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Revolutionizing Implantable Drug Delivery: A Review of Curcumin Nanofibers Fabricated via Electrospinning Method for Cancer Therapy

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ABSTRACT:

The comprehensive overview gazed at the current state of the art use of curcumin-loaded nanofibers made by electrospinning as an implanted cancer medication delivery system. The powerful anticancer properties of curcumin, a naturally occurring polyphenol, are well known. Still, its quick systemic metabolism, low bioavailability, and poor water solubility make it difficult to translate into clinical practice. A clever way around these obstacles is to use electrospun nanofibers, which provide curcumin with a flexible encapsulation medium and allow for regulated release kinetics. By carefully regulating factors like polymer makeup, fiber structure, and medication loading, electrospun nanofibers show great promise for improving curcumin stability, and solubility, delaying its release, and enabling tailored administration to malignant regions. This study highlights the curcumin loaded nanofiber's potential efficacy and safety profiles in preclinical investigations while thoroughly examining their production methods, physicochemical characteristics, and biological applications. It also addresses the difficulties that lie ahead and potential paths forward in integrating this cutting edge technology into clinical practice and transforming cancer treatment approaches.

KEYWORDS: Implantable drug delivery system, Curcumin, Nanofibers, Electrospinning method, and Cancer.

INTRODUCTION

Implantable Drug Delivery System [1]

The innovative drug delivery system is made to assist in delivering the medication to the intended site or organ where localization of action is necessary. The two scientists Deansby and Parkes introduced the idea of an implantable pharmaceutical administration device in 1938. They did this by subcutaneously introducing a compressed pellet. An implanted medication delivery system is one in which the implant is surgically placed into the body.

An implantable drug delivery system is able to reduce the chance of adverse effects from medical assistance while increasing patient compliance. By avoiding initial pass metabolism and chemical degradation within the abdomen and viscus, this type of system together has the potential to deliver medications that would typically be inappropriate orally, hence enhancing bioavailability.

The goal is Increasing the medication's beneficial effects and reducing the risk of potentially fatal conditions including cancers, ischemic heart attacks, cerebral strokes, and aids are the goals of implants, a new medical innovation. For the range of medications that the digestive system is unable to effectively handle orally, implants seem to be a far stronger drug delivery method. These medications are ones with lower bioavailability. Ex-steroid and contraceptive.

The required features for implants include: [2]

- ❖ To improve patient compliance, the frequency of dosing should be decreased, and the medication should be released continuously throughout the treatment.
- ❖ The implant must be inexpensive and simple to manufacture.
- ❖ Applying the implant shouldn't require any specific techniques and should be a simple process.
- ❖ Along with to having adequate mechanical strength, the implant should be stable, safe, and effective.
- ❖ The implant should not have any possible issues.

The classification of implants: [3]

While categorization is a complex procedure, the Implantable drug delivery system divides implantable devices into various active and inactive categories. Since both the biodegradable and the non-biodegradable implantable devices use the passive diffusion releasing method,

A. The passive implantable device can be broadly classified into two categories: biodegradable process and non-biodegradable device. Non-biodegradable implants are commonly prepared using polymers such as silicones, poly(urethanes), poly(acrylates) or copolymers such as poly (ethylene vinyl acetate) Over their lifetime, these devices exhibit structural resilience and robustness. Therefore, the primary disadvantage of non-biodegradable implants is that they must be removed once their medication supply is exhausted. These devices' components have strong long-term biocompatibility, although occasionally they can lead to infections, tissue damage, or cosmetic deformities. To avoid any negative consequences, the drugs are typically removed once they have been released in their whole. The shortcomings of non-biodegradable implants led to the development of biodegradable implants. These gadgets are composed of polymers or block copolymers, which are biodegradable and can fragment into tiny pieces that the body will either ingest or excrete. Typically, polymers like poly (lactic acid) (PLA), poly(caprolactone) (PCL), or poly (lactic-co-glycolic acid) (PLGA) are used to make them. These substances have undergone a great deal of research, and it is simple to modify their degradation kinetics in order to modify the drug release rate. The primary benefit of this kind of implant is that the patient's body will break them down naturally, negating the necessity for extraction following insertion.

a) Implants of the monolithic kind are composed of a polymer matrix with uniform drug dispersion.

b) Conversely, implants of the reservoir type have a small drug core encased in a non-biodegradable membrane that is permeable. The drug's permeability through the membrane and the thickness of the membrane will control the release kinetics.

B. The active system requires energy in order to release the drug. The positive driving force in these implants regulates the medication release from the apparatus. They thus offer a greater level of medication release control. But their intricacy means that their development expenses are higher. This category of implants mostly consists of electronic systems composed of metallic components. However, only polymeric implants will be discussed in order to stay within the purview of this paper. The majority of dynamic medication delivery implants are of the pump type. Osmotic pumps are the primary class of polymeric active implants. This kind of device is primarily composed of a drug reservoir encircled by a semipermeable membrane. An aperture in the membrane that permits medication release is necessary. Osmotic gradients will provide a constant fluid influx into the implant. The pressure inside the implant will rise as a result of this action, forcing the medicine to pass through the aperture. Drug release is continuous thanks to its design (zero order kinetics). The medication loading capacity of this kind of device is restricted, yet it permits a favorable release rate. These energy sources could be anything from electromechanical drives to osmotic pressure gradients.

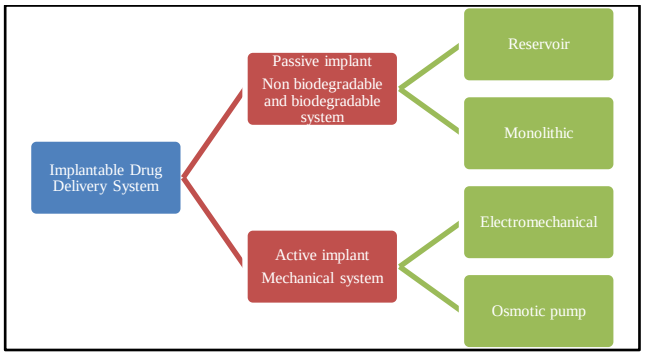

Figure 1 classification of implant

The benefits of implant: [4]

Convenience: Continuous IV infusions or frequent injections can sustain drug concentrations in the blood for extended periods of time. Under these regimens, patients are usually required to stay in the hospital for the duration of treatment in order to get constant

medical surveillance. On the other hand, patients who have implantation medical assistance are able to obtain medication outside of a hospital setting with no further medical police examination. In addition, compared to an indwelling catheter-based infusion system, implant treatment is associated with a reduced incidence of infection-related complications.

