes it easy for drugs to access both malignant and healthy tissues. Cisplatin and carboplatin are examples of platinum-based medicines that have been used as the first-line chemotherapy agents. Some of these side effects are dose-dependent and can include anemia, nephrotoxicity, cardiotoxicity, peripheral neuropathy, and damage to the intestines. One can also find mild symptoms like nausea, fatigue or discomfort. Therefore, it is common practice to prescribe other anti-cancerous agents alongside platinum drugs in order to overcome those adverse reactions. In this case, administration via combination therapy, including two or three substances reduces the amount of each drug but promotes overall efficacy. Typical combinations include platinum drugs with paclitaxel, gemcitabine, etoposide, or vinblastine. Contrary to the viral vectors, nanotechnology offers some exciting and hopeful developments in the construction of the drug delivery system capable of effectively tracking target tumors, ushering in an absolutely new era of cancer management and treatment.[4] Nanoscale drug delivery systems can be effectively used to formulate a diverse range of anticancer drugs and enhance their therapeutic efficacy. Using nanoparticles to optimize the biodistribution would reduce the nonspecific toxicity caused by the potent antitumor drugs and increase their therapeutic impact at the same time. Globally, lung cancer is still one of the most prevalent and lethal cancer types, accounting for a significant portion of cancer-related yearly deaths.[5] The text message from the user is vacant. Notwithstanding the advancements in medical research and treatment methods, the prognosis for individuals with The main reason lung cancer is still unfavorable is because of late-stage recognition and the rise of opposition to conventional treatment.[6]

Recent Advances in Nanoparticle Systems Hugely Advanced Drug Delivery Technology

Research in the field of nanomedicine is expected to continue and achieve highly sensitive and specific new diagnostic and imaging agents and safe and effective methods for drug delivery. However, there are a few challenges that are attached with radical innovation and translation into clinical applications. The design of nanoparticle drug delivery systems to target specific sites and to deliver therapeutic or gene payloads effectively remains a challenge. Possible problems arising in the biological environment include suboptimal surface chemistry, unclear structural properties, poor biocompatibility, and an improper size distribution. Moreover, the large variety of physicochemical properties and biological activities of nanoparticles further complicates the design of an ideal system to deliver drugs to the lungs. As a variety of challenges, such as immune response, rate of circulation clearance, targeting efficiency, and capacity to traverse biological barriers, come up, these nanoparticle systems proceed to preclinical and clinical testing. That's why the proper understanding of the biological activity of nanoparticles requires the best efficiency in drug transport. Determining the physicochemical properties is crucial for understanding the intracellular trafficking of nanoparticles, protein adsorption on the surface of nanoparticles, aggregation tendencies, and particle-particle

interactions within a biological milieu. Any one of these variables, in significant fluctuation, may be a cause in toxicity, inadequate drug delivery, and/or decreased therapeutic efficacy. Therefore, the physicochemical characteristics of nanoparticle systems play a major role in determining their efficacy-toxicity balance. Since larger particles are quickly removed from the circulation, intravenous injection of particles larger than 500 nm is not advised. These physical properties probably help the nanoparticles take advantage of the solid tumors' increased permeability and retention (EPR) impact. Because of impeded lymphatic flow, passively targeted nanoparticles are able to permeate solid tumors through their leaky vasculature and remain there for lengthy periods of time. Numerous FDA-approved nanoformulations, including abraxane and doxil tap into the distinct micro physiology of tumors. The EPR effect is a significant factor in assessing the effectiveness of nanoparticle-based drug delivery systems in solid tumors, including lung cancer.[7] Determining the physicochemical properties is crucial for understanding the intracellular trafficking of nanoparticles, protein adsorption on the surface of nanoparticles, aggregation tendencies, and particle-particle interactions within a biological milieu. Any one of these variables, in significant fluctuation, may be a cause in toxicity, inadequate drug delivery, and/or decreased therapeutic efficacy. Therefore, the physicochemical characteristics of nanoparticle systems play a major role in determining their efficacy-toxicity balance. Since larger particles are quickly removed from the circulation, intravenous injection of particles larger than 500 nm is not advised. These physical properties probably help the nanoparticles take advantage of the solid tumors' increased permeability and retention impact. Because of impeded lymphatic flow, passively targeted nanoparticles are able to permeate solid tumors through their leaky vasculature and remain there for lengthy periods of time.

