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Revolutionizing Lung Cancer Therapy with Nano-Fiber -Based Drug Delivery System

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Abstract:

Lung most cancers continues to pose giant challenges to clinicians and sufferers alike, with conventional treatment modalities regularly falling brief in phrases of efficacy and safety. In latest years, nanotechnology used for revolutionizing lung cancer therapy. Among the numerous nano-materials being explored, nano-fiber-primarily based drug shipping structures have garnered sizeable attention due to their particular homes and capability for targeted and controlled drug delivery. This complete evaluate presents a top-level view of the modern-day brand new in nanofiber-based totally drug transport systems for lung most cancers remedy, highlighting their blessings, challenges, and future possibilities. Chemotherapy including general anticancer medicines is linked to serious adverse effects because of the large dosage required. Researchers have lessened the environmental impact of nanofiber manufacturing by using water as an efficient solvent in place of hazardous chemicals. The environmentally benign properties of this green method of creating nanofibers make it a promising tool for regenerative medicine, including cancer treatment. However, a wealth of research studies on the use of nanofibers are accessible. This review article focuses just on using nanofibers for cancer treatment.

Keywords: Lung cancer therapy, nanofibers, drug delivery system, electrospinning, targeted drug delivery, nanotechnology, controlled release, biocompatible polymers, cancer nanomedicine, tumor targeting, pulmonary drug delivery, biodegradable nanofibers, smart drug carriers

Introduction

Lung cancer accounts for 18% of all cancer fatalities globally and is the most common reason of cancer-related deaths. Lung cancer kills about 35,000 people in the UK annually, with a 10% survival rate. The two main risk factors for lung cancer are tobacco use and smoking is 66% of lung cancer fatalities. The 1950s saw the discovery of the link between smoking and lung cancer. Numerous carcinogens (>60r) found in cigarettes have been demonstrated in lab settings to cause cancer.[1] About fifty distinct carcinogens that damage both the central and peripheral alveolar regions of the lungs have been recognized by the IARC as being present in cigarette smoke. The genes in charge of cell division, growth, and apoptosis may become mutated as a result of these carcinogens. [2]

Hyperplasia, a condition marked by a significant rise in collagen, is the first sign of lung cancer. The stage known as dysplasia occurs when cells lose their capacity for differentiation after hyperplasia. The advanced stage of dysplasis known as carcнита is characterized by non-invasive, malignant cells. About 17.8% of lung cancer patients had a five-year survival rate. In industrialized nations, its prevalence and death rate are extremely high, but in underdeveloped nations, they are continuously rising. [3] Numerous genetic changes, such as EGFR overexpression, tumour suppressor gene inactivation, telomerase activation, etc., are to blame. Lung cancer is known to have several "key attributes".Human lung diagram given in figure 1.

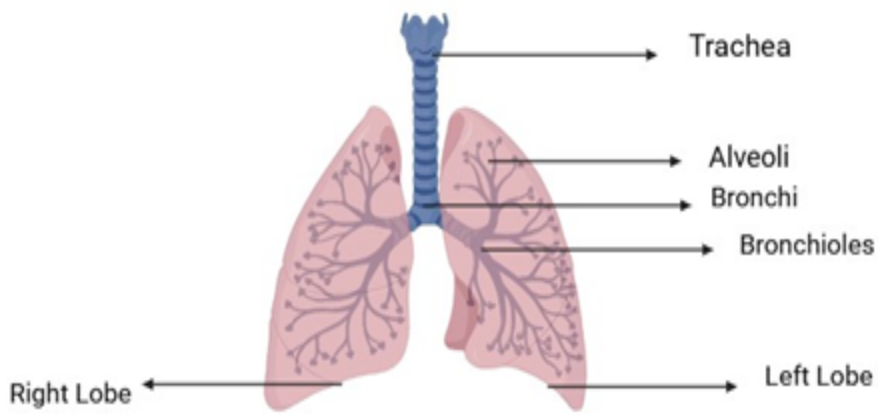

Fig.1. Human Lungs

The global issue, however, a variety of treatment modalities, including surgery, biomarker testing, hormone therapy, photodynamic therapy, radiation, chemotherapy, stem cell transplantation, and photodynamic therapy, are now being researched and studied. Among these, radiation therapy, chemotherapy, and heat shock have all been shown to be effective cancer treatment strategies.[4]