Compliance: By allowing a reduction in or outright removal of patient-involved dosage, compliance is greatly increased. Sometimes a person forgets they need to take a pill, but the medication delivered by an AN implant is essentially independent of the patient. Periodic filling is a problem with some implantable devices, yet despite it, the patient has less control over administering the prescribed drug. Allowing a decrease in or outright removal of patient-involved dosage greatly increases compliance. Although a patient may forget to take their medication, an implant does not require patient input for drug administration.

The risks of implant: [4]

Invasive: To start medical therapy, either a small or large operation is required. It requires qualified surgical experts and ought to be a drawn-out, stressful procedure. cause minor scarring where the implantation is placed, and a minuscule percentage of the patient may experience surgical complications. Therapy cannot begin until either a minor or large surgical operation has been completed. This requires the right surgical expertise and could be unpleasant and time-consuming. The surgical operation that the patient must undergo can be either major or small.

Termination: At the end of treatment, non-biodegradable implants and diffusion pumps may even be surgically removed. However, surgical removal is not necessary for a perishable implant. It is challenging to stop drug delivery because of its ongoing biodegradation. Non-biodegradable polymeric implants require surgical removal.

The implant preparation methods are as follows: [5]

The preparation of implants can be done in three primary ways:-

a) Extrusion method: To create a solution, the chosen medicine is first dissolved in an appropriate solvent system. Following that, the polymer is gradually added to the mixture and left to stand for ten to fifteen minutes in order to soak. The resulting swelled material was homogeneously combined to create a dough-like substance. After being placed within the extruder cylinder, the dough was extruded by the assistance nozzle into the shape of long rods. The implants were left at room temperature for the entire night before being sliced to the ideal size and dried at 40 degrees Celsius.

b) Compression Method: The solution was created by dissolving the medication and polymer.
For the purpose of creating a consistent cake, the generated solution was freeze-dried. Compression was applied to the cake in order to form the implant. Implants have been created using a Carver hydraulic press operating at a pressure of one metric ton. A stainless steel system consisting of a set of cylindrical punches with a diameter of one millimeter was specifically designed for this purpose.

c) Molding Method: Prior to the prepared cake being molded into rods, a Teflon sheet heated to between 100 and 120 degrees Celsius was placed on a hot plate. The polymer and drug solution were first made in an appropriate solvent system, after which it was subjected to lyophilization and transformed into a homogenous cake.

The evaluation parameters of implant: [6]

Following any appropriate form of preparation, an implant is evaluated by several parameters:

1) Shape and size: implants are assessed in a light environment, and the Vernier Caliper was used to measure the implant's size.
2) Uniformity of thickness: Each implant is individually tested for thickness using Vernier Calipers, which provide an accurate measurement of thickness and reveal variations in each implant's thickness. To get the mean value, at least three samples must be assessed.
3) Weight uniformity: The weight variation test is another name for this one. It is carried out to ascertain whether each implant weighs consistently. 20 implants were chosen at random, and the mean weight was computed. Out of twenty implants, two should not weigh more than the average weight, and none should weigh twice as much as the average.
4) Percentage swelling index: Ready Implants were dipped into the swelling medium (neutral pH) and allowed to sit at room temperature for one hour. This resulted in the percentage swelling index. The free solution was eliminated from the implant after it had been weighed by tapping the surface with the dry filter paper. The following formula was used to

calculate the swelling index:

WU = ([W2] - [W1]) / [W1] x 100

The weight of the implant in its dry form is W1, and the weight after an hour is W2.

5) In Vitro dissolution: These are crucial for figuring out how drugs release and how stable finished products are. The rotating paddle is used to facilitate in-vitro dissolution studies; this method falls under apparatus 2. After the dissolution media was added to the vessel and the ideal temperature and rotational speed were established, the implant was added, the paddle was rotated, and the sample was taken at predefined intervals of time. Additionally, the gathered samples were analyzed at a certain wavelength using a UV-visible spectrophotometer. The dissolving study is conducted at least three times, with an average observation being made each time.

Applications of implant:[7]

1) Diabetes- Implantable technologies have the potential to revolutionize the present paradigm for diabetes diagnosis and treatment, as it is a chronic illness.
2) Cancer- Developing implants to safely and effectively deliver chemotherapy medicines without adverse effects is the main problem in anticancer therapy—for example, Zoladex.
3) Tuberculosis- Long treatment periods and medication side effects are the main issues with TB treatment. This may negatively impact the patient's way of life, resulting in treatment failure, noncompliance, and the emergence of drug-resistant strains.
4) Contraceptive- Apart from subcutaneous implants, innovative drug delivery methods such as intrauterine devices and intravaginal rings are increasingly being utilized in the field of women's health. The popular five-year non-biodegradable implant Norplant was an example.
5) Ocular therapy- Prolonged ocular delivery has been tested with membrane-controlled devices, implantable silicone devices, and implantable infusion systems.
6) Pain management- An implantable drug delivery device would be the best way to ensure that patients follow their treatment plans and comply with them. Inadequate patient adherence to tranquilizer therapy may also be common and increase the likelihood of recurrence, therapy, and other adverse effects.

Curcuma longa linn [8]

In addition to the culinary world, the scientific and medical communities have shown a great deal of interest in turmeric. The use of turmeric dates back nearly 4000 years to the Vedic culture in India in North India, turmeric is commonly called “haldi,” and in the South, it is called “manjal,”. Curcuma longa, the plant used for turmeric, belongs to the ginger family and is a rhizomatous herbaceous perennial. Curcumin's source by turmeric, has been used for millennia for its therapeutic benefits. Only recently, however, have researchers been able to pinpoint the precise mechanism or mechanisms of action as well as identify the bioactive components. Curcumin, commonly referred to as (1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione)diferuloylmethane, is the primary organically formed polyphenol prevalent in the rhizome of Curcuma longa (turmeric) and other Curcuma genera.

Curcumin, Demethoxycurcumin (DMC), and Bisdemethoxycurcumin (BDMC) are the constituents of turmeric and are collectively known as curcuminoids which are form of flavonoids of The chemical makeup of Curcuma longa includes 1.4% DMC, 1.2% BDMC, and more than 3% curcumin. Curcumin has been used in tradition as a medical herb due to its various advantages such as antioxidant, antiinflammatory, antimutagenic, antimicrobial, and several therapeutic Properties. There are several forms of curcumin that may be purchased, including as ointments, pills, and capsules. The US Food and Drug Administration (FDA) has recognized curcuminoids as "Generally Recognized as Safe" (GRAS).