Types of New Drug Carriers New System

The creation of microspheres carrying both hydrophilic and hydrophobic medications encased in biocompatible polymers has been made possible by microencapsulation, which has proved crucial to the development of novel treatments. By achieving a controlled release, these carriers are intended to decrease systemic absorption while preserving therapeutic drug levels for a predetermined amount of time.[8] These methods have found use in the pharmaceuticals,[9,10] food and cosmetics industries.

Nanoparticle-Based Delivery Systems:

Liposomes

These lipid-based nanoparticles can encapsulate both drugs that are hydrophilic and hydrophobic drugs, improving the stability and bioavailability of chemotherapeutic agents.[11] They can also be designed to target lung cancer cells more precisely, reducing off-target effects.

Nanocarriers

Nanoparticles like dendrimers and quantum dots are being used to deliver drugs directly to cancer cells.[12] They can be engineered for specific targeting and controlled release.

Targeted Therapies

Monoclonal antibodies and conjugates

To improve delivery and effectiveness, antibodies that target certain antigens on lung cancer cells are conjugated with medications or poisons.[13] Antibody-drug conjugates are a type of medication that combines a cytotoxic chemical with a monoclonal antibody to specifically target and kill cancer cells.

Small molecule inhibitors

To enhance their delivery to lung cancer cells, medications that selectively block molecules implicated in cancer cell signaling pathways are being developed.[14]

Inhalation-Based Delivery

Dry powder inhalers (DPIs)

Drugs may now be delivered to the lungs more effectively because to advancements in DPI technology.[15]

Smart inhalers and nebulizers

To increase the precision and effectiveness of medication delivery to the lungs, more advanced models of these devices are being created.[16]

Gene Therapy and RNA-based Therapies:

Delivery of siRNA and mRNA

Technologies are developing to transport messenger RNA (mRNA) or small interfering RNA to cancer cells.[17] These treatments try to increase the expression of therapeutic proteins or interfere with the expression of genes in cancer cells.

Combination Therapies

Combination of chemotherapeutic and Immunotherapy

To increase overall treatment efficacy, drug delivery methods are being devised to deliver immune checkpoint inhibitors and chemotherapeutic drugs at the same time.[18]

Combination with radiotherapy

To enhance treatment results, systems combining focused radiation therapy and drug administration are being developed.[19]

Advanced Imaging and Tracking:

Imaging-guided drug delivery

Real-time monitoring of drug distribution and accumulation in lung tumors is made possible by the integration of drug delivery systems with imaging techniques (such as MRI and PET)[20] and some tracking is shown in Figure 1.

RNA Based Therapies

Lung cancer continues to be among the most significant causes of cancer mortality for men and women globally.[21] As of 2020, the number of new cases was approximately 228,820 and deaths related to LC were reported as 135,720 in the United States alone[7]. In general, there are two subtypes of LC: small-cell lung cancer (SCLC) and non-small-cell lung cancer (NSCLC). These have two principal subtypes that can be classified higher into causes and mutations and are characterized by marked