However, radiation and chemotherapy have relatively significant levels of toxicity and adverse effects. In the end, the course of treatment may be more hazardous, involved, and occasionally result in injury to healthy tissue. For this reason, it is critical to identify tumor cells early on. By introducing foreign chemicals into the tumor, heat is produced in the tumor location during hyperthermia treatment in order to kill the afflicted cells. The target tissue is heated using a variety of techniques for energy transmission using external equipment. Furthermore, magnetic hyperthermia can assist in overcoming the drawbacks of the conventional hyperthermia procedure and is less damaging to healthy cells.[5] On the other hand, in an effort to facilitate quicker and more accurate cancer therapy, imaging, and diagnosis, have emerged as a very intriguing subject of study in the medical sector. An illustration of the process for creating electrospun magnetic nanofiber mats is provided in Figure.2.

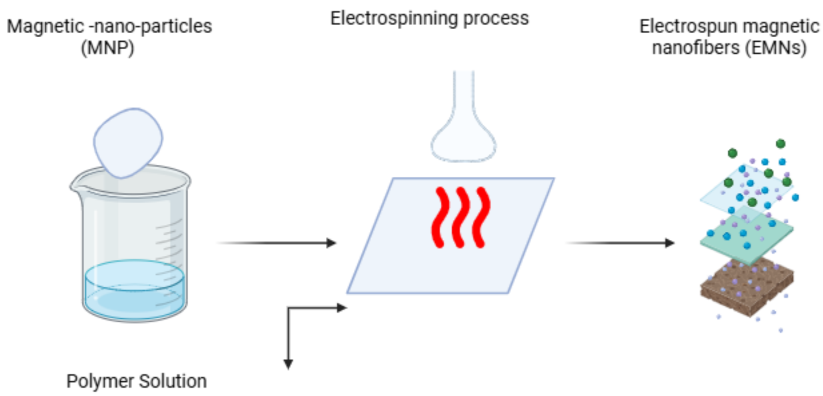

Fig.2. Electrospun magnetic nanofiber mats

A. Symptoms of Lung Cancer

Some persons with carly lung cancer do experience symptoms, but most lung cancers do not until they have spread. Lung cancer is not likely to be the source of the majority of these symptoms. Kretch et al. summarized the symptoms experienced in patients in lung cancer (100 consecutive patients), Pain, dyspnea, and anorexia were the most prevalent and severe symptoms, occurred in 86, 70, and 68 patients, respectively. Lung cancer subtype, location and Description is given in table.1.and Fig.3.[6]

Table I: Lung Cancer subtype Location Description [7]

Lung Cancer Subtype	Location	Description
Adenocarcinoma (40%)	Peripheral	It develops in small airways epithelial and type 2 alveolar cells and in the most common type of the non-smoker
Squamous cell carcinoma (20%)	Central Peripheral	It is strongly link to smoker and developed in proximal airways epithelial cells
Large cell carcinoma (3-5%)	Peripheral	It appears similar to Adenocarcinoma and lesion developed is typically larger
Small cell Lung cancer (15%)	Central	It is strongly associated with smoking and develops from neuroendocrine cells, which produces neurotransmitters, growth factors and vasoactive chemicals. It is associated with paraneoplastic syndrome.

