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"A Review of Nanofiber: Current Progress in Application of Polymeric Nanofibers to Tissue Engineering"

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Abstract

Numerous types of polymer nanofibers have been developed to serve as synthetic alternatives to extracellular matrix (ECM). Among these, electrospinning is a widely used technique for the production of nanofibrous scaffolds. This method creates nanofibers having a porous structure and a large specific surface area. Both organic and artificial Electrospun polymers have been used to create a fibrous framework that mimics the ECM and promotes cell activity. Tissue engineering is a technology that uses biomaterials, chemistry, and cell biology to create tissues in three dimensions (3D) that closely resemble the matrix extracellular in structure. The ECM is formed by braiding nanofibrous structures together. Electrospinning is widely used in the creation of nanofibrous scaffolds. It produces porous nanofibers with a highly particular surface area. The electrospinning technique and the parameters of the solution strongly influence the nanofibers' structural shape and assembly. By combining natural or synthetic polymers used in electrospun nanofibers, their function can be modified. Furthermore, electrospun nanofibers can be functionalized using a range of surface modification methods. This work presents the latest advancements in electrospun nanofiber synthesis and describes various methods for surface modification of the scaffolds to increase their activity. There is also discussion of the use of cutting-edge polymeric nanofibrous scaffolds in human vascular tissue regeneration, ligaments, and tendons.

KEYWORDS: Electrospinning, Nanofibers, Tissue engineering, polymers.

INTRODUCTION:

Organ transplants are becoming more necessary each year due to the high incidence of organ failure and tissue damage **[1].** However, tissue engineering provides an alternative method of repairing damaged tissue without the problems related to traditional tissue transplantation **[2].** For creating three-dimensional tissue, researchers

must know a variety of fields such as nanotechnology, materials science, chemistry, cell biology, and micro- and nanofabrication [3]. Numerous scientists have made an effort to modify the biological activity of cells with the use of biomaterials with specified three-dimensional structures and messages that guide cells, enhanced along with elements similar to extracellular matrix (ECM) **[4].** Extracellular matrix (ECM) molecules possess intricately woven fibrous patterns at the range of nanoscale that facilitate cell adherence as well as bioactivity. Therefore, tissue engineering research focuses on creating scaffolds featuring a design similar to the ECM molecule **[5].** Various methods have been employed to produce scaffolds built using a nanofibrous structure, such as phase separation, self-assembly, and electrospinning **[4,5].** Of these methods, The use of electrospinning has gained great attention as a result of its ability to create nanofibrous scaffolds with elevated porosity and adjustable pore size distribution. When combined with other components, The electrospun nanofibers' high surface area and porous structure can improve the performance of the cell **[6].** The choice of materials used to create nanofibrous scaffolds is crucial **[6].** Various types of polymers, such as natural, synthetic, as well as composite ones, have been utilized to generate nanofibers produced by electrospinning **[3,4].** The electrospinning process has undergone significant technological advancements that have enabled the development of novel polymeric materials with desirable characteristics. These materials can modify the hydrophilicity, conductivity, and antibacterial activity of nanofibers, as well as their structural diversity. Numerous investigations have investigated applying nanofiber scaffolding for engineering vascular, bone, neuronal, as well as cartilage tissue **[6,7].**

GENERAL FABRICATING NANOFIBROUS SCAFFOLDS:

Biomolecules, including polysaccharides and proteins, make up the extracellular matrix (ECM), which provides cells in natural tissue with a complex microenvironment. **[8]** This ECM performs various functions, including maintaining mechanical integrity and controlling cell signalling. For example, the strength and tenacity of the ECM in withstanding external strain are attributed to its robust protein macromolecules. Moreover, the ECM proteins are linked to the shifting patterns (migration) and destiny choices (proliferation, death, and development) of cells employing their universal mechanical attachment to cell receptors like integrins. **[8]** Therefore, constructing scaffolds that can imitate the fibrillar shape and range of activities of the extracellular matrix is vital to quickening the processes of tissue genesis, differentiation, proliferation, and cell adhesion. To create an extracellular matrix (ECM) equivalent, it is important to consider the geometry and topographical features at different scales - macro, micro, and nano. Scaffolds made from high specific surface area nanoscale Fibers could potentially resemble the native ECM morphology. **[9]** The most common methods to create nanofibrous structures are phase separation, electrospinning, and self-assembly. **[7]**

POLYMER SELF-ASSEMBLY:

Polymeric materials often self-assemble through the intermolecular connection of peptides, which rapidly form stable and well-defined structures through the action of non-covalent interactions like hydrogen bonding, interactions such as van der Waals, electrostatic, and π–π stacking. Although typically, these connections are weak, they have a significant impact on the communication between other molecules, cells, and tissues and the supramolecular structure when they combine during the assembly procedure, into a single unit. This helps to regulate the assembly's stability and structural conformance. A sequence of amino acids in the initial self-assembling peptide can be adjusted to enhance the basic concepts for creating other self-assembling peptides **[10].** Peptide self-assembly can be triggered by electrolytes' existence in the mixture. Peptide monomers may experience mild electrostatic repulsion when peptides that self-assemble with a little net charge, positive or negative are present. As a result, these peptides dissolve in water in reasonable amounts and remain dissolved for a long time. Self-assembly of peptides is not yet completely comprehended, but A few research has suggested that it takes place because electrolyte ions cause peptide monomers with similar charges to repel each other less strongly **[10].**

