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Review

Applications of nanofibers in the diagnosis and treatment of cancer

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Abstract

When a cell's DNA is damaged, the injured cells react by changing from normal to malignant cells, rather than dying or repairing the damage. Metastatic cancer is the deadliest kind of cancer since it refers to cancer that has spread to other parts of the patient's body. The need for cancer detection techniques that are rapid, non-invasive, and accurate is growing. Cancer diagnosis, monitoring, therapy, and prognosis may all benefit from a diagnostic tool that can quickly and efficiently detect changes in cancer biomarkers in biological samples. Medication delivery, biomarker mapping, molecular imaging, drug transport, gene therapy, targeted therapy, and detection and diagnostics are some of the possible nanotechnology uses in cancer diagnosis and treatment that have been discovered. Nano-carriers for pharmaceutical delivery are critical in the medical business. Nanotechnology-based molecular diagnostics has the potential to accurately and quickly identify cancer. Nanotechnology-based treatments may ensure precise malignant tissue targeting. As their name suggests, nanofibers are fibers with a single dimension in the nanoscale region. Also, because of its simplicity and ease of parameter control, electrospinning is the most often utilized. In this paper, we look at how prepared nanofibres may be utilized to detect and cure cancer.

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1. Introduction:

Cancer is a serious public health issue that affects people worldwide, and it is the leading cause of death in the United States [1]. When a cell's deoxyribonucleic acid (DNA) is damaged, the damaged cells respond by transforming from normal to malignant cells instead of dying or healing the damage. These transmuted cells divide and replicate, ultimately becoming havoc cells. The most serious kind of cancer is metastatic cancer,

Abbreviations: DNA, Deoxyribonucleic acid ; ECM, The extracellular matrix ; PLA, Polylactic acid ; FDA, Food and Drug Administration ; Cur, Curcumin ; DOX, doxorubicin hydrochloride ; 17-DMAG, 17-dimethylaminoethylamino-17-demethoxy geldanamycin ; PCL/PEG, Poly (caprolactone)–poly (ethylene glycol); CS, Chitosan; Cur-CD-GO, curcumin-loaded cyclodextrin-graphene oxide cores ; BGs, bioactive glasses; MOFs, metal-organic frameworks ; CA, Cellulose acetate ; DS, degree of substitution ; PHAs, polyhydroxyalkanoates ; PHBV, poly (3-hydroxybutyrate-co-3-hydroxyvalerate) ; CP, collagen peptide ; 5-FU, 5-fluorouracil ; DCA, dichloroacetate ; IONPs, iron oxide nanoparticles ; SPH, supramolecular peptide hydrogel ; FITC, fluorescein isocyanate ;PtOEP, platinum octaethylporphyrin

which refers to cancer that has spread to other parts of the patient's body. The majority of cancer-related deaths are caused by metastatic cancer. The need for cancer detection methods that are quick, non-invasive, and accurate is increasing. As a result, detecting and treating malignancies as soon as possible is critical to preventing disease spread and mortality. Nanotechnology is now one of the most extensively utilized cancer research techniques. Medication delivery, gene therapy, detection and diagnostics, drug carriage, biomarker mapping, targeted therapy, and molecular imaging are some of the possible nanotechnology uses in cancer diagnosis and treatment that have been discovered [2]. As a consequence of nanotechnology, nanomaterials have been created [3]. Nanotechnology-based molecular diagnostics, such as the development of biomarkers, may help doctors identify tumors more accurately and quickly. Nanotechnology-based treatments, such as nanoscale drug delivery, may provide precise malignant tissue targeting while decreasing undesirable side effects [4]. Because of their great surface to volume ratios, adjustable size, and other benefits over ordinary materials, nanomaterials are widely used in nearly every sector of life sciences. Nano-carriers for medicine delivery in the medical industry are crucial. Nanotechnology-based medication delivery techniques, such as nanoparticles, have substantial downsides. The drug-loaded nanoparticles' commercialization is hampered by their burst release and poor drug trapping efficiency [5]. Nanofibers are fibers with a single dimension in the nanoscale region, as their name suggests. The surface area of these nanofibers increases considerably as a consequence of their reduced size, providing a significant benefit [6]. Bicomponent spinning, drawing, flash spinning, melt blowing, phase separation, and force spinning are some of the procedures used to make nanofibers, although electrospinning is the most extensively used due to its simplicity and ease of parameter control [7]. In this review, we will look at how prepared nanofibers may be used to diagnose and treat cancer using this technology.

2. Nanofibers

2.1. Definition of nanofibers

Nanofibers are one-dimensional materials formed from polymer solutions or melts with dimensions ranging from 50 to 500 nm. Multilayer structures, core shells, ribbons, porous wells, necklace-like architectures, web architectures, multi-channel architectures, and single-layer designs are all possible. The widths of polymeric nanofibers vary from 1nm to 1μm, approximately corresponding to the extracellular matrix size scale (ECM fibers) (**Fig. 1**) [8]. The diameters and architectures of fibers varied when the concentration, viscosity, kind of polymer solution, and preparation technique were adjusted. Because of their unique size and form, nanofibers offer a better potential for drug encapsulation than other nanomaterials. The first burst release of pharmaceuticals happened when single-layer nanofibers were used as drug carriers in the early phases of therapy [9]. Multilayers and core-shell nanofibers, on the other hand, did not show this phenomenon in their release mechanism. Because pharmaceuticals are loaded in multi-layers or core-shell nanofibers, respectively, on the inner surface or core of nanofibers The inclusion of hydrophobic nanofibers in the outer or shell layers of multilayers, as well as core-shell nanofiber carriers, resulted in a delay in the release of medication [10]. Creating multi-drug/nanofiber combinations improves the therapeutic effectiveness of anticancer drug/nanofiber systems [11], 2) creating temperature and pH-sensitive polymers to construct dual-sensitive drug/nanofiber systems [12], or 3) hyperthermotherapy and drug delivery matrices based on medication/nanofibers-magnetic nanoparticles [13], the design of these carriers increases the amount of cancer cell death.