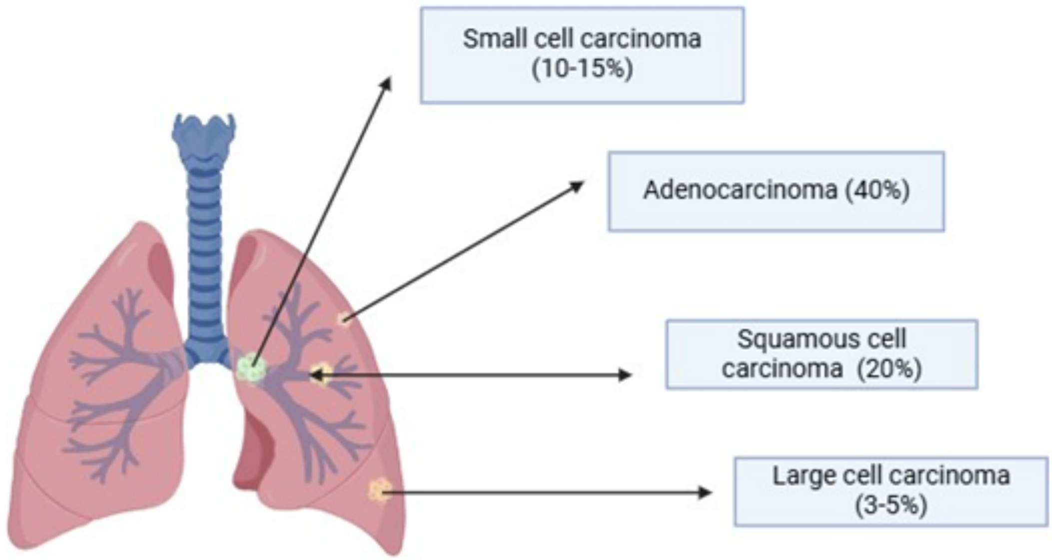

Fig.3. Lung cancer subtype

B. Nanofiber

Nanofibers are biocompatible and biodegradable, and they function well as a medication delivery mechanism. They can be made with a combination of various polymeric solutions or a single polymer solution. Low solubility and low permeability medicines are well suited for delivery via nanofibers. Nanofibers distribute medications over a predetermined time with little to no adverse effects, functioning as a controlled release drug delivery device.[8]

Although electrospinning is the most popular method, nanofibers can also be prepared by other methods such self-assembly, template synthesis, electrospinning, and drawing. Nanofibers can be made from polymers or a combination of other polymeric solutions. PVA may combine with water despite not being a naturally occurring polymer. PVA is odorless, colorless, and non-toxic. PVA is biodegradable and biocompatible. PVA has a wide range of applications, including the creation of films, membranes, and polymer composites. It is also employed as a medication delivery system in the biological fields. Gums, paper cutting, textile coating, and fiber preparation are more applications for PVA.[9]

HPMC belongs to the class of cellulose ether. HPMC is a hydrophilic, recyclable, and biocompatible polymer that finds use in the pharmaceutical, cosmetic, and agricultural sectors as well as in the formulation of coating agents, gums, dyes, and medications.

Chitosan is a linear polymer that is made by treating chitin shells with alkaline chemicals. Due to its numerous uses in biomedical settings, as a means of delivering food and medications, and for purifying water, chitosan.

The innovative nanofiber mesh is a synthetic polymer technology that incorporates a bioadoptable and biodegradable component that rapidly delivers anticancer medications to the cellular level, increasing their efficacy.[10]

The development of nanodrugs has been significantly aided by the electrospinning process, a versatile and cost-effective technique for producing ultrafine fibers with diameters in the nanometer range. Electrospinning allows for the encapsulation of therapeutic agents—such as small molecule drugs, proteins, or nucleic acids—within nanofibers, enabling controlled and sustained drug release. This method enhances drug stability, improves bioavailability, and allows for targeted delivery by modifying the fiber composition, morphology, and surface functionality. The high surface-area-to-volume ratio of electrospun nanofibers facilitates efficient drug loading and rapid cellular interactions, making them ideal for transdermal, oral, and implantable drug delivery systems.[11]Furthermore, the electrospinning process is compatible with a wide range of biodegradable and biocompatible polymers, including cellulose acetate, poly(lactic acid), and polycaprolactone, thus advancing the design of smart nanodrug platforms tailored for cancer therapy, wound healing, and tissue regeneration. “The drug loading rate and its delivery in nanocomposites were examined over a period of 60 days, with the nanofibers tested on A549 lung cancer cells. Most anticancer drugs exhibit low selectivity and high cytotoxicity; therefore, a drug delivery system must be designed to enhance the efficacy of chemotherapeutic interventions while minimizing the detrimental effects of the drugs on adjacent tissues.,”. Nanofiber structure is given below fig.4.