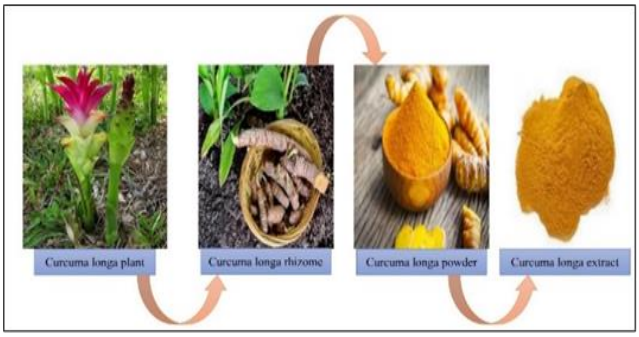

Figure 2 synthesis of curcumin from plant

Taxonomy of Curcuma longa:[9]

Scientific Name: Curcuma longa
Kingdom: Plantae
Sub-kingdom: Tracheobionta -Vascular plants
Super division: Spermatophyta
Division: Magnoliophyta – Flowering plants
Class: Lilliopsida-monocotyledons
Subclass: Zingiberidae
Order: Zingiberales

Genus: Curcuma L. curcuma

Species: Curcuma longa L

Chemistry of curcumin:[9]

Chemical analyses have shown that turmeric contains carbohydrates (69.4%), moisture (13.1%), protein (6.3%), fat (5.1%) and minerals (3.5%). The essential oil (5.8%) obtained by steam distillation of the rhizomes contains a-phellandrene (1%), sabinene (0.6%), cineol (1%), borneol (0.5%), zingiberene (25%) and sesquiterpenes (53%), curcumin (3-6%) is responsible for the yellow color. curcumin's low bioavailability when taken orally; seems to be mostly because of inadequate absorption, quick metabolism, and quick excretion. Curcumin's bioavailability has been studied using several drugs that target these different processes. To boost curcumin's bioavailability, the majority of them have been designed to obstruct its metabolic route. For example, piperine, a known bioavailability enhancer, is the major active component of black pepper and is associated with an increase of 2000% in the bioavailability of curcumin.

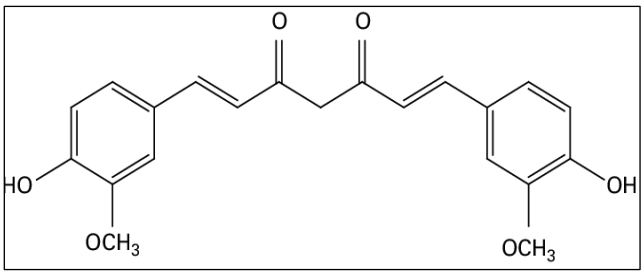

Figure 3 structure of curcumin

Curcumin has the chemical formula C21H20O6 and a molecular weight of 368.385g/mole. Curcumin's structure is made up of three different chemical entities: a seven-carbon chain made up of an unsaturated β-diketone moiety and two oxy-substituted aryl moieties with ortho-methoxy phenolic OH– groups. Curcumin, a tiny molecular weight polyphenolic molecule that is lipophilic in nature and insoluble in both ether and water, is one of the most intriguing parts of curcuminoid. but soluble in ethanol, dimethyl sulfoxide, and other organic solvents.

Pharmacology of curcumin: [10]

a) Anti-Angiogenesis Activity: The ability of curcumin to prevent primary endothelial cell proliferation in the presence or absence of basic fibroblast growth factor (bFGF) as well as the ability to prevent the proliferation of an immortalized endothelial cell line were both examined. The ability of curcumin to suppress phorbol ester-stimulated vascular endothelial growth factor (VEGF) mRNA synthesis was investigated. In a dose-dependent way, curcumin significantly suppressed the proliferation of endothelial cells. In mice, curcumin significantly inhibited the bFGF-mediated neovascularization of the cornea. The synthesis of VEGF induced by phorbol ester was unaffected by curcumin. These findings suggest that curcumin possesses direct anti-angiogenic properties both in vitro and in vivo.

b) Anti-oxidant Activity: Curcumin was evaluated using a variety of in-vitro antioxidant assays, including hydrogen peroxide scavenging, ferric thiocyanate determination of total antioxidant activity, ferric thiocyanate determination of total reducing ability, superoxide anion-free radical scavenging by the riboflavin/methionine/illuminate system, and ferrous ions (Fe^{2+}) chelating activities. These assays were used to demonstrate the antioxidant activity of curcumin.

c) Anti-inflammatory Activity: In both acute and chronic models of inflammation, curcumin has strong anti-inflammatory properties. In the carrageenan oedema test, it is just half as strong as phenylbutazone, but it is half as potent in the chronic testing. Six trials involving humans have shown that curcumin is safe and has anti-inflammatory properties. It may work as an anti-inflammatory agent through inhibiting several different molecules involved in inflammation. Numerous transcription factors, cytokines, protein kinases, adhesion molecules, redox state, and enzymes connected to inflammation have all been demonstrated to be regulated by curcumin.

d) Anti-allergy Activity: Curcumin relieved nasal congestion, rhinorrhea, and sneezing, which reduced the nasal airflow resistance. Moreover, it increases the levels of soluble intercellular adhesion molecules and IL-10 while suppressing IL-4, IL-8, and tumor necrosis factor α. In a model of allergic asthma in mice, curcumin delivered by nasal route prevented allergic airway inflammations while preserving anatomical integrity. The ovalbumin (OVA) of Balb/c mice treated with varying doses of curcumin (2.5 and 5.0 mg/kg) significantly regulates airway inflammation and obstruction, primarily through modulating cytokine levels (IFN-, IL-4, 5, and TNF-α) and sPLA2 activity, which in turn inhibits PGD2 release and COX-2 expression.

e) Anti-arthritis Activity: Synovial fibroblast hyperplasia is a hallmark of rheumatoid arthritis (RA), a chronic inflammatory illness. It is well

known that curcumin has strong anti-inflammatory and anti-arthritic effects. Patients with active rheumatoid arthritis were treated with curcumin and compared to a reference group receiving diclofenac sodium. Curiously, the patients in the curcumin group had a considerably higher percentage of improvement in their total rheumatoid arthritis ratings compared to those in the diclofenac sodium group. More significantly, compared to the diclofenac sodium group, the curcumin group was determined to be safe and did not correlate with any side outcomes. It is thought that the anti-inflammatory, immune-suppressive, antioxidant, and proliferative properties of curcumin contributed to the reduction of rheumatoid arthritis patients' symptoms.

f) Anti-venom Activity: Curcumin was identified as a metabolite from an herbal plant that is efficient against PLA2 snake venom. Researchers looked at the structural relationships between Russell's viper PLA2 and medicinally significant herbal substances such as acalyphin, chlorogenic acid, stigmasterol, curcumin, and tectoridin. Favorable interactions with the amino acid residues in the venom PLA2 active site were identified by the molecular modeling studies as potentially causing the inhibition.