2.2. Different types of nanofibers

Thermal-induced phase separation [14], chemical vapor deposition [15], drawing [16], phase separation [17], melt blowing [18], selfassembly [19], template synthesis [20], template melt extrusion [21], interfacial polymerization [22], wet spinning [23], force spinning [24], electrospinning [25], and other chemicals, physical, mechanical, and electrical processes are used to make micro and nanofiber architectural compounds. Electrospinning technology with multi-needle and multiple-jet needleless spinnerets systems is often utilized in research projects and commercial applications for manufacturing low and large-scale micro and nanofibers [26].

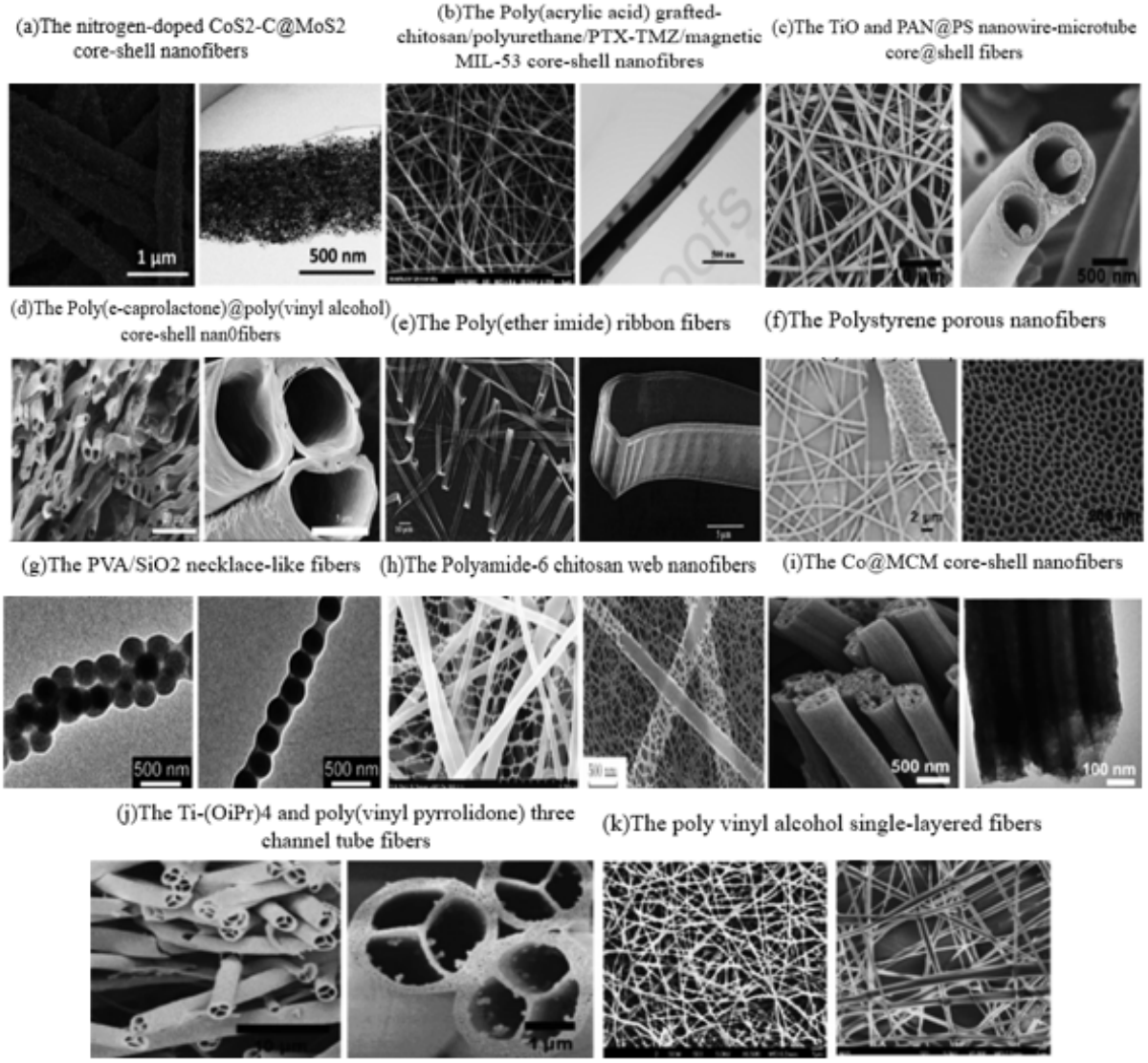

Figure 1: Nanofibers with (**a-d**) multi layers and core-shell, (**e**) ribbon, (**f**) porous well, (**g**) necklace-like, (**h**) web, (**i, j**) multi-channels, (**k**) single layer structures [8].

2.2.1. Electrospun Nanofibers: Recent Advances

Kenawy et al. employed electrospun nanofibers in drug delivery for the first time in 2002. Because of their unique properties, such as ease of drug incorporation during electrospinning, large surface area to volume ratio, highly porous and interconnected architecture, and tailorable material properties, electrospun nanofiber membranes have been extensively researched as drug delivery carriers since 2002 [27]. The polymer composition, fiber diameter, porosity, shape, and ease of surface functionalization all impact the material's flexibility in terms of features. All of the aforementioned properties make it possible to manage exact medication release patterns [28]. Some of the medicinal substances that have been effectively effectively integrated into such fibers include antibiotics, genes, proteins, DNA, siRNA, and oligo/polypeptides. **Table 1** shows anticancer drugs, gene therapy therapies, and viruses encased in polymers of various compositions. It is worth noting, however, that all electrospun nanofiber-based cancer research solutions are still in the early stages of development or testing. **Fig. 2A** demonstrates two popular drug integration methods for cancer research utilizing electrospun nanofibers: simultaneous encapsulation and surface modification. Surface immobilization of certain species is used for cancer cell detection and sensing, cancer cell capture, separation, isolation, and surface modification with proteins or growth factors is

Table 1: Encapsulation of a representative anticancer medication, gene, and virus into electrospun nanofibers with varying polymer compositions.