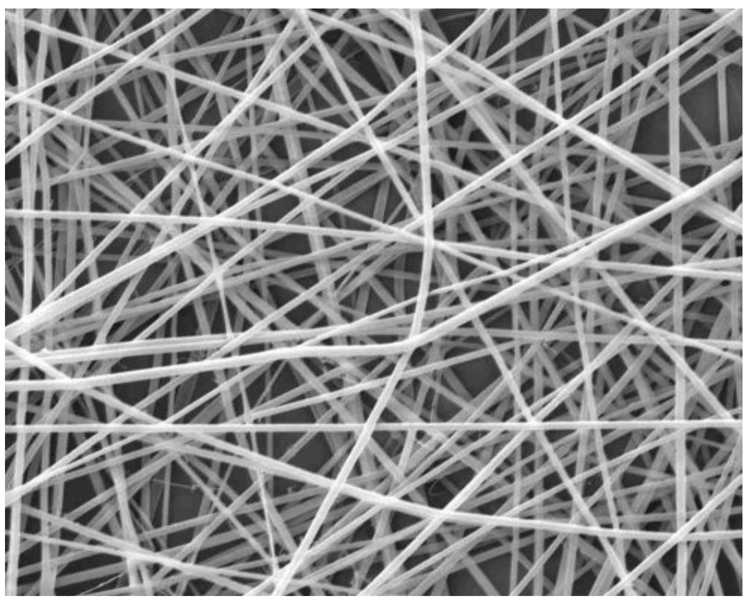

Fig.4. Nano Fiber structure [12]

Nanofibers for Cancer Therapy

It has been documented in the literature that various polymer types can both ensnare and distribute anti-cancer medications to targeted locations with prolonged release. Some of the nanofibers utilized in cancer therapy are listed in Table 2. The electrospinning conditions under which the corresponding polymers were spun to produce defect-free nanofibers are also described. When dealing with cancer cells, the selection of the polymer, medication, fabrication technique, and post-modification are crucial factors to take into account. Systems for cancer treatment based on nanofibers are now using a variety of polymers;[13]

Table: 2: Nanofibers Reported for Cancer Treatment [14,15,16,]