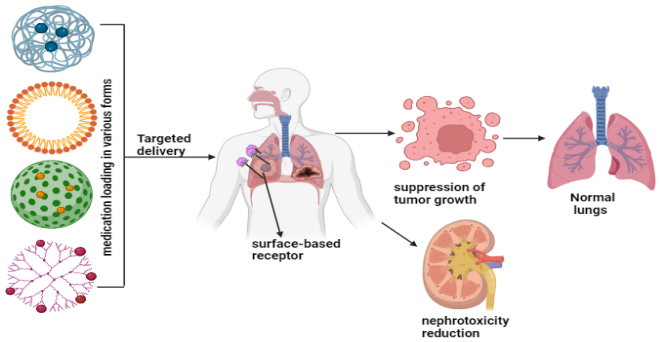

Figure 1: Drug delivery system on lungs

intratumoral variation in their composition.[22,23] Around 80 to 85% of LC can be classified as NSCLC; among them you will find large cell carcinoma, squamous cell carcinoma and adenocarcinoma.[24,25] Roughly 10 to 15% of the different types of SCLC are represented in the SCLC.[26,27] SCLC has a 5-year survival rate of almost 5%, while NSCLC has a figure below 20% if viewed from the past 20 years.[28,29] Some frequently analyzed oncogenes for NSCLC include KRAS, EGFR, and EMAP-like 4-ALK. In SCLC, certain genes are related to poly (ADP-ribose) polymerase, Aurora kinases and vascular endothelial growth factor.[30-34] KRAS is among the potential targets for LC therapy because it contains activating mutations in about 30% of LC patients. Similarly, tyrosine kinase inhibitor therapy did not provide any benefit regarding OS to patients following activating mutations of EGFR.[35-38] Similar lacunas exist in the management of SCLC: most of the patients develop resistance to chemotherapies and immunotherapies have very low efficacy because the receptor antigens have very sneeze-like expression.[39-43] Failure of present-day therapeutic approaches, as highlighted by the use of certain medicines that have really been shown to work, occurs mainly because of the affectation of drug-resistant mechanisms, including gene mutation; generation of cancer stem cells; oncogene overexpression; loss or inactivation of tumor suppressor genes.[44-48] It has been observed from the above studies that patients suffering from LC need a completely new approach to treatment. The rapid advancement in strategies for addressing such limitations using RNA interference and RNA-based drugs is impressive. Some research efforts show how combinations of silencing certain genes either alone or with additional mediators like immunotherapy or chemotherapy can be effective.[49-57] The general types of recent drug carrier system and advancement are mentioned in Table 1 and Figure 2, respectively.

General Mechanism Consideration

The surface of a specific material can be modified to form stronger bonds with it, release drugs in a systematic way, and target tissues that need to be treated:

Many strategies have been studied to direct medication delivery to a particular region of interest, either by active diffusion (using ligands to target a specific target) or passive diffusion (increased accumulation owing to passive physiological factors).[64] Drug absorption can be enhanced by adsorbing, coating with or linking bioactive molecules to surfaces of drug carriers that bind to cell receptors showing a selective affinity to specific cells or tissues. This may also involve the use of modified coatings that the inhibition of enzymatic decline. within the gastrointestinal (GI) tract and plasma, including chitosan and albumin.[65] Research has been done on monoclonal antibodies (or fragments) and non-antibody ligands, such as cell surface-specific carbohydrates like lectins.[66] Moreover, for instance small molecules or peptides that act as agonists/subtractors or antagonists/inhibitors targeting receptors overexpressed on the cell surfaces of specific tissues (like folate, transferrin, and galactosamine) have also shown good results in recent times. The use of targeting ligands should be taken into consideration in several ways because they can enhance distribution to secondary target sites of unintended tissues. Indeed, a major drawback to non-antibody ligands is their unspecificity when produced. On the other hand, immuno-conjugates have problems with respect to immunogenicity and reticuloendothelial system (RES) retention. Carrier surfaces can be modified by adding some coatings that change their lipophilicity/hydrophilicity profiles, minimize uptake by immune cells while at the same improving cell recognition (such as the synergy between