Drug	Carrier	Loading method	Type of cancer	Ref.
CPT11, SN-38	PCL/PGC-C18	Encapsulation	Colorectal cancer	[29]
Cisplatin	PEO/PLA; PCL/PGC-C18	Encapsulation	Cervical cancer; lung cancer	[30]
Doxorubicin	Chitosan/PLA; PLGA/HAp; PLA/mesoporous silica nanoparticles; poly(NIPAAm-co-HMAAm); silica nanoparticles-DOXCaCO3/ PLLA; polydopamine/PCL; gelatin/PCL-PEG micelle	Encapsulation immobilization	Graffi myeloid tumor; epithelial carcinoma; orthotopic secondary hepatic carcinoma; postsurgical cancer; skin cancer; HeLa cells; H1299 cells; breast cancer	[31]
Doxorubicin and camptothecin	PLGA/gelatin/ZnOnanospheres	Encapsulation	Liver cancer	[32]
Paclitaxel	PLGA; chitosan/PEO	Encapsulation	Glioma; prostate cancer	[33]
Paclitaxel and doxorubicin	PEG-PLA	Encapsulation	Glioma	[34]
5-Aminolevulinic acid	PVA	Encapsulation	Cholangiocarcinoma	[35]
Hydroxycamptothecin	PEG-PDLA	Encapsulation	Hepatoma	[36]
Combretastatin A-4 and hydroxycamptothecin	PEG-PLA	Encapsulation	Breast cancer	[37]
Titanocene dichloride	PLLA	Encapsulation	Lung cancer	[38]
Temozolomide	PLGA/PLA/PCL	Encapsulation	Glioma	[39]
1,3-Bis(2-chloroethyl)-1-nitrosourea	PEG-PLLA	Encapsulation	Glioma	[40]
Green tea polyphenols	PCL/MWCNTs	Encapsulation	Lung cancer and liver cancer	[41]
Curcumin	PCL-PEG-PCL; PLGA	Encapsulation	Glioma; skin	[42]
Daunorubicin	Poly (N-isopropyl acrylamide)-co-polystyrene	Encapsulation	Leukemia	[43]
Daunorubicin and Fe3O4 nanoparticles	PLA	Encapsulation	Leukemia	[44]
Cdk2 siRNA	Plasmid DNA/PCL	Encapsulation	Breast cancer	[45]
MMP-2 RNAi and Paclitaxel	PEI/DNA nanoparticles/PLGA	Encapsulation	Brain tumor	[46]
Inactivated Sendai virus	PCL	Surface immobilization	Prostate cancer	[47]
Fe3O4 nanoparticles	Chitosan	Surface immobilization	Colon adenocarcinoma	[48]

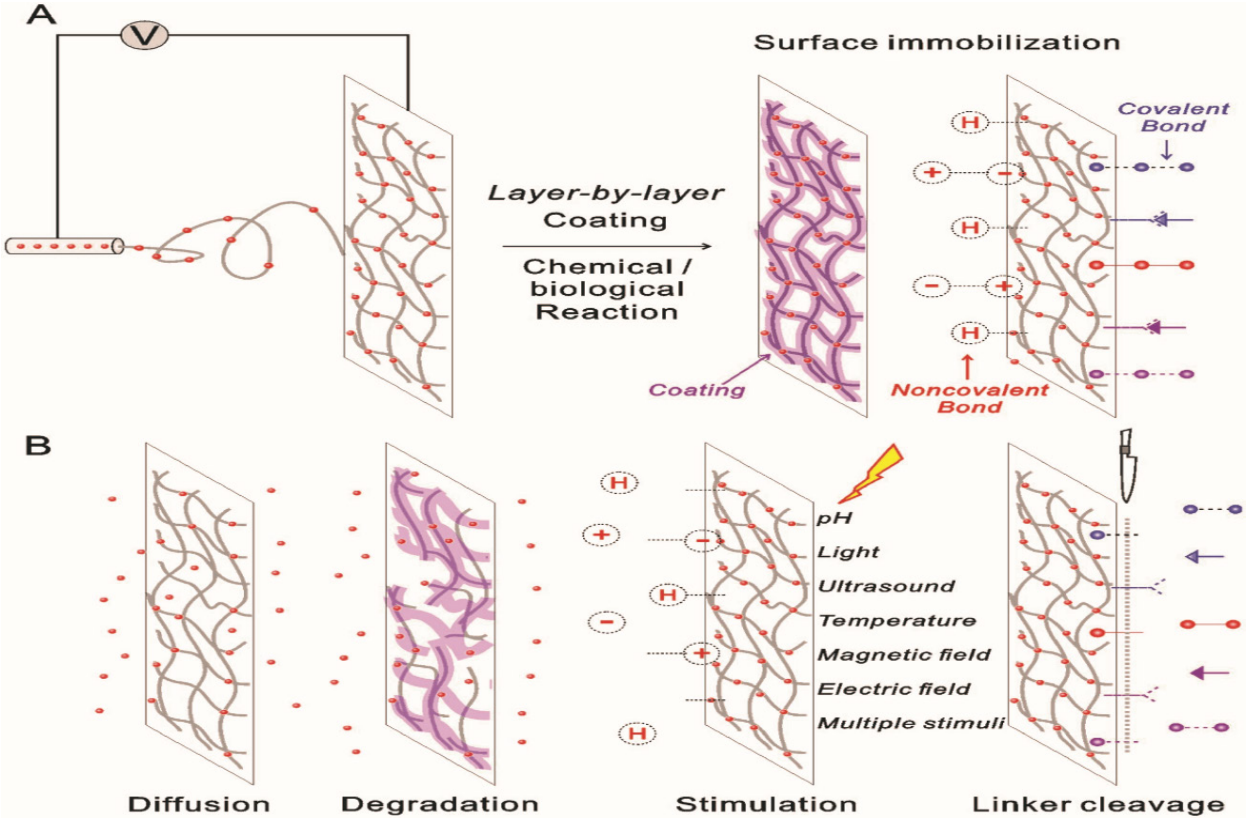

Figure 2: Therapeutic ingredients are loaded and released from electrospun nanofibers. **A)** Different loading techniques of medicinal compounds onto electrospun fibers and **B)** their related release processes are shown in this diagram [49].

used to create 3D in vitro cancer models. For medicinal reasons, anticancer drugs and genes are generally encapsulated. **Fig. 2B** depicts the equivalent release processes. In the literature, a variety of polymers have been reported for encasing and delivering anti-cancer medications to particular regions with long-term release. Various polymers are now being employed in nanofiber-based cancer treatment systems [49].