S.No	Polymer	Conc. W/V	Solvent	Drug	Spinning conditions Volt.KV	Dist(cm)
1.	PCL	20%	Chloroform/methanol	CPT-11, SN-38	12-18	12-25
2.	PLA	10%	DMF/methylene chloride	Doxorubicin	10	15
3	PLA	5%	Dichloro methane	Titanocene dichloride	12-22	15
4.	PEG-PLA	7.5%	Chloroform	BCNU (1,3-bis(2-chloroethyl)-1-nitrosourea)	35	24
5.	PGLA	2-30%	DCM	Paclitaxel	5-12	-
6.	PCL	5%	Trifluoroethanol	Indomethacin, doxorubicin	10	10
7.	PCEC	8%	DCM/isopropanol	Curcumin	18	12
8.	CO-PLA	5%	DMF/DMSO	DOX and quaternized chitosan	40	18
9.	CO-PLA	5%	DMF/DMSO	DOX and quaternized chitosan	25	18
10.	PELA	N. A	Methylene chloride	DOX and quaternized chitosan	25	18
11.	PLA	10%	Chloroform	Hydroxycamptothecin	20	---
12.	PLGA	2%	DCM/DMF	Daunorubicin	10	10
13.	PLA	N. A	Chloroform	Ferulic acid	18	12
14.	Chitosan/PEO	5%	Acetic acid	Curcumin	20	13
15.	PEG/PLA	6%	Chloroform	Doxorubicin hydrochloride	43-48	24
16.	Cel-Acetate	17%	Acetone/dimethylacetamide	Curcumin	17.5	15
17.	PLA	10%	DMF/methylene chloride	Doxorubicin hydrochloride	10	15
18.	Chitosan	8%	Acetic acid	Doxorubicin hydrochloride	20	15
19	PGLA -Gelatin	16%	Hexafuoro-2-propanol	Doxorubicin hydrochloride and camptothecin	18-20	15
20.	PCL	15%	DMF/dichloromethane	Green tea polyphenols	21	20
21.	PCL	10%	Methanol/chloroform	Curcumin and natural extracts (neem and Aloe vera)	12	12
22.	PHBV	8%	Trifluoro-ethanol	Irinotecan, PCT, Oxaliplatin, Cisplatin and 5-fluorouracil	13	12

Description about Polymers used In Nanofiber Formulations

A. Poly (lactic acid)

PLA has found several uses in the medical sciences because of its exceptional qualities and non-toxic nature. Lactic acid is the breakdown product of PLA, which, combined with its strength, makes it a perfect fit for usage in medical. For instance, medication laden these would release the medication by polymer degradation and diffusion. Therefore, by modifying the morphology of the resulting PLA, which would modify the drug's release, the diffusion rate of the drug can be changed.[17] Due to the hydrophilic drug's incompatibility Paclitaxel and doxorubicin, two hydrophobic medications that are compatible with PLA, were found to have zero order kinetics of drug release, which decreased the initial burst release. Consequently, adjusting the desired release from PLA fibers depending on the kind of medication being loaded would be simple.[18]

As a result, the desired burst and sustained discharge may be accomplished. electrospun fibers have been reported to exhibit early burst release followed by persistent drug release during in vitro drug release study, reducing the survival of rat Glioma C6 cells by up to 60–80%. After 192 hours, up to 86.7% drug release was seen.[19] Fiber mats and virgin drug both had reductions in cancer cell proliferation of 68.20 and 73.10%, respectively. The medicine was first delivered in a burst, but after a while, a prolonged, gradual, and regulated release was seen, which is advantageous. When dichloroacetate and oxaliplatin were injected into PLA-based multilayer nanofiber constructs, the cancer cells were more effectively killed in vivo and in vitro. made of PLA might be conveniently placed to a surgically excised tumor site.[20]

B. Poly(caprolactone)

PCL is a significant polymer that finds usage in a variety of medicinal applications since it is both biocompatible and biodegradable. This aliphatic polyester is the breakdown products are nontoxic. PCL is readily spun into nanofibers using solvent or melt electrospinning techniques. Its non-toxic characteristics and subsequent FDA approval in the United States have led to its widespread use in medical applications, including as absorbable sutures, tissue engineering, medication delivery, and nerve guidance. For mixing, PCL exhibits strong compatibility with natural polymers.[21]

C. Cellulose acetate Cellulose acetate

Cellulose acetate is a semi-synthetic, biodegradable polymer derived from cellulose, the most abundant natural polymer found in plant cell walls. It is produced through the acetylation of cellulose, typically using acetic anhydride and acetic acid in the presence of a catalyst. Known for its excellent film-forming ability, biocompatibility, and ease of processing, cellulose acetate is widely used in biomedical applications such as drug delivery systems, wound dressings, and tissue engineering scaffolds.[22] In nanofiber form, particularly via electrospinning, cellulose acetate enables controlled drug release and high surface-area interactions, making it ideal for advanced therapeutic delivery systems. Additionally, it offers environmental advantages due to its biodegradability, making it a sustainable alternative to synthetic polymers in medical.[23]