Table 1: Types of recent drug carrier systems

S. No	*Carrier system*	*Description*
1.	Microsponges	Synthetic polymer-based microsponges are biologically porous, non-reactive sediments that can support an active substance equal to its own mass within the same volume.[58] They are able to provide a regulated release while shielding the medication from the elements. Products, which contain fluorouracil to treat actinic keratosis, and Retin-A micro®, which treats acne vulgaris, are readily available.
2.	Nanotechnology	The term "nanomedicine" first appeared when commercially available devices were quickly generated through use of nanotechnology for the drug delivery system. The creative use of materials at the nanoscale to create novel treatments and methods is known as nanomedicine. Materials exhibit varying physicochemical properties at this scale because of their high surface area, surface structure.
3.	Immunoconjugates	Recombinant antibodies are covalently attached to a drug through a linker to form antibody drug-conjugates, also known as immunoconjugates.[59] The concept behind this method is to use the specificity of monoclonal antibodies (mAb) to deliver powerful medications to the intended spot, preventing toxicity to non-targeted organs.[60]
4.	Virus	Because viruses may naturally infect particular cells and transfer genomic material to the nucleus, they are promising delivery systems for medication and gene therapies.[61–63] Recombinant virus technology can increase medication delivery by improving transfection efficiency and avoiding lysosomal degradation.

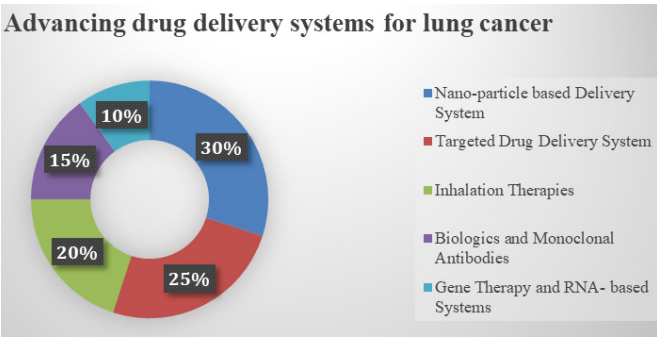

Figure 2: Advancement in drug delivery systems in lung cancer

antibody dispersion and signaling). Because of opsonization and subsequent phagocytosis by the RES cells, for instance, nanoparticles are removed from the plasma shortly after IV infusion.[67] In fact, PEG-coated liposomes and in vivo nanoparticles lengthen human residency lengths by up to 200 times and prolong circulation times by several minutes to several hours.[68-70] Conversely, PEG's efficacy is contingent upon its surface density, chain length,[71] and capacity to evade hepatic absorption. PEG carriers, however, are meant to penetrate intracellularly, and occasionally PEG stops the carrier from negatively interacting with cells. Furthermore, after repeated injection, PE-Gylated nanocarrier systems have been demonstrated to cause an immunological response known as the accelerated blood clearance (ABC phenomenon), which is followed by increasing accumulation on the liver and spleen.[72] The surface charge, or zeta potential, is another important component to enhance carrier targeting. This eventually affects clearance and distribution patterns by influencing the interaction with plasma proteins, cell membranes, and surfaces. Because of their overall anionic charge, cationic surfaces—obtained, for example, by coating cells with chitosan—show a high interaction with surfaces and cell membranes. But because PLGA nanoparticles have a slightly negative surface charge, it tends to inhibit both their intracellular absorption and interaction with negatively charged plasmids.

Concurrently Embedded Medications Using Combined Therapy

These are systems that possess possibility of administering many medications at once. Herein are contained PLGA nanoparticles carrying both vincristine sulfate and verapamil hydrochloride for an effective way to illicitly deliver strong anticancer agents while preventing P-gP output route. This approach improves the therapeutic index and helps overcome tumor insensitivity. Consequently, administration of doxorubicin and cyclosporine A was scheduled using the same approach.[73,74] Nevertheless, it appears from recent research that PLGA-PEG interacts with P-gP, Improvement on the efficiency of this system could possibly arise. It is important to consider the properties of drugs that will be encapsulated when designing such systems. To illustrate, hydrophobic polymers are more probable to encapsulate hydrophobic drugs and vice versa.[75] For better treatment outcomes, another way involves using two separate rates of release for the two drugs (for instance, cold treatment for cancer). Herein, paclitaxel and C6-ceramide have been encapsulated using the controlled blend polymer PLGA-PbAE to evade mechanisms of resistance against cancer therapy.