2.2.2. Polylactic acid

PLA provides a broad variety of therapeutic purposes owing to its unique properties and non-toxic nature. One of the most important variables in effective medication administration and release kinetics in cancer treatment is drug compatibility with the polymer solution. PLA's breakdown product is lactic acid, which, together with its great strength, makes it an attractive choice for therapeutic uses [50]. PLA nanofibers loaded with medicine, for example, would release the drug by diffusion and polymer breakdown. As a consequence, altering the morphology of the PLA formed might alter the drug's diffusion rate, resulting in a change in drug release. Mixing PLA nanofibers with other polymers to make nanocomposites is another technique to modify their composition. The core of PLA nanofibers becomes amorphous when electrospun, whereas the sheath becomes semi-crystalline. PLA nanofibers that were aligned (collected using a spinning collector) showed a smoother morphology than PLA nanofibers that were oriented randomly (collected on a grounded plate collector) [51]. According to Kochi, H., et al. [52], A novel anticancer drug delivery system including PLA nanofibers with encapsulated paclitaxel was produced by electrospinning the matching nanofibers on top of a spin-coated thin film with the same chemical compositions. HCT-116 cells were killed by PLA nanofiber supported on corresponding polymeric films at various paclitaxel loadings and inhibited HCT-116 cell growth. This study is part of a larger effort to build a strong relationship between PLA-based nanofibers and their related films to boost composite film stability and prolonged release capabilities. Mehnath, S., et al. [53] discovered that electrospinning Poly (L-lactic acid-co-caprolactone) in the core shell

resulted in controlled PTX release for 60 days and effectively killed HeLa cells. A core-shell structure comprised of PLGA polymer, hydroxyapatite, and silica nanoparticles is utilized to deliver anticancer medicines. A doxorubicin-loaded porous silica nanoparticle combined with PLA nanofibers has a very stable structure, allowing for regulated drug release.
PLA was used to create anticancer drug-loaded nanofibers that released anticancer medicines over 90 days. These fibers demonstrated efficacy against a range of cancer cell types by combining an early burst with a continuous release. Fiber breakdown in vivo and in vitro, on the other hand, are not the same. As a result, extensive study is required to demonstrate a reliable association between in vitro and in vivo degradation.

2.2.3. Poly caprolactone

Because of its biocompatibility and biodegradability, PCL is one of the most frequently utilized polymers in medical applications. Because the breakdown products of aliphatic polyester are non-toxic, it is a popular option for medical purposes. Melt or solvent electrospinning may be used to create PCL nanofibers. Because of its non-toxic nature and later clearance by the FDA, it has been widely used in medical applications such as drug administration, tissue engineering, absorbable sutures, and nerve guidance [54]. PCL is compatible with natural polymers like hyaluronic acid and chitosan when it comes to mixing. Folate (FA) modified MPEG-PCL micelle Cur (FA/Nano-Cur) is a colorectal cancer treatment. In addition, FA/Nano-Cur micelles had a substantially larger influence on tumor formation, apoptosis, and angiogenesis than Free Cur and Nano-Cur micelles in vivo studies [55]. For the first time, a group of Iranian researchers has shown that electrospun nanofibers can control drug release and cytotoxicity in MCF-7 breast cancer cell lines. Diffusion was used to control the release of DOX after it was injected into the center of a nanofiber. The slow degradation of the fiber mats revealed diffusion-controlled drug release and cytotoxicity [56]. H. Mellatyar, et al [26], undertook a new investigation to see whether implantable 17-DMAG-loaded PCL/PEG nanofibers might boost anti-cancer effects by reducing HSP90 expression and telomerase activity. According to an MTT assay, incorporation of 17-DMAG into PCL/PEG nanofiber dramatically improved cytotoxicity in lung cancer cells. In A549 cells treated with nanofibers, this was associated with lower HSP90 mRNA expression and telomerase activity. As a result, implantable scaffolds might be an effective way to remove cancer cells that have remained in the lungs. A new study was conducted by Talaei, S., et al.[26] The chemical and physical characteristics of electrospun 17AAG-loaded PCL/PEG nanofibers were investigated using FTIR and FESEM. The cytotoxicity of T47D cancer cells, which were utilized as an in vitro breast cancer model, was assessed using the MTT assay. In treated cells, 17AAGs reduced telomerase activity and mRNA expression. As a result, they could be a better option for removing any remaining malignant cells in the breast and preventing local cancer recurrence.

2.2.4. Chitosan

CS is a natural polymer that has been extensively studied for tissue engineering, drug delivery, and other medicinal uses [57]. Chitosan nanofibers have also been investigated for medicinal purposes [58, 59]. Sattari, S., et al. [60] have shown that single-drug-loaded nanofibers with Cur@CD-G O outperform co-loaded delivery systems with gallic acid-loaded chitosan shell nanofibers. Cur-Ga NF's anti-cancer, antibacterial, antioxidant, and anti-inflammatory activities have all been enhanced. In medical applications, this kind of co-delivery fiber technology might be employed as a nanocarrier. For regulated Cisplatin release at varied pH and temperature levels, BGs and magnetic biorhythms were doped into poly (caprolactone) nanofibers. The drugs in the core were released in a controlled and consistent manner. Amini, Z., et al. [61] studied the simultaneous effects of chemotherapy and hyperthermia on MG-63 osteosarcoma cells treated with Cs-g-PCL/MBGs/Cisplatin in an alternating magnetic field. When coupled with Cs-g-PCL/MBGs, cisplatin-loaded nanofibers from BGs and MBGs were shown to be the most efficient in killing MG-63 cells. At a pH of 5.5 and a temperature of 43°C, the rate of drug release into the circulation was increased. 100 mg/ml of 100mg/Cisplatin was demonstrated to be a successful therapy for MG 63 cells based on the apoptotic and necrotic effects. The creation and testing of novel chitosan derivative nanofibers for the prevention of local breast cancer recurrence were examined by Sedghi, R., et al. [62] Nanofibers are extremely efficient against E. coli and Staphylococcus aureus bacteria, and they have outstanding anticancer activity against 4T1 breast cancer cells while causing

little harm to normal cells. These findings suggest that nanofiber might be used to prevent breast cancer recurrence.