D. Poly(hydroxyalkanoate) Polyhydroxyalkanoates

(PHAs) are materials that many microorganisms make that are green, biocompatible, and biodegradable. PHAs have several uses in the medical field because of their remarkable qualities. According to reports, PHAs are safe for use in medicine and are excellent for tissue regeneration and cell proliferation without increasing the danger of tumor formation. PHA nanofibers displayed a lower degree of crystallinity in comparison to bulk film, but a larger contact angle (130°) in comparison to bulk film (77°), which may have resulted from these fibers' rougher surfaces. while there haven't been many reports of PHAs being utilized as nanofiber drug carriers for anticancer medications.[24]

Because of these PHA polymers' excellent biocompatibility and environmentally friendly qualities, they are widely employed in medical applications. However, because these polymers are made from microbes, their main drawback in terms of commercialization is the high expense of purity required. Poly(styrene) Polystyrene (PS) has an extremely slow rate of biodegradation and is a synthetic polymer. After being subjected to an alternative magnetic field, the PS nanofibers containing IONPs produced heat and eliminated all of the human ovarian (SKOV3) cancer cells that were adhered to their surface in less than ten minutes. Moreover, the addition of collagen to the PS nanofibers' surface improved the cancer cells' adherence to the nanofibers.[25]

E. **Poly (vinyl alcohol) Polyvinly alcohol (PVA)**

Early cancer detection has several advantages. The method was predicated on the ability to identify cancer cells with overexpressed CD44 receptors. The resulting nanofibers were efficient, smooth, and hemocompatible. Prior to this, Fan et al. reported using folic acid-based receptors to identify cancer cells. PVA/PEI nanofibers were produced, and folic acid was immobilized on them to detect and identify cancer in its early stages. It has been observed that these loaded with micelles carrying Pt(iv) and dichloroacetate (DCA) exhibit synergistic effects on cancer cells. When intravenously administered, chemotherapy based on micelles delivers medications to the tumor poorly and frequently results in systemic damage. Less systemic toxicity and the anti-cancer system's efficacy was increased. These nanofibers had good performance and were biocompatible when tested against SKOV3 cancer cells. [26,27]

F. **Peptides**

A natural occurrence, peptides are short chain monomers of amino acids joined by amide bonds, three distinct types of ovarian cancer cells showed of peptide RADA16-I nanofibers for the purpose of screening anticancer medicines. Because of the acidic pH of the stomach, intact peptide-based nanofibers are challenging to administer drugs orally.[28] These peptide nanofibers were effective in targeting three distinct tumor cell types, namely MCF-7 breast cancer cells, 293 T embryonic kidney cells, and HepG2 liver carcinoma cells. Additionally, the biodistribution of curcumin medication in mice was investigated. According to Yang et al, when D- and L-peptide nanofibers are injected into mice, their stability varies both in vivo and in vitro, leading to a modified bio-distribution. However, there have only been a few documented uses of these peptide nanofibers; more research could yield greater results.[29]

G. **Smart polymer nanofibers**

For the treatment of cancer Another name for smart polymers is stimuli-responsive polymers. These polymers exhibit remarkable conformational adaptations to very small changes in pH, temperature, voltage, and other parameters, and are widely used in biological applications. using electrospun nanofibers loaded with DOX.

The temperature-responsive copolymer acted on cancer cells in two ways: it released the anticancer medication DOX and produced heat through MNPs. In a 5-minute in vitro study, the fibers revealed up to 70% killed cancer cells. The combination of the medication and the heat caused the rapid activity. The hyperthermia smart nanofibers have the potential to be highly effective switchable agents against cancer. However, it is difficult produce electrospun such sensitive nanofibers since the polymer's responsiveness is affected by even small changes to the process and solution parameters.[30]