Figure 4 application of curcumin

Side effects of curcumin: [11]

Curcumin has a well-established track record of safety. For instance, curcumin's Allowable Daily Intake (ADI) is 0–3 mg/kg body weight, per reports from the European Food Safety Authority (EFSA) and the Joint United Nations and World Health Organization Expert Committee on Food Additives (JECFA). The efficiency and safety of curcumin have been verified by numerous studies conducted on healthy participants. Even with its well-established safety, there have been a few unfavorable side effects noted. In a dosage response study, seven patients received 500–12,000 mg and were monitored for 72 hours. Symptoms included headache, rash, diarrhea, and yellow stools. In another trial, individuals who received 0.45 to 3.6 g/day of curcumin for one to four months also saw an increase in the levels of lactic dehydrogenase and alkaline phosphatase in their serum, together with symptoms of nausea and diarrhea.

Limitations of curcumin: [12]

Curcumin has a restricted physicochemical stability, which makes it vulnerable to chemical breakdown and degradation, and weak water solubility, which means it dissolves slowly in water. firstly, when curcumin is taken orally, it has a low oral bioavailability, which means that the body has difficulty absorbing it. secondly, it is not well absorbed from the digestive system, which reduces its potency even further. thirdly, curcumin is rapidly excreted from the body due to its quick metabolism and brief biological half-life. Finally, because it degrades at an alkaline pH, less of it is absorbed and bioavailable in the pre-intestinal area. As a result, the drug's dosage required to produce the intended therapeutic effects is finally reduced. By addressing these restrictions with cutting-edge delivery techniques, like nanofiber-based drug delivery systems, curcumin's therapeutic potential for the treatment of cancer can be increased and some of its related difficulties can be resolved.

NANOFIBER [13]

The science and design of materials, structures, and devices with at least one dimension of 100 nm or less is referred to as nanotechnology. Due to their remarkable physicochemical properties and the availability of ultra-fine solid fibers with diameters of less than 50–500 nanometers, nanofibers have become popular one-dimensional nanomaterials for a variety of scientific and industrial uses. It involves them as nanostructured materials. Compared to other frequently used base materials, nanofibers have superior mechanical properties (such as stiffness and tensile power) and a diameter a thousand times smaller than a human hair. Pharmaceutical compounds from BCS classes II and IV may become more soluble and permeable with the use of nanofibers. Nanofibers lessen toxicity and side effects, facilitate easier alternate administrations, and

have a more extended-release profile due to their high loading capacity and high encapsulation efficacy.

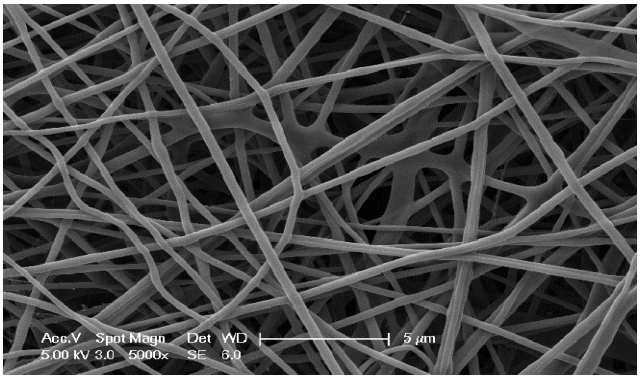

Figure 5 SEM image of nanofiber

Key features of nanofiber: [14]

a) High surface-to-volume ratio
b) Good porosity and permeability
c) Lightweight and density
d) Physico chemically stability
e) High loading capacity

Fabrication techniques for nanofiber: [15]

1) Drawing technique: Stretching of the polymer in solution is done throughout the drawing process for each individual nanofiber. Only viscoelastic materials have been spun into nanofibers using this technique. A cooling system is required to solidify the fiber if the polymer is melted. On the other side, a heating mechanism is required to evaporate the solvent if the polymer is in solution. This is a relatively slow procedure best suited for small-scale experiments.
2) Self-assembly technique: A bottom-up method called self-assembly gathers tiny components to create specified molecular structures like nanofibers. Peptide nanofibers are created by the process of self-assembly. This is an extremely complicated procedure best suited for producing nanofibers on a lab scale.
3) Phase separation technique: Polymer dissolution, polymer gelation, solvent extraction, freezing, and freeze-drying are the five phases in this method. Using a solvent such as THF (tetrahydrofuran), a polymer is dissolved to create a homogenous polymer solution. Subsequently, they will be permitted to divide into two phases based on physical inconsistency, with the bottom solvent phase and the upper polymer phase formed either by heat treatment or by the addition of a nonsolvent, which will cause gelation. This technique does not provide for control over fiber dimensions. It turns out this is only appropriate at lab scale.
4) Template synthesis technique: This technique makes use of nonporous membranes with cylindrically shaped pores. These pores all have uniform diameters. When solid polymers are created, their diameter matches the size of the pores one of the remarkable techniques frequently employed to create nanomaterials such as rods, tubes, and strands This technique can be used in conjunction with a few other production techniques, such as sol-gel and chemical vapor deposition, to create a wide range of nanomaterials, including metals, semiconductors, electroconductive polymers, and carbon nanotubes. the main limitation of this method is the removal of templates after synthesis.
5) Centrifugal spinning technique: Force spinning, another name for centrifugal spinning, This method's underlying idea is comparable to that of making cotton candy. Using centrifugal force, centrifugal spinning produces a variety of nanofibers more quickly and safely, including metal, carbon, ceramic, and polymer nanofibers. The polymer solution injected in the spinneret with two or more orifices is first ejected by centrifugal force in this production method. Next, the polymer material's surface area is increased by the jet stretching process before it is deposited on the collector.
6) Electrospinning technique: The electrostatically driven classical method of electrospinning is widely utilized to produce nanofibers due to its simplicity, low cost of manufacturing, easy adaptation, and efficiency. As the fiber discharge passes across the airspace, solid polymer fiber settles on the metal collector. This causes the solvent in the jet to evaporate, resulting in the development of the nonwoven web.