Dizaji, B.F., et al. [11] reported, that zeolites and MOFs were integrated into PLGA/chitosan nanofibers for regulated release of Paclitaxel anticancer medication against prostate cancer. Researchers examined it in vitro and in live cells to see what proportion of cells died and how effectively it inhibited tumor growth. The MTT test and DAPI staining studies were used to investigate the cytotoxicity and apoptotic effects of nanofiber containing paclitaxel on LNCaP prostate cancer cell lines.

Nanosystems based on CNCs and a CS derivative are studied by Pinto, R.J., et al. [63] In MDA-MB-231 breast cancer cells, fluorescent CNCs/FA-CS-FITC nanosystems with a rod-like shape displayed good stability and were non-cytotoxic. They might be used as nanocarriers with imaging characteristics for active targeted treatment since they have a great affinity for FR-positive cancer cells. To allow continuous-release, these nanofibers, like CS and other hydrophilic materials, must be coupled with other polymers, restricting their application in long-term treatment.

2.2.5. Cellulose acetate

CA is generated when cellulose reacts with acetic acid and acetic anhydride in the presence of sulphuric acid. For fiber manufacture, a CA solution is required, which is defined by DS of CA. CA has a DS of 2–2.5 and is soluble in acetone, methyl acetate, and dioxane, among other solvents [64]. Nanofibers are commonly made from cellulose or cellulose mixed with additional polymers when great absorbency is required. Because of their biocompatibility and biodegradability, CA nanofibers have proven a promising option for medicine administration and wound dressing applications [65]. Ag+ and Au+ ions are reduced and stabilized by silk fibroin and cellulose acetate. Due to its excellent IC50 value, it also considerably enhances cytotoxic activities against MCF-7 and MDA-MB-231 human breast cancer cells. According to their research, CA/SF/Au-Ag composite nanofibers are a great material for safer anticancer applications [66].

According to Liu, Y., et al.67), many natural chemicals have been shown to have significant benefits in the treatment and prevention of diseases [67]. Using an electrospinning process, paclitaxel and rectorite were loaded into cellulose acetate nanofibers to develop a drug carrier with good biocompatibility for use in the treatment of stomach cancer. Rectorite was employed to aid paclitaxel attachment without compromising the Nanofibrous mats' thermal performance. The mats made human gastric adenocarcinoma SGC7901 cells more cytotoxic. According to recent research, Arumugam, M., et al. [66] present an electrospun silk fibroin/cellulose acetate/gold-silver nanoparticles (CA/SF/Au-Ag) composite nanofiber for anticancer applications. After being exposed to CA/SF/Au-Ag nanofiber, human breast cancer cells MCF-7 and MDA-MB-231 become substantially cytotoxic. Silk fibroin and cellulose acetate both help to decrease and stabilize Ag+ and Au+ ions, making them more biocompatible. The CA/SF polymer matrix was produced in needle and rod morphologies with diameters ranging from 86.02 to 57.35 nm.

2.2.6 Poly hydroxyalkanoate

Many bacteria make PHAs, which are biocompatible, biodegradable, and environmentally friendly compounds. Because of their distinct characteristics, PHAs have a broad variety of applications in the medical field [68]. PHAs have been shown to be safe and effective for cell proliferation and tissue regeneration, with no risk of tumor formation. Electrospinning parameters and drug loading determine the final morphology, size, and release rate of a drug-loaded nanofiber [69] PHA nanofibers displayed less crystallinity than bulk film but a larger contact angle (130°) than bulk film (77°), which could be related to the fibers' increased surface roughness [70]. Researchers created (R)-3-hydroxydecanoic acid (R10) by depolymerizing PHAs and combining them with cationic peptides to improve cationic peptide anti-cancer activity. In lung carcinoma, colorectal cancer (HT-29), T-cell leukemia, human glioma (SNB-19), and human pancreatic carcinoma (MiaPaCa) cell lines, conjugated peptides were more cytotoxic than unconjugated peptides [71]. PHAs have been employed as drug delivery nanocarriers within cells in the past, although they are seldom used as anticancer drug carriers in the form of nanofibers. To test 3D tumorigenicity against gastric MKN28 cancer cells, researchers employed PHBV and CP, as well as five different anticancer medicines [72]. Drug-loaded nanofibers were 270 nanometers in diameter, compared to 520 nanometers for pure carbon nanomaterials. The decrease in fiber size was attributed to a negative association between viscosity solution and CP concentration. The molecular mass ratio of PHBV/CP (7:3) created substantially more proliferation than the other mass ratios when electrospun the different solutions. To have the

same effect on cancer cell growth rate in 3D systems as in 2D systems, more medicine was required. Because of their outstanding biocompatibility and environmental friendliness, these PHA polymers are widely employed in medical applications. However, since these polymers are produced from microbes, their major economic drawback is the high expense of purity necessary to utilize them as medical-grade goods [73].

2.2.7. Poly vinyl alcohol

PVA (polyvinyl alcohol) has been employed as a capping agent in drug delivery applications since it is biocompatible and biodegradable. Esfahani, R.E., et al. [74] developed an optimized nanofibrous sample based on a poly (vinyl alcohol)/CS blend and tested it for shape, drug release, and cell growth using 5-FU. Electrospun nanofibers with a diameter of 150.8 nm have the potential to be a useful cancer therapy. An MTT test paired with NIH cell culture revealed that the chemical destroyed over 80% of the NIH 3T3 cells. There were no chemical interactions between the polymers and the medication during the electrospinning process.