Impacts of Nanofiber-Based Drug Delivery Systems

A. **Benefits of Nanofiber-Based Drug Delivery Systems**

Nano-fiber matrices permit precise manage over the discharge kinetics of healing marketers, taking into account sustained drug release on the tumor website and retaining healing concentrations over an extended period.[31] Nanofibers allows green drug loading, ensuing in greater cellular uptake and improved therapeutic effects in comparison to conventional drug formulations. Encapsulation of medicine within nanofibers protects them from degradation and clearance, prolonging their circulation time and improving their bioavailability. Nano-fiber-based drug shipping systems provide flexibility in phrases of cloth composition, floor amendment, and drug loading potential, making an allowance for tailored layout to meet precise therapeutic needs.[32]

B. **Limitations of Nanofiber-Based Drug Delivery Systems**

Fabrication of nanofibers regularly calls for specialised gadget and know-how, making scale-up and commercialization hard and steeply-priced. Some artificial nano-fiber materials may additionally elicit immune responses or cytotoxic consequences in vivo, necessitating thorough biocompatibility trying out prior to clinical utility.[33]

Nanofibers may undergo degradation or structural modifications over the years, affecting the release profile and efficacy of encapsulated drugs. Not all healing agents are suitable for encapsulation inside nanofibers, specially people with negative solubility or balance beneath processing conditions.

Regulatory acclaim for nanofiber-primarily based drug shipping structures may be extra stringent as compared to standard drug formulations due to issues concerning protection, efficacy, and manufacturing consistency.

Prevention

1. Nanofiber-based totally drug delivery systems can be engineered to goal particular cells or tissues associated with lung most cancers development, including precancerous lesions or areas with high-danger factors like publicity to carcinogens (e.G., tobacco smoke).[34]
2. Slow-Release Formulations: These structures can be designed to launch chemopreventive marketers' step by step, making sure sustained exposure to the drugs over an extended duration. This approach can assist in stopping the initiation or development of cancerous cells.
3. Combination Therapy: Nanofiber structures permit for the transport of a couple of dealers concurrently, enabling combination remedy strategies that focus on distinct pathways involved in lung most cancers development.[35]

Treatment

1. Nanofiber-based totally drug transport structures can supply chemotherapy drugs without delay to tumor websites at

the same time as sparing healthful tissues, thereby lowering systemic toxicity and side outcomes associated with conventional chemotherapy.

2. Nanofibers can penetrate deeply into tumors due to their high floor region-to-quantity ratio and small size, taking into consideration extra powerful drug transport to most cancers' cells for the duration of the tumor mass.[36]
3. These systems can be engineered to release tablets in response to unique stimuli present within the tumor microenvironment, along with low pH or high enzyme degrees, ensuring top-rated drug shipping and efficacy
4. Nanofiber systems can also be used to deliver immunotherapeutic dealers, together with checkpoint inhibitors or cancer vaccines, immediately to tumor web sites, improving the immune reaction against cancer cells.
5. Some nanofiber systems can contain sensors or imaging dealers to screen the tumor response to therapy in actual-time, taking into consideration changes in treatment regimens as needed.

Table 3: Nano-Fiber Delivery Systems Incorporated with Chemical Components for Lung Cancer Treatment [37,38]

Loaded agent	Type of polymer	Applied cell animal	Main finding
Polycaprolactone	PVP	Breast cancer (MCF7) and lung cancer (A459)	Long-term medication release Over time, the release of curcumin was examined to determine whether the device might be used as a drug-eluting implant.
PLA50/PVP50/Cur15		HeLa	Studies have demonstrated that the high surface/volume ratio and porosity of nanofibers enhance curcumin bioavailability.
17-DMAG	PCL/PEG	A549 cells	Enhancing its biological half-life and therapeutic efficacy by employing the electrospinning technique.
Superhydrophic Meses	polycaprolactone and poly (glycerol monostearate-co-caprolactone)	LLC	Underline how crucial it is to use local drug delivery techniques in addition to cytoreductive surgery to help lung cancer patients having tumor resection have better prognoses.
		HSP90	By optimizing their pharmacological structure and combining them with other medications including low-dose HSP90 inhibitors in combination therapies, HSP90 inhibitors can be made more therapeutically effective while also posing less