Carrier Distribution

As mentioned earlier, because of their phagocytosing and clearing action in the systemic circulation, RES, present in the liver and spleen, principally act as barriers to carrier systems. Actually, upon IV infusion of PLGA nanoparticles, maximum accumulation (about 40%) was observed in the liver, followed by the kidney with about 26%, heart with about 12%, brain with about 13%, and only a trace amount in the plasma. With PLGA-PbAE, comparable outcomes were attained.Because of lymphatic clearance, the administration route affects the distribution pattern of all charged particles after IP injection. Furthermore, the lipophilicity of carriers affects cell absorption, which may lead to the quick elimination of more hydrophilic particles.The pH of the medium affects surface charge, which alters cellular absorption and, in turn, the carrier's distribution throughout the system. Due to electrokinetic effects created by a group of surface modifiers like cetyltrimethylammonium bromide (CTAB), di(2-ethylhexyl) sodium sulfosuccinate (AOT), polyvinylpyrrolidone (PVP), etc., it was found that zeta potential of these particles vary from positive through neutral to negative values for selective and simultaneous delivery of therapeutic agents into cancer tissues under IV and IP injections as a result monitoring their biodistribution with fluorescence microscopy. Tenfold reduction recordings from plasma concentration peaks had been observed among positively charged ones after intravenous administration whereas their clearance was more pronounced within 15 minutes in case of both negative as well as positive drug carriers. Conversely, minimal amounts of both positive and negative charged particles were discovered following IP injection. These findings demonstrate the increased circulation of neutral and zwitterionic nanoparticles. Drugs can be delivered to particular tissues and organs by modifying nanocarriers. So, dendrimer branching size can be adjusted to allow controlling for dendritic distribution and excretion across the body systems. Hence, it may dissolve from renal elimination when 40 to 60 kDa cutoff is chosen or about G7. From G3 to G7, the dendrimers can mainly be found in circulation. They are rapidly cleared from G1 to G5 kidneys and bladder but stay in lymph nodes then the liver which is greater than G9. PEG plays a crucial role in drug distribution in an organism. Usually, with increasing molecular weights of PEGylated dendrimers, the uptake rate from an injection point into lymph is notably a larger part of the whole absorption pattern indicating their possible application as drug delivery systems and also more advanced imaging agents targeting lymphatic tissues.

Pharmaceutical Applications

Brain delivery

This amazing barrier holds back the enigmatic exogenous chemicals to the brain; it is on record that 98% of drugs

never pass to the brain therapeutically. Experimental approaches have been proposed as solutions to these issues and to improve the bioavailability of the brain for presently available therapies to the central nervous system.[76] Ultrasound-focused and MRI-guided, slow-release devices, injection of chemical lysosomes are filled with osmotically active compounds such as mannitol or vasoactive agents that open tight junctions temporarily to allow drug penetration in the brain (or CSF). Intra-cerebral (IC) implants and/or continuous infusion via convection-enhanced delivery (CED) are also other means of getting medication into brains directly. The drugs are directly administered to the brain through different methods, including intraparenchymal (into parenchyma) or intracerebral (within the cranium) infusion, use of various types of implants and convection-enhanced drug delivery techniques, whereby osmolarity-modifying substances like mannitol, among other things, serve to chemically or osmotically open blood-brain barriers' tight junctions.[77] The concept of transport across the BBB-appropriate drug carrier is being resurrected. The tissue specificity of the nano vectoring targets the delivery of hydro-, lipophilic-but not forget the macromolecules-and controlled release profile of peptides and genes with a prolonged profile.[78] Because they are of very small size, nanoparticles can easily diffuse through the physical barriers of the brain interstitium even into small capillaries; thus, diffusion inside the cells, which allows the drug to be accumulated at a certain sitting in the body.[79] Nonetheless, the cost for nanoparticles to be able to pass through the blood-brain barrier (BBB) is often very high if there are receptor-mediated transporters. Certainly, some peptides allow transcytosis across the blood-brain barrier via receptors; thereby, they can serve as a targeted drug delivery mechanism to the brain. The emergence of polymer-based drug transporters has provided an alternative means of accessing brain interstitium directly.[80] There are several research strategies that have been adopted in recent times whereby two techniques are combined to offer more accuracy in targeting and better absorption rates. Such strategies include antibodies directed against various receptors, and chimeric particles are among the frequently employed approaches in addition to fusion agents and natural ligand-mimicking pro-drugs or viral vectors.[81]