In unique research by Jajaei, M.S., et al., poly (lactide-glycolide) was synthesized using two distinct solvent evaporation processes [75] to analyzing the influence of particle size in cancer treatment. The anti-cancer medication oxaliplatin was added to the sub-microscopic particles. The viscosity of the dispersed phase and the size of the droplets dictated the medication loading rate. As the process parameters changed, sub-micron-sized particles were generated from PLGA solutions of varying concentrations in a 1 percent poly (vinyl alcohol) solution. When administered intravenously, micellar chemotherapy has poor drug distribution to tumors and often causes systemic toxicity. The treatment of cancer cells with DCA and Pt (iv) loaded micelles inserted into PVA nanofibers produced synergistic advantages. DOX and nickel ferrite nanoparticles were combined in nanofiber coatings to deliver controlled DOX to MCF-7 breast cancer cells. In the battle against the illness, these coatings have been found to be both efficacious and biocompatible [76].

2.2.8. Polystyrene

The synthetic PS degrades slowly in the environment. Magnetic hyperthermia treatment of cancer cells using PS nanofibers coated with IONPs has been found to be successful [77]. Hyperthermia treatment kills cancer cells by applying heat to a specific location. When the PS nanofibers loaded with IONPs were exposed to a different magnetic field, they created heat and killed all of the human ovarian (SKOV-3) cancer cells clinging to their surface in less than 10 minutes. Increased cancer cell adherence to the nanofiber was also a consequence of the collagen addition. The mats were also tested in a water bath; however, the SKOV-3 cells responded better to alternating magnetic heating [78]. MDR Leukemia 562 cancer cell lines were treated with daunorubicin-loaded poly (N-isopropyl acrylamide)-co-polystyrene electrospun fibers, which successfully reduced MDR and hence increased drug absorption [79]. The activity of nanofiber on P-glycoprotein increased the medicine's cellular absorption (multi-drug resistant protein). The medicine repels the MDR-protein in its pure form, but it attaches to nanofibres and enables it to pass through. Increased fluorescence (showing that the drug has penetrated cancer cells) and, eventually, MDR cancer cell death follow [79]. Because of their low disintegration rate, PS-based nanofibers have not been explored for anti-cancer medicine delivery. PS has been combined with other polymers or magnetic nanoparticles to generate hyperthermia treatment, which uses heat to destroy cancer cells. The slow degradation rate of PS is a drawback since it delays the drug's release.

2.2.9. Peptides

Peptides are short-chain monomers of amino acids that are bonded together by amide bonds in nature. Ionic-complementary self-assembly is used by designer self-assembling peptides to form entangled nanofiber networks in hydrogels. This kind of hydrogel exhibits realistic biological and physicochemical characteristics, making it ideal for biomedical applications as a biomimetic ECM [80]. Because of its excellent biocompatibility, multifunctionality, and injectability, the potential of SPH in cancer treatment has been intensively investigated during the last decade. Depending on its design, the SPH may provide localized cancer treatment as well as systemic anticancer immunity to prevent tumor recurrence. Peptide amphiphiles are made up of two, three, or four distinct building pieces, each with its own structural and functional properties as well as an affinity for interacting with cellular membranes or intracellular organelles [81].

3. The role of nanofibers in cancer diagnosis

Current nanofiber-based drug delivery technologies for treating cancer cells, on the other hand, provide considerable advantages over standard chemotherapy. Hair loss, mouth sores, weariness, nausea, and cell damage are all possible side effects of chemotherapy. Brittle bones, diarrhea, exhaustion, hot flashes, digestive problems, and headaches may all benefit from hormone therapy [82]. Nanotechnology and polymer research have yielded unique answers to issues ranging from basic household utilities to health care. To achieve the desired results, researchers employed simulation to change morphology at the nanoscale. Researchers used bovine serum album as a model active component to evaluate nanoparticles and nanofibers for drug delivery. Due to drug adsorption during nanoparticle encapsulation, drug-loaded nanoparticles generated both burst and sustained drug releases, while drug-loaded nanofibers produced solely diffusion-related drug releases due to their core-sheath structure [83]. As a consequence, drug delivery using nanofibers reduces the first burst of medicine while increasing potency against cancer cells by allowing for a more steady release over time [7]. Aside from long-term drug release, nanofibers are easy to make, have a tuneable final form with simple parameter control, and are re-producible. Nanofibers are a unique kind of material that may be used for a variety of purposes, ranging from basic filtration to more intricate tissue engineering and therapeutics. These fibers, in contrast to nanoparticles, can be easily duplicated and are less vulnerable to form changes due to human error. A little error in nanoparticle synthesis might result in a completely different form and batch-to-batch variation [84].

4. Nanofibers as biosensors

The use of nanofiber-based drug delivery systems provides several advantages over traditional chemotherapy, but the use of toxic solvents is the primary drawback. If a solvent residue gets stuck within one of these strands, it may injure the cell in the same way. The problem of cell damage has been discussed in a number of studies published by some of the world's most prestigious academic institutions [85]. The use of toxic solvents is the principal drawback of nanofiber-based drug delivery methods compared to traditional chemotherapy. If a solvent residue gets stuck within one of these strands, it may injure the cell in a normal way. The problem of cell damage has been discussed in a number of publications published by some of the world's most prestigious academic institutions. When compared to nanospheres and nanocapsules, oral approaches have a variety of difficulties, such as the difficulty of delivering nanofibers orally to a specific tumor area. Clinical studies will be necessary before electrospun Nanotechnology can be economically feasible, even though extensive research is being done to assess its practicality [86].

5. The role of nanofibers in cancer treatment

Nanoparticles are nanoparticles having unique optical, magnetic, and structural features not seen in other molecules. They've recently acquired popularity in cancer research and detection because of their tiny size, improved biocompatibility, and high atomic number. In recent decades, nanoparticles have sparked a lot of interest in cancer diagnosis and monitoring. A gadget that can detect matrix metalloproteinases 9, a protein that might be used to diagnose cancer, has been created by researchers. Due to its high levels of expression in the body, MMP-9 is overexpressed in malignant tissues. For fluorescence detection, FITC specific peptides were covalently bonded to an electrospun nanofiber matrix. Due to the porous structure of the material, it had a short response time of 30 minutes and a lower detection limit of 10 1012 m [87].