			toxicity.
MSNs-HA	HA	A549	The tremendous potential of Metf@MSNs-HA in targeted therapy of lung cancer cells was revealed by this exploratory investigation.
SLB and SLB-loaded PLGA NFs	lactic-coglycolic acid,PLGA	BEAS-2B	The findings showed that while free SLB and SLBloaded NFs were cytotoxic against A549 cells and increased intracellular ROS levels in cancer cells, they had no effect on BEAS-2B cells. Furthermore, apoptotic protein gene expression was stimulated by both agents, and the SLB-loaded NFs had a higher level of activity than the free SLB.

Limitations for Nanofibers-Based Cancer Treatments

The primary disadvantage of the current methods for treating cancer cells with drug delivery systems based on nanofibers is the use of hazardous solvents, which may interact with the drug and defeat the intended purpose. Despite this, the methods offer significant advantages over conventional chemotherapy. If the solvent residue becomes stuck in one of these threads, it could cause typical cell damage. The world's top research groups have previously produced publications that effectively highlight this problem of cell destruction. Due to their hydrophilic character, water soluble polymers have certain advantages, but they also have a major disadvantage in terms of the drug's burst release from entrapment.[39]

Researchers have also suggested using aqueous solutions for electrospinning as a means of encouraging environmentally friendly nanofiber synthesis.It would be beneficial if this method could also lower the polymer concentration needed for electrospinning. These nanofibers are often placed transdermally or during surgery at the tumor location to provide prolonged medication release. When it comes to delivering nanofibers orally to a particular tumor site, even though there is a lot of research being done to determine whether electrospun nanofibers are feasible for use in cancer therapy, the outcomes of clinical trials are crucial before these nanofibers are commercialized because anything that works incredibly well in vitro does not always work similarly in a complex biological environment (in vivo).[40]

Due to their easy dispersibility in water as micelles or nanoparticles. These amphiphilic block copolymers have a drug reservoir in one half. It has been shown that these block copolymers are temperature, light, and pH-responsive drug delivery agents. Additionally, it has been observed that these ABCPs can deliver anticancer drugs as conjugates or micelles. These nanofibers may find application in the fields of pharmacy, medicine, and agriculture, despite being used in many drug delivery methods, the effectiveness of these ABCPs against cancer cells has not yet been investigated.

Future Scope & Conclusion

Looking ahead, further research is wanted to optimize the layout and system of nanofiber-based drug shipping systems for lung most cancers therapy. This includes exploring novel substances and fabrication techniques, improving the scalability and reproducibility of manufacturing procedures, and carrying out rigorous preclinical and medical research to assess protection and efficacy. With continued innovation and collaboration throughout disciplines, In this keep the capability to revolutionize the remedy of lung cancer and enhance patient consequences. In conclusion, nanofiber-based drug delivery structures represent a promising approach for revolutionizing lung most cancers remedy. By allowing focused drug shipping, managed launch, and enhanced drug balance, those systems offer sizeable blessings over traditional drug transport techniques. With ongoing advancements in nanotechnology and translational studies, nanofiber-based therapies have the capability to transform the panorama of lung most cancers treatment and improve the lives of sufferers worldwide.

Selecting the appropriate medication and polymer combination is critical for long-term drug delivery. High concentrations of various anticancer medications, natural extracts helpful in cancer treatment, anticancer medications can all be encapsulated in nanofibers. Nanofibers can be used to distribute water soluble and poorly soluble drugs, such as curcumin, locally. As a result, nanofibers have enormous benefits for helping humanity fight cancer. Given that water-soluble materials have been successfully, it is important to explore the full potential of water as a solvent or co-solvent. Although it is difficult and there is still a significant gap, other polymers with medical uses from water-based electrospinning methods should also be investigated.

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