Characterization of nanofiber:

a) Characterization of chemicals- Fourier transform infrared spectroscopy (FTIR) and nuclear magnetic resonance (NMR) can be used to ascertain the chemical structure of nanofibers. With these techniques, we can identify the molecular interactions and molecular structure of the polymers combined to produce nanofibers. The macromolecule structure in a nanofiber can be determined by small-

angle X-ray scattering, differential scanning calorimetry (SAXC), and wide-angle X-ray diffraction (WAXD). Water contact angle measurements and FTIR-ATR analyses are used to evaluate the surface chemical characteristics.

b) Characterization of mechanicals- It is possible to assess the mechanical characteristics of nanofibrous nonwoven membranes using conventional methods. Tensile strength of a nanofibrous mat was found to be comparable to normal skin. It was discovered that the electrospun nonwoven mats showed distinct characteristics in different orientations when the membranes were being spun on a drum. A number of electrospinning parameters and the drum surface's linear velocity both have an impact on the fiber orientation. Nanofibers cannot be evaluated using the same criteria and procedures that are currently utilized to evaluate the mechanical properties of conventional fibers.

c) Characterization of Geometric- Geometric characteristics of nanofibers include fiber diameter, fiber morphology (such as surface roughness and cross-section shape), and fiber orientation. Atomic force microscopy (AFM), transmission electron microscopy (TEM), field emission scanning electron microscopy (FESEM), and scanning electron microscopy (SEM) are used to assess the geometric properties of nanofibers. The diameter of fibers can be measured using the AFM technique, although exact readings are challenging to get. Very small fiber diameters can be measured with TEM. Another method for figuring out the forms and sizes of fibers is SEM. One of its drawbacks is that at higher magnifications, the resolution becomes less clear. SEM is still a quick way to look at the fibers that are created, and it works best with a small sample size.

Release mechanism of nanofiber:

The use of nanofiber drug delivery systems may shed light on how bioactive growth factors might be directly added to scaffolds. Furthermore, implantable scaffolds for tissue engineering can be used in conjunction with drug delivery devices to guard against infection while regeneration and repair take place. Drugs are released from biodegradable polymers by erosion or diffusion. Both mechanisms work together to control release from biodegradable polymers and their relative rates of erosion and diffusion determine this. Hydrolysis is the process that breaks down the majority of biodegradable polymers utilized in medication delivery. When water molecules react with the bonds that make up the polymer backbone usually ester bonds the polymer chain is repeatedly broken until it splits back into monomers. This process is known as hydrolysis. Another kind of chain scission that can be found in other biodegradable polymers is enzymatic degradation. Drug release occurs when the physical integrity of the polymer deteriorates due to the breaking of chemical bonds by water molecules along the polymer chain.

Challenges of nanofiber: [16]

Because of the high cost of technology and the low production rate, the process of creating nanofibers is more expensive than creating regular fibers. Additionally, it is necessary to recover or dispose of the vapors that the electrospinning solution released during the web-forming process in an environmentally responsible manner. This calls for more money and equipment. There is significant worry regarding the potential health risks associated with inhaling fibers due to their fineness and evaporated vapor. costly, dangerous for one's health, Vaporizing solvents; packing, transportation, and handling.

Commercial characteristics of nanofiber: [17]

1. Nanofibers are a great choice for drug and cell administration because of their sterility, controlled release pattern, enhanced mechanical qualities, biocompatibility, and biodegradability.
2. The compositions of nanofiber scaffolds are highly biocompatible with biological tissues and incorporated chemicals.
3. Nanofibers are easily removed from the implantation site or absorbed into nearby tissues due to their high biodegradability profile and nontoxic breakdown products.
4. The open, interconnected porous structure of nanofiber compositions allows for the best possible interaction with bioactive substances.
5. Nanofiber compositions are excellent in delivering medication encapsulation to the desired location with the least amount of side effects.
6. Because of the enormous ability of nanofibers to trap and load, medication can be injected into the body and then continually administered for a prolonged amount of time.
7. Because of their biocompatibility, nanofibers and the breakdown chemicals they produce are non-toxic to the body.
8. After being inserted into the body, nanofiber scaffold

formulations have a strong enough binding affinity to maintain cells in their pore structures or to permit the continual release of the drug that is encapsulated.

Application of nanofiber: [18]

a) Because of its special qualities, a nanofiber mat is an excellent choice for wound dressing. Its small pores and high specific surface area help to manage fluid drainage in addition to preventing the infiltration of external microorganisms. Furthermore, a straightforward method for incorporating medications into the nanofibers for potential antibacterial and therapeutic uses.

b) In medicine, getting pharmaceuticals or chemicals to patients in a form that is more physiologically acceptable has long been a concern. Orally administered medications for a variety of illnesses reach the injured area, albeit the dosage is lowered from the starting point. To maintain an effective drug concentration at the injured site, the composition, porosity, and shape of the nanofibers can be changed, hence controlling the drug's release rate from them.

c) In order to treat skin cleansing, skin healing, and other medical and therapeutical qualities, nanofibers have been employed as a skin care mask. The increased specific surface area of the nanofibrous skin mask accelerates the rate at which additives are transferred to the skin. Electrospun nanofibers have the potential to be employed as face masks due to their small pore size and high surface area to volume ratio. Skin energizing ingredients can also be used to nanofiber masks to enhance skin health. The ability of the electrospun nanofiber mask to be applied directly, gently, and painlessly to the skin to promote skin healing is its most intriguing feature.

d) Filtration is one area where polymeric nanofibers have found extensive application. The filter should have these characteristics in order to facilitate the easy entrapment of particles for the purpose of filtration. Because of their extremely high specific surface area to volume ratio, polymeric electrospun nanofibers are excellent filters for capturing particles smaller than 0.5 mm. Small particles, or droplets, are captured by both physical entrapment and electrostatic attraction. Certain chemical and biological warfare substances can also be detected and filtered using nanofiber membranes composed of certain polymers.

e) Because it increases a soldier's chances of survival against hostile environments, biological, chemical, and nuclear warfare agents, and extreme environmental conditions, protective clothing finds use in combat situations. Because they have all the characteristics of the perfect protective clothing, including being low weight, very porous, having a wide surface area, being resistant to the penetration of dangerous chemicals, and having good filtering efficiency, nanofibers have been acknowledged as viable candidates for applications involving protective clothing.

f) Chemical reactions can be accelerated by the use of enzymes as catalysts. Enzyme immobilization has various benefits, including improved reaction control and reusability, which enhance the functionality and performances of enzymes for bioprocessing applications. Both the carrier system's porosity structure and the matrix-enzyme interaction are major factors in immobilization efficiency. Enzymes have been immobilized on electrospun nanofibers using a variety of techniques, such as physical adsorption, grafting enzyme on the fiber surface, and introducing enzyme into the nanofiber by procedures that are then followed by a cross-linking reaction.

g) Energy sources such as hydrogen gas and natural gasses have been stored in nanofibers. Materials made of nanofibers can transform a variety of energies into electrical power, helping to address the energy crisis. Solar energy is used by solar cells to generate power. The market for solar cells is now dominated by single-crystal and polycrystalline solar cells. Fuel cells are machines that use a metal catalyst to transform hydrogen or fuels high in hydrogen into electric current. There are several types of fuel cells available at the moment, including solid oxide fuel cells, alkaline fuel cells, direct methanol fuel cells, and proton exchange mat fuel cells. Fuel cells with proton exchange mats are the most significant due to their high power density and low operating temperature.

h) One use for affinity membranes is the extraction of organic compounds from wastewater. In one study, for instance, β-cyclodextrin was physically mixed into a polymethyl methacrylate nanofiber membrane. The results showed that the β-cyclodextrin combined with hydrophobic organic molecules from waste water to create an inclusion

complex. Electrospun nanofiber mesh has been employed as an affinity membrane and functionalized surface with ligands in a number of studies.