Peptides can be positioned closer to one another as a result of this process, strengthening hydrophobic contacts and creating stable nanofibers. Pore widths range from 5 to 200 nm as a result of further organizing nanofibers into 3D structures and hydrogel production **[11].** Phenotypic hydrogel mechanical characteristics are known to be controlled by several variables, such as the pH of the solution, temperature, hydrophobicity/hydrophilicity, charge of the amino acid, concentration and type of electrolyte ions, hydrophobicity/hydrophilicity, and amino acid sequence **[11].**

Because they are simple to utilize, nonimmunogenic, and nontoxic (requiring no hazardous chemicals), Self-assembling hydrogels of peptides provide an excellent foundation for designing tissues including liver, cardiac tissue, neuron, cartilage, bone, and angiogenesis [10,11]. These hydrogels are biodegradable, and cells may metabolize the byproducts of their breakdown. The mechanism by which polymers self-assemble results in

significantly lessened nanofibrous structures than scaffolds made by the electrospinning approach. Self-assembled nanofibers have certain drawbacks despite their benefits, including difficult processing, low productivity, and comparatively expensive cost **[12].**
Furthermore, self-assembled systems may diffuse in vivo before gelation because of their inadequate mechanical characteristics (as in contrast to those made using alternative methods) and lower kinetic rate of formation than existing shear-thinning injectable hydrogels **[12].**

PHASE SEPARATION:
Separation of phases is yet another method accustomed to generating an architecture of porous nanoscale for polymer scaffolds used in 3D tissue engineering. The dissolving, gelation and water-based solvent extraction from the gel are the three primary processes needed for this approach. Freezing-lyophilization is then performed under a vacuum **[13].** A polymer is first dissolved in a solvent at a high temperature, and then either cooling or non-solvent exchange is used to cause the polymer to undergo a liquid–liquid or solid–liquid phase separation. At that point, phases high in polymers emerge within the solvent because the polymer is no longer thermodynamically soluble. The scaffold is in a frozen state and preserves its arrangement once the solvent has been extracted. By lyophilization, extremely porous fibrous polymer scaffolds with Circular pores at the microscale are eventually produced **[13].** Zhang et al. developed a method in an attempt to replicate the extracellular matrix's (ECM) nanofibrous structure by creating 3D interwoven poly-l-lactide (PLLA) fibrous networks using a liquid-liquid phase separation technique. The diameter of these artificial Fibers ranged between 50 and 500 nm, which is Comparable to a collagen matrix. **[13,14]**
Phase separation allowed for the creation of 3D scaffolds with predetermined dimensions by employing particular Molds. Complex constructions, like the jawbone or ear of a human, can be created by using computer-aided design for the Molds **[14].** Phase separation is used to create scaffolds that have large hole diameters that can enhance cell infiltration, similar to more traditional foams **[15].**

ELECTROSPINNING:

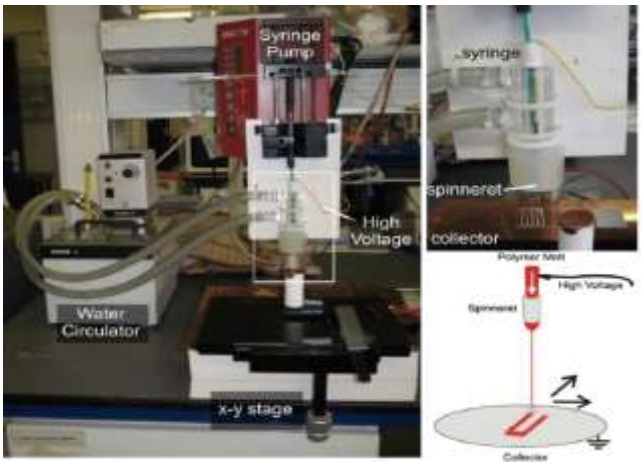

Fig 1: Electrospinning equipment

Tissue engineering researchers have shown a growing interest in electrospinning since the discovery that the structural characteristics of Many materials are involved in a critical part in regulating cell function. Electrospinning is a method for creating synthetic fibers using electrostatic forces**.** In a standard electrospinning setup, a field of electricity is generated between a charged object and spinneret which includes both a polymer solution and a counter electrode **[16].** When a polymer solution is charged by an electrostatic charge, it forms a jet towards the end of a metal needle because of the lower surface tension. This charged jet then passes through a spinneret and reaches a counter electrode where it turns into continuous polymer fibers. These fibers are collected on a collector and their diameter can vary from dozens of nanometres to a small number of micrometres based on the type of polymer mixture and the electrospinning parameters. **[16]** The process of electrospinning fibers is influenced by various factors, such as the characteristics of the resolution including polymer content, processing, solvent volatility, and solution conductivity (including flow rate, applied voltage, and needle-to-collector distance) **[17].** The ability to create steady strands, known as well as spinnability, mainly relies on the polymer chains' entanglement in the solution. The concentration of the polymer affects this entanglement, as well as the solution's viscosity and surface tension. When the polymer concentration is too

low, it results in the creation of polymer droplets or mechanically weak fibers. On the other hand, when the concentration is too high, the creation of fibers is prevented altogether **[17].**