Mucosal drug delivery

It is the route of preference due to convenience and the avoidance of all complications involved in more invasive techniques while maintaining the ability to deliver the proper dosage. When designing such a formulation, one must consider multiple factors including the solubility of the drug carrier, in addition to those charges from both the carrier system as well as the content itself. At the final destination, they will change the way that they are absorbed through the mucosal membranes. So far, drugs can be spontaneously cleared by mucosal surfaces' mechanisms for mucus clearance, but there exist various challenges posed by the digestive system (GI) as a physiological and chemical barrier. Also the very fact that some drugs can irritate tissues makes them less suitable for this route. Several strategies have been used to overcome these limitations and nanoparticles are another advantageous device for delivery via mucosae. It is known that they can increase the bioavailability of protein and peptide drugs by overcoming their limited absorption across the intestinal epithelium, avoiding efflux mechanisms while protecting against enzymatic degradation.[82] Particularly, longer residence times in the enterocytes, targeting to M cells,[83,84] or surface-specific targeting receptors can all be used to uptake nanoparticles. Additionally, a number of research have been conducted and fresh insights into oral vaccination have been obtained.[85] Live attenuated organisms,[86] peptides, and most recently DNA vaccines[87,88] have been used in oral immunization. Effective oral vaccination is still constrained, though, by issues such the vaccine not being swallowed, inactivation in the GI tract, or disruption of the gut flora. When particular ligands, like the RGD peptide, are used to target M cells, promising outcomes have been seen as well as humoral and cellular in vivo responses. Additionally, in cases where the target antigen is insufficiently immunogenic, vaccination with carriers might be the best option. Merits and demerits in drug delivery system in lung cancer[89,90] are depicted in Table 2.

Table 2: Merits and demerits in drug delivery system in lung cancer

S. No	*Advantages*	*Disadvantages*
1.	Targeted therapy	Technical Challenges
2.	Improved efficacy	Cost
3.	Reduced system side effects	Safety concerns
4.	Personalization	Regulatory hurdles
5.	Non-invasive options	Patient Adaptation

CONCLUSION

Lung cancer has become more treatable and patient-specific because of the new innovations in the field of drug delivery systems. This is due to nanoparticle-based systems that can specifically target tumor cells so they have little systemic toxicity and deliver drugs directly into tissues that are affected by cancer. For example, an inhalable drug delivery method, such as a dry powder inhaler or nebulizer, could provide localized treatment within the lungs, thereby increasing drug concentration at the tumor site and decreasing systemic exposure. Personalized approaches use patients' genetic or molecular profiles to customize therapies based on their individual tumor characteristics for better effectiveness and safety. It is also possible to deliver drugs in this way by using intelligent drug delivery systems that respond physiologically or externally on demand. All these innovations are likely to enhance the results and experience of patients suffering from lung cancer. Ultimately, the combination of these improvements provides better performance, personalization and less toxicity medication alternatives against lung cancer providing hope for better survival chances as well as enhanced satisfaction with living standards by patients.

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