Figure 6 application of nanofiber

Electrospinning method: [19]

A prominent by electrostatic force driven traditional technique of fabricating nanofibers is electrospinning, which is beneficial due to its simplicity, affordability, ease of adaptation, and efficiency. This method's produced nanofibers are thought to be more beneficial because of their improved porosity, smaller fiber diameter that falls between nano and microscale, and larger surface area. It is also known as electrohydrodynamic process.

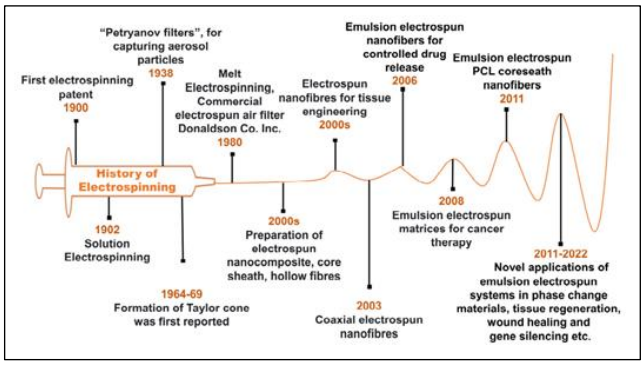

Figure 7 history of electrospinning method

Four main parts make up an electrospinning setup:

a) a collector (rod or plate)
b) a syringe pump or infusion pump
c) a spinneret (a needle with a blunt tip)
d) a high-voltage power source (15-50 kV)

Principle of the process of electrospinning, in which a high voltage is applied to the liquid polymer to cause the spinneret to eject an endless stream of jet strands towards the grounded collector. This process allows for

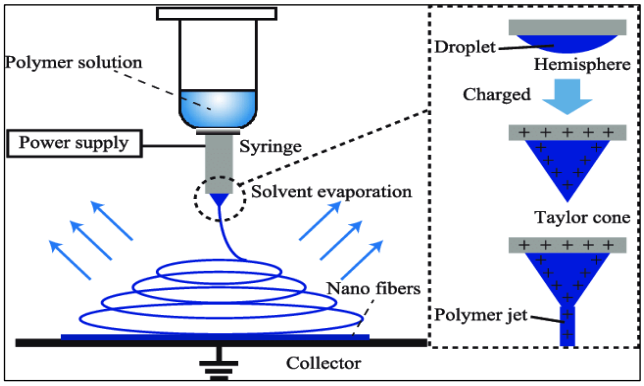

Figure 8 principal image of electrospinning

the creation of nanomaterials using a preferred polymer and an appropriate solvent to prepare polymer solutions along with drugs, peptides, nanoparticles, etc. An applied electric field regulates the polymer droplet's interfacial tension. After that, the droplet elongates to create a "Taylor cone" which is then separated from the droplet to create a fiber jet that extends toward the collector and solvent evaporates while drug containing polymer will solidify in the form of fibrous mesh. The type of polymer, depending on the concentration, conductivity, viscosity, flow rate, and nozzle to collector distance, are crucial characteristics to take into account in this procedure.

Formulation components: [20]

This is based creation of custom Solvents, surfactants, single and multiple polymers, etc. are the foundation of electrospun nanofibers. Drug release, solubility, stability, mechanical qualities, etc. can all be altered depending on the kind of polymer. Various solvent types, including organic and inorganic solvents, are utilized in the creation of polymeric solutions. The list of excipients utilized in the creation of nanofibers is provided here as

a) Polymers are a kind of spun material that are frequently utilized to create Electrospun Nanofibers for usage in a variety of biomedical and pharmaceutical applications. The following are lists of synthetic and natural polymers used in electrospun: - 1) Polyglycolic acid (PGA), Polyethylene terephthalate (PET), Poly(ε-caprolactone) (PCL), Polystyrene, Polyurethane (PU), Polylactic acid (PLA), and Poly L-lactic acid-co-polyε-caprolactone (PLACL) are examples of synthetic polymers. 2) Alginate, collagen, hyaluronic acid, chitosan (CS), silk fibroin, chitin, heparin, and cellulose are examples of natural polymers.
b) Typically, the polymer must dissolve in an

appropriate solvent before being spun into nanofibers with a diameter of between several nanometer. Selecting the right polymer-solvent system combination is necessary to achieve it. A list of some of the solvents used in electrospinning is provided. Water, hexafluoro isopropanol, trifluoroacetic acid, toluene, sulfuric acid, formic acid, chloroform, ethanol, acetone, phenol, dimethyl formaldehyde, dimethyl acetamide, dimethyl chloride, etc.

c) These days, surfactants are used in the electrospun nanofiber manufacturing process. It improves the active's stability and solubility in the electrospun polymeric solution. It can be applied alone or in conjunction with two distinct surfactants. These are mentioned below, Ion-based surfactants: SDS, or sodium dodecyl sulfate, Surfactants that aren't ionic: Triton X-100 iii. Hexa-decyl-tri-methyl ammonium bromide (HTAB) and cetyl-tri-methyl ammonium bromide (CTAB/SDBS) are examples of cationic surfactants.

d) The medication must be incorporated into and compatible with the solvent polymer composition, even if it exists in the solid state as a solid powder. additionally, Medicine The process of loading a medicinal substance into nanofibers entails dissolving the medication in the polymer solution prior to spinning. Another way to control medication release is through covalent attachment to polymers. Additionally, it has been proposed that the large porosity of nanofibers facilitates the quick spread of product degradation. The sudden release, though, can also mean that the medication is merely surface-attached. Given that the medication and carrier materials can be combined to electrospun nanofibers, the following are the most likely drug modes in the resultant Nano structured products:

The drug is present as particles that adhere to the carrier polymer's surface to create nanofibers. Because the medication and carrier polymer are both in the form of nanofibers, there are several types of nanofibers woven together. The combination of medication and carrier materials is incorporated into a single type of fiber that has both parts. The drug particles are enclosed in a tubular form created by electrospun of the carrier material.