6. Nanofibers for drug delivery

In this field, electrospun fibers are appealing because bioactive compounds like cell-recognizable ligands may be chemically and physically enhanced. Sensor reduction may assist multiplexed, portable, wearable, and implanted medical equipment. Electrochemical transduction is the mechanism of action, with enzymes, antibodies, and, less typically, DNA strands or aptamers serving as sensing components [88].

Ali et al. [89] announced the development of a label-free, selective, and highly repeatable immunosensor for the early detection of a breast cancer biomarker with remarkable sensitivity (femtomolar). The sensor's excellent impedimetric response allows for fast detection (128 s) across a wide detection test range (1.0 fM–0.5 M) and can detect concentrations as low as 1 fM (4.34 105 ng/mL). Paul et al. [90] developed a new biosensor technology for the ultrasensitive detection of cancer antigen-125 based on multi-walled carbon nanotubes embedded with zinc oxide nanofibers. Simple ES was used to create the system.

The differential voltammetry technique was used for label-free detection, and it had a high sensitivity (90.14 A (U mL1)1 cm2) and a detection limit of 0.00113 U mL1 concentration. Soares et al. [91] described the development of immunosensors based on electrospun polyamide 6 and poly (allylamine hydrochloride) nanofibers coated with multi-walled carbon nanotubes or gold nanoparticles, the three-dimensional structure of which was suitable for immobilizing anti-CA19-9 antibodies for detection of the pancreatic cancer biomarker CA19-9. The sensitivity and selectivity of the device were evaluated using blood serum samples from people with varying amounts of the cancer-causing gene CA 19-9. A new kind of pH-sensing ES fiber scaffold has been developed by putting ratiometric pH sensor capsules directly into the lumen of electrospun organic fibers. Proton-induced switching causes optical changes, which may be recorded using fluorescence detectors and linked to the local proton concentration with micrometer-scale spatial accuracy. Drug screening and development might use biocompatible ES fiber mats with pH sensing capabilities to analyze the efficiency of anti-cancer drugs in real time **(Fig. 3)** [88,89]

7. The limitations and benefits of nanofibers application in cancer detection and therapy

To mention a few applications, electrospun nanofibers might be employed for tissue engineering (bone and skin), wound healing, and the treatment and detection of cancer cells. There are numerous great review articles available that investigate the possible uses of nanofibers, such as the treatment and identification of cancer cells. Tumor cell recurrence following tumor cell elimination surgery is a serious problem that must be addressed. Cancer drugs have poor specificity, meaning they may harm both healthy and malignant cells. A suitable amount of anticancer medicine should be maintained in the immediate region following surgery to avoid harm to normal cells [92]. Nanofibers laden with anticancer medicines might permit long-term pharmacological release in local locations **(Fig. 4A)**. They may be injected directly into solid tumor cells for therapy and are successful in lowering the likelihood of local cancer recurrence following surgery. As a consequence, in cancer treatment, nanofiber beats nanoparticles **(Fig. 4B)** [93]. Nanofibers were employed to construct fibers for paper-based conductive platforms, and monoclonal carcinoembryonic antibodies were physically adsorbed onto them by antibodies from the body, according to research. In another research, cancer biomarkers were detected using a hybrid polyvinyl alcohol/poly (3,4-ethylenedioxythiophene): polystyrene sulfonate (PVA/PEDOT: PSS) carrier [94] With a linear detection range of 0.2–25 ng mL1, high sensitivity of 14.2 A ng1 mL1 cm2, and shelf life of 22 days, this conducting paper-based biosensor demonstrated better sensing performance for the detection of a cancer biomarker carcinoembryonic antigen (Figure 4C). Based on the phenomenon that cancer cells consume glucose and release lactate, Thundat and colleagues deposited pH-sensitive PVA/PAA electrospun nanofibers on the light addressable potentiometric sensor surface to measure cancer cell acidification in a noninvasive manner to understand cancer cell metabolic activities and their response to chemotherapies (Figure 4D) [95]. The electrospun nanofibers detected localized changes in the medium pH with a sensitivity response of 74 mV pH1. Oxygen is another crucial component in cancer cell development. For oxygen detection, Lannutti and colleagues used PCL as the shell and oxygen-sensitive probes tris(4,7-diphenyl-1,10-phenanthroline) ruthenium (II) (Ru(DPP) and PtOEP as the core, as well as PDMS as the core [96]. PDMS sensors were discovered to react swiftly within 0.5 seconds of contact with a person's body due to their porous nature and high oxygen permeability.

8. Conclusion and future perspective

The most regularly used chemotherapeutics' clinical effectiveness against a variety of solid and hematological malignancies, including breast cancer, is hampered by severe and deadly side effects that occur at therapeutic levels. In order to develop innovative cancer-targeting medications, researchers are focusing their efforts on postoperative chemotherapy uses [97]. Pharmaceutical controlled release is a difficult task in which devices send the right quantity of medication to the right target at the right time and the right place. Targeted microcarrier technologies like micro-and nanoparticles, liposomes, and nanofibrous materials are used to deliver drugs. With just one injection, a controlled release method keeps the medicine in the right therapeutic range in circulation, eliminating the ineffectiveness and toxicity