Advantages of electrospinning method: [21]

Various materials and polymers are used to create nanofibers. The following factors are crucial: molecular weight, solution viscosity, charge carrier mobility, tensile modulus and tensile strength, wettability, thermal stability, and degradation. physicochemical characteristics of polymers and materials.

Fiber functionalization ease of use: Surface functionalization can be achieved by core-shell electrospinning or by spinning a basic polymer solution first.

Combining materials is simple: There are few prerequisites for producing fibers when using different materials for electrospinning.

Relatively cheap initial outlay: Usually, a simple electrospinning setup is less expensive. Store-bought pieces can be used to self build a setup in a laboratory environment.

Simple to learn: The principles of electrospinning can be understood in a matter of weeks by someone who has some acquaintance with polymers and electrostatics, as well as mentorship.

Numerous nanofibrous structures have been built. Electrospinning setup and method modification have enabled the production of three-dimensional blocks of nanofibers, yarns, and tubular nanofibrous structures.

Mass production capability: Large scale manufacture of nanofibers can also be achieved by commercially available electrospinning technologies.

Electrospun fibers are commonly deposited on different surfaces as water, glass, metal, and mats.

Disadvantages of electrospinning method: [21]

The difficulties in obtaining in situ nanofiber deposition on various substrates.

It requires a high working voltage and has a low yield.

Large-scale production of nanofibers with these characteristics is still difficult.

Because the polymer's aspect ratio falls short of expectations in terms of toughness and impact resistance, it is brittle.

If dangerous compounds are employed in the solvent bioaccumulation process, it could be toxic and dangerous for both human health and the environment.

Because the chemicals, equipment, and energy can be expensive, producing and scaling up nanofibers can be costly as well.

Drug loading techniques in electrospinning: [22]

a. Blend electrospinning- When the therapeutic substances are dissolved or distributed in the polymeric solution, drug encapsulation is accomplished through electrospinning in a single step when employing the mixing electrospinning process.

Drug loading techniques in electrospinning: [22]

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c. Coaxial electrospinning- The primary aim of coaxial electrospinning is to produce fibers that possess a core-shell configuration. Using this method, fibers with certain medications encapsulated in the fiber's core can be produced, resulting in a controlled and prolonged release of the drug. These fiber types offer a three-dimensional network with a large surface area.

d. Emulsion electrospinning- One of the most crucial ways to quickly and cheaply prepare core-shell electrospun nanofibers is through emulsion electrospinning, a versatile and promising technology for encapsulating many medications into nanofibers. the control of the emulsions' water and oil phases to modify the medication release rate and achieve the intended drug release.

e. Surface modified electrospinning- By adding certain molecules that can camouflage the surface by providing an environment similar to the tissue that will surround the implanted material, a specific conductive surface can be chemically changed and altered to modify the external properties of the coated device. This tactic is typically used to delay the rate at which biological molecules immobilize on a given surface and prevent rapid initial burst release. Furthermore, 3D surfaces can be coated with nanoparticles or homogenous surfaces using effective electrospinning technology and a standardized technique for producing an electric field within a camera.

f. Electrospray electrospinning- One of the best techniques for creating nanoparticles and nanospheres is electrospraying. The easiest strategy for incorporating drugs is this one. Because of surface tension, the liquid in this process that emerges from the nozzle into the electrical field forms the Taylor cone. The Taylor cone splits into highly charged droplets as the electric field rises, which provides the right environment for the production of nanoparticles or microparticles. Solvent evaporation produces solid particles.

Parameters affecting electrospinning method: [23]

A. Solution Parameter
   a. Molecular Mass- Higher molecular mass results in a more uniform morphology
   b. Concentration- Increases viscosity and amount of deposited nanofibers
   c. Viscosity- Increased viscosity fiber diameter increases and decreases bead formation
   d. Conductivity- Increasing conductivity fiber diameter decreases; ionic materials can reduce atomization of polymer jet

B. Operational process parameter
   a. Applied Voltage- Decreasing fiber diameter with increasing voltage supply
   b. Distance of collector from nozzle- Fiber solidification; deposition area, increases with increased distance between collector and nozzle
   c. Solution Flow Rate- Higher flow rates - larger diameter fibers and Lower flow rates- smaller diameter fibers
   d. Tip- Increasing tip diameter increases the diameter fiber
   e. Collector Type- Aligned fibers, yarns, braided, or random fibers can be obtained by changing from a plate to a drum, area, etc. type collector

C. Environmental Conditions
   a. Temperature- High temperature reduces the viscosity of the polymeric solution, resulting in a low diameter of fibers
   b. Humidity- High humidity resulted in the bead and circular pore formation in fibers, low humidity may produce thicker fibers due to quick solvent evaporation

Electrospinning step from initial to final:

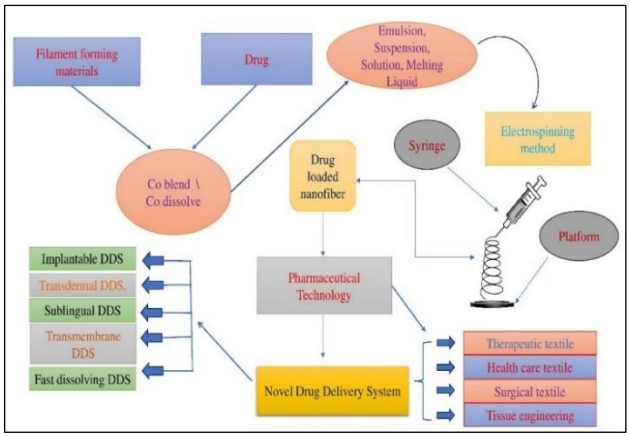

Figure 9 complete step of electrospinning

Cancer: [24]

Cancer is a sickness characterized by uncontrolled cell growth that can spread to other body areas and is caused by genetic or epigenetic changes in the somatic cells. They comprise a subset of tumors. The uncontrollably growing cells in a group known as a tumor or neoplasm form a lump or mass that may be widely dispersed.

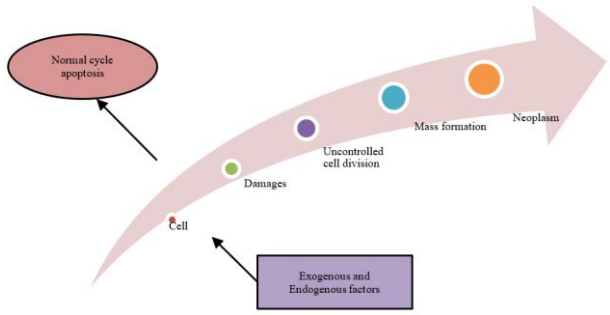

Figure 10 step of cancer cause

Causes of cancer:[25]

Numerous factors can contribute to the development of cancer in various body parts. For example, tobacco use accounts for 22% of deaths, while poor diet, obesity, inactivity, and excessive alcohol consumption account for 10% of deaths. Other factors that may contribute to the development of cancer include specific exposure to ionizing radiation, environmental pollutants, and infections. Hepatitis B, hepatitis C, human papillomavirus infection, helicobacter pylori, immunodeficiency virus (HIV), and Epstein-Barr virus are among the illnesses that cause about 15% of cancer cases worldwide. The genes have changed, at least in part, because of these influences. Fifteen to twenty percent of cancer cases are also caused by genetic abnormalities inherited from the patient's parents. Three types of chemicals that we consume externally, in addition to genetic factors, interact to cause cancer:

1. Physical Carcinogens: Ionizing radiation such as radon, ultraviolet rays from sunlight, uranium, and radiation from alpha, gamma, beta, and X-ray-emitting sources.
2. Chemical Carcinogens: Compounds like nitrosamines, asbestos, cadmium, benzene, vinyl chloride, nickel, and benzidine and contain about 60 known potent cancer causing toxins or chemicals in cigarette smoking or tobacco consumption, a drinking water contaminant (arsenic), a food contaminant (aflatoxin).
3. Biological carcinogens include infections caused by certain bacteria, viruses, or parasites. Examples of pathogens include Epstein-Barr virus (EBV), human papillomavirus (HPV), hepatitis B and C, Markel cell polyomavirus, KSHV, Schistosoma species, and Helicobacter pylori.

Types of cancer: [26]

a. Carcinomas: They begin in the tissue or skin that covers the surface of the internal organs and glands. It solidifies as a tumor. lung cancer, colorectal cancer, prostate cancer, and breast cancer.
b. Sarcomas: The tissues that support and link the body are where it begins. It can develop in blood vessels, bones, muscles, cartilage, tendons, joints, nerves, or lymph vessels.
c. Leukemias: Leukemia is a type of blood cancer. It starts when normal blood cells start to expand and alter out of control. Acute myeloid leukemia, acute lymphocytic leukemia, chronic myeloid leukemia, and chronic lymphocytic leukemia are its four subtypes.
d. Lymphomas: The lymphatic system, which is a network of glands and tubes that aids in the body's defense against infection, is where lymphamic cancer starts. Two types of lymphomas: non-Hodgkin and Hodgkin.
e. Melanoma: it begins in cells that eventually develop into melanocytes. These cells are specialized cells that produce melanin, the pigment responsible for the skin's color. Melanomas typically arise on the skin, although they can also occur in other pigmented tissues, such as the eye.
f. Cancers known as adenomas can develop in the adrenal gland, thyroid, pituitary, and other glands.
g. Cancers that originate in the brain and spinal cord. Other types of cancer include meningiomas, vestibular schwannomas, gliomas, pituitary adenomas, primary CNS lymphomas, and primitive neuro-ectodermal tumors.

Symptoms of cancer: [27]

Early Symptoms: Cancer does not exhibit any signs or symptoms in its early stages, making it impossible to diagnose the illness. Additionally, the indicators or symptoms are displayed in a damaged state.

a. Continuous Cough or Saliva with Blood Tinting
b. A Shift in the Bowel Pattern
c. Stool with Blood
d. Inexplicable Anemia
e. lump in different bodily parts
f. nausea and stomach ache
g. back and bone pain

Late Symptoms: These signs vary according on the type of cancer, its location, and the extent to which its cells have disseminated.

a. noticeable alterations to a mole's or wart's size, color, shape, or thickness
b. a hard time swallowing a persistently painful throat sibilant voice
c. Low-grade fevers that go undiagnosed might either continue or not.
d. Recurrent Infections

Diagnosis of cancer: [27]

When a patient exhibits no symptoms, their cancer is identified during testing for other illnesses or problems; if the patient does, the physician will do a number of tests. Physicians diagnose cancer by having patients undergo screening tests. For instance, a pet, pap and hpv test, mammography, and colonoscopy. Before screening testing, further tests are run to look for any anomalies in the body. For instance, ultrasonography, X-rays, MRIs, CT scans, biopsy, lab scan and bone tests. For this reason, radionuclide tests are carried out in areas that are difficult to see, such as inside bones or some lymph nodes. Gene testing is covered in the Understanding Cancer Series tutorial, which also defines genes, describes how mutations in genes develop and are detected, and highlights the advantages of gene testing for cancer and other diseases.

Treatment of cancer: [28]

The treatment depends on the kind of cancer and its stage of progression, there are several kinds of cancer therapies. While some cancer patients only receive one treatment, the majority have many therapies, such as radiation therapy and surgery.

a. Surgery: A surgeon may remove lymph nodes in order to stop or slow the disease's progress and eradicate cancer from the body.
b. Radiation therapy: In this treatment, large radiation doses are utilized to destroy cancer cells and shrink tumors.
c. Chemotherapy: Although it has serious adverse effects, chemicals are used to treat cancer by shrinking tumors and destroying cancer cells.
d. Immunotherapy: This type of therapy involves using medicine or other treatments to strengthen the immune system. Take the use of checkpoint inhibitors and adoptive cells as examples.
e. Targeted therapy: This treatment targets and strengthens the immune system to assist cancer cells in proliferating, disseminating, and dividing. For instance, small-molecule medications and monoclonal antibodies.
f. Hormone Therapy: This treatment uses hormones to block and slow the growth of cancers, including breast and prostate cancer.
g. Stem Cell Transplantation: This treatment helps cancer patients regain their stem cells, which have been damaged by extremely high radiation or chemotherapy dosages.

Precision medicine is a more recent technique where genetic testing is used to decide the optimal course of treatment for a patient.

Side effects of treatment of cancer: [28]

Healthy cells are harmed by side effects. Those are the adverse effects:
Hair loss & mouth ulcers
Feeling queasy Tired
Inflammation of the organs
Heart palpitations
Congestion in the sinuses

CONCLUSION

In conclusion, using electrospun curcumin nanofibers appears to be a highly promising approach to enhance cancer therapy. Drugs may be released gradually through these nanofibers, increasing their safety and efficacy. They also decompose over time and are compatible with the body. However, further study is still needed to refine the procedure and comprehend how effectively they function over the long term. Overall, this analysis indicates that curcumin nanofibers may represent a significant advancement in cancer treatment; however, further research is required to be certain.

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