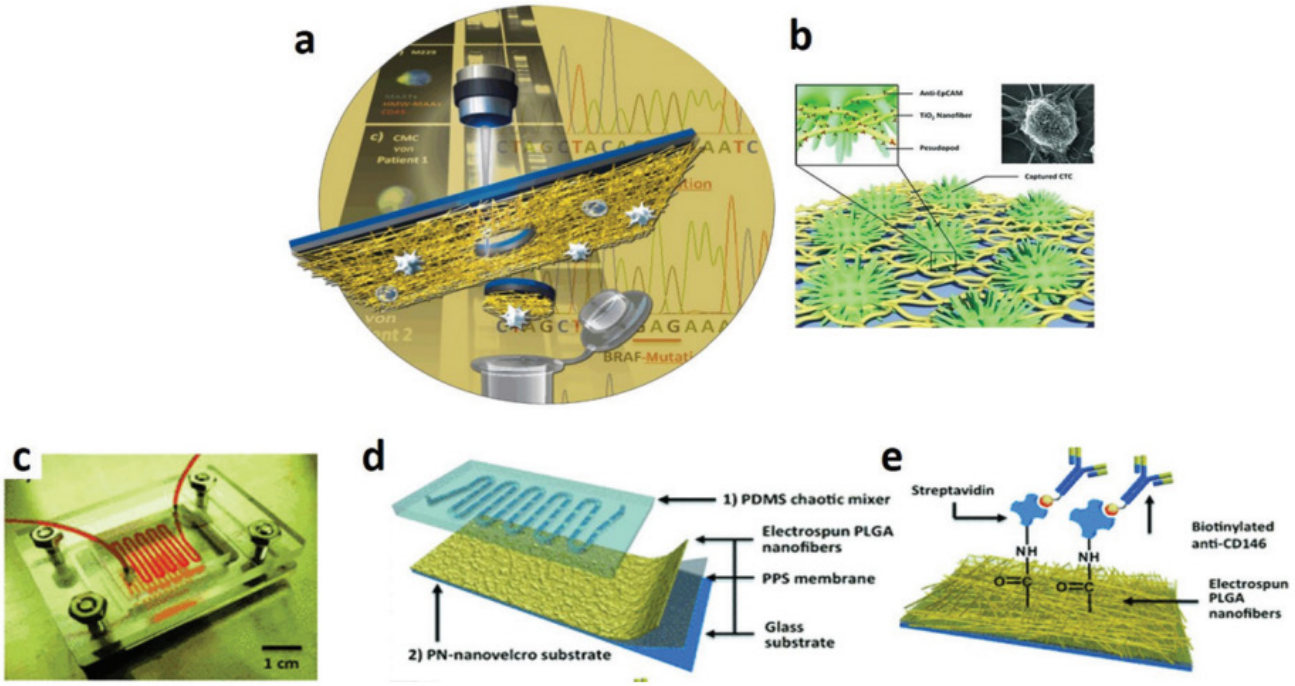

Figure 3: Laser microdissection is a method for detecting and isolating single circulating melanoma cells from normal white blood cells. (a) A TiO2-based nanofiber platform with a biological cell-capture agent has been designed to trap circulating tumor cells. (d) To covalently bind streptavidin for conjugation of biotinylated anti-CD1, a melanoma-specific antibody, a transparent NanoVelcro substrate, and an overlaying PDMS chaotic mixer are used. NHS chemistry is used to covalently bind streptavidin for conjugation of biotinylated anti-CD1, a melanoma-specific antibody [88].

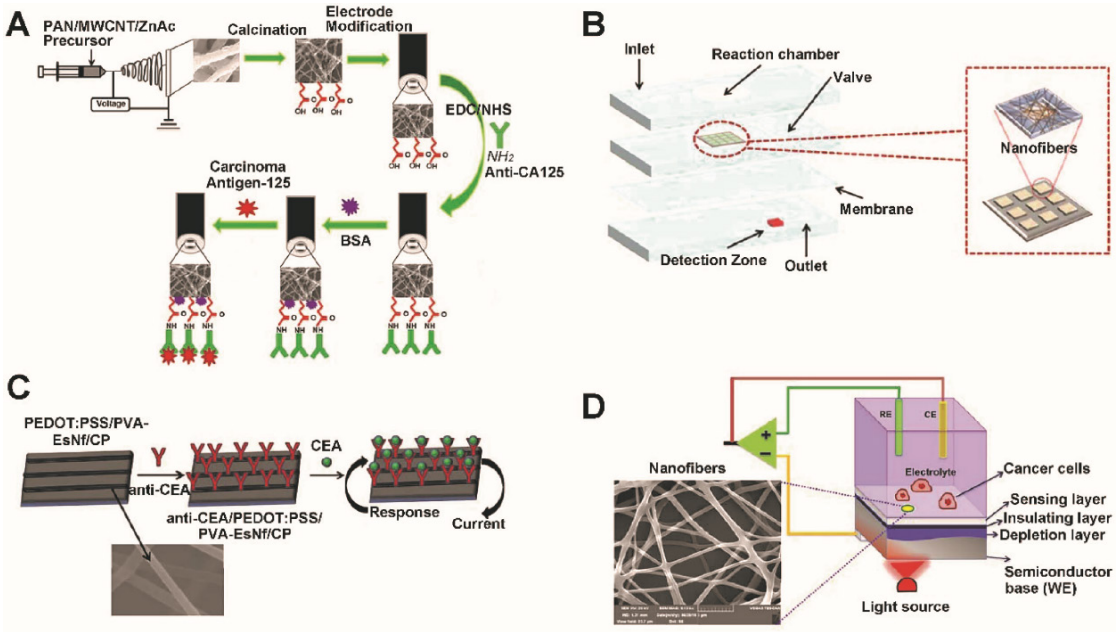

Figure 4: **Using nanofiberselectrospun, cancer cells may be identified and detected. A)** Illustration of a biofunctionalized electrospun multiwalled carbon nanotube with a zinc oxide nanowire interface for cancer antigen-125 detection with extreme sensitivity. **B)** A hydrogel-framed electrospun nanofiber matrix was used to build the MMP-9 microfluidic device. **C)** A biofunctionalized electrospun PEDOT:PSS/PVA nanofiber for carcinoembryonic antigen detection, shown schematically CEA. **D)** A real-time cancer cell metabolism and response to anticancer medicines is represented schematically using a light-addressable potentiometric sensor with pH-sensitive hydrogel nanofibers [49].

of injectable pharmaceuticals [90]. Controlled-release systems maintain the medicine in a polymeric matrix rather than being affected by external factors or susceptible to human variability. Drug release across a polymeric system network is influenced by two main processes: (1) drug diffusion, which is the most prevalent, and (2) chemical mechanisms, such as polymer degradation or drug cleavage from a polymer link. Because of their enormous surface area to volume ratio and ability to release a significant quantity of medication, electrospun fibers are an excellent drug delivery platform. Different delivery mechanisms have been developed for antibiotics, anticancer medicines, proteins, and nucleic acids. Electrospun fiber administration has acquired popularity as a local drug delivery method after surgical treatment to remove solid tumors [98]. Active molecules may be physically or chemically bonded to the surfaces of the fibers, or they may be combined with polymers. The next sections will go through the different loading procedures.

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