Various experimental setups of the electrospinning process have been employed to alter the main characteristics of fibres, like the solution or nozzle arrangement (coaxial nozzles) versus spin melting. Electrospinning in coaxial form, which employs two needles in alignment, enables the simultaneous spinning of two distinct polymer solutions. By working at the chemical droplet at a comparable voltage the tip of both metal syringes is deformed. This results in the development of a jet on the deformed droplet tip, producing core-shell nanofibers, where large fibers encase tiny fibers. Precise core-shell nanofibers have been developed by using the right amount of solution **[18].**
There is an alternative method to coaxial electrospinning that avoids potential toxicity and solvent buildup, known as melt electrospinning. In this process, a strong electric field is created between the heated extruder's polymeric melt and the metal-based collecting rotor. This causes nanofibers to form during the stage transition brought on via cooling after the polymer has initially melted. Similar to coaxial electrospinning, the formation of fibers is driven by the spin line's attenuation subjected to the forces of electrostatics. While in transit, the electrostatic forces acting on the jet cause its diameter to continuously decrease until the jet cools, and its viscosity overcomes the electrostatic forces. **[19]**

MATERIALS FOR ELECTROSPUN NANOFIBER FABRICATION:
Nanofibrous scaffolds have been designed using a range of natural and manmade polymers, each with their unique properties. Synthetic polymers are generally more cost-effective and offer greater flexibility in terms of synthesis, processing, and modification. However, they require more alterations and are not inherently bioactive. Conversely, naturally occurring polymers promote improved cell adhesion, growth, and differentiation as a result of their intrinsic
bioactivity and cell-interactive domains. Additionally, the breakdown products of natural polymers are relatively weak and chemically harmless to the immune system**.[20]**

NATURAL POLYMERS:

Fig 2: Natural Polymers

Natural polymers with biocompatibility and bio-functionality, such as silk, hyaluronic acid, collagen, gelatin, chitosan, and fibrinogen, have been utilized as gratings for a long time **[21].** Crosslinking is frequently utilized to increase the strength of natural polymers electrospun while maintaining their fibrous shape **[22].** After electrospinning, Crosslinking collagen nanofibers can be achieved by a variety of techniques, such as stabilisation using formaldehyde, epoxy resins, or vapours of glutaraldehyde, as well as UV light exposure **[22].**
Gelatin nanofibers, which are created by denaturing collagen, can be stabilized through physical blending with other polymers or through chemical crosslinking with genipin, glutaraldehyde, and carbodiimides. For example, gelatin scaffolds that were electrospun and crosslinked with genipin had A mean diameter measuring 570 ± 140 nm. These scaffolds showed limited fused patches where the fibers overlapped, retaining more crisscrossed than non-crosslinked structures **[23].**
Chitosan, a polysaccharide made from deacetylated chitin, can also be electrospun. It is typically electrospun using acidic mixtures, like acetic acid, formic acid, diluted hydrochloric acid, and trifluoroacetic acid. The outcome chitosan scaffolding is suitable for wound healing applications because of its low immunogenicity, hemostatic properties, and antibacterial characteristics **[24].** When fibrinogen scaffolds are crosslinked, it

enhances their power and dexterity and slows down their rate of deterioration, similar to other natural polymers. For instance, when using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide and genipin to crosslink electrospun fibrinogen, the scaffold remains mechanically stable for up to 14 days **[25].**

SYNTHETIC POLYMERS:

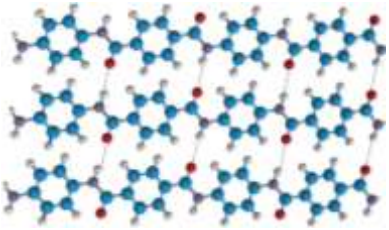

Fig 3: Synthetic Polymers

Many synthetic polymers have been used to create electrospun scaffolds. The primary advantages of synthetic polymers include their cost-effectiveness, exceptional mechanical integrity, and spinnability. Electrospun materials have been used for tissue engineering applications, including polyesters like poly (e-caprolactone) (PCL), polyethers, polyglycerol sebacate, polylactic acid, and polyglycolic acids like Polyethylene oxide (PEO), polyurethanes, and polyvinyl alcohol (PVA)-functionalized polyolefins **[26].** Poly(caprolactone) or PCL is a type of artificial substance that is biodegradable additionally is often utilised in various applications. Its unique viscoelastic and rheological characteristics make it an ideal material for submissions where mechanical strength is critical. **[26]** created PCL fibres measuring 1833 ± 369 nm on average in diameter. Electrospun nanofibers with natural degradation products and quicker rates of breakdown have been produced using **PLA, PGA,** and **PLGA** as copolymers.

Because PLA hydrolyzes to produce lactic acid, it is suitable for use in medicinal applications. Other benefits of PLA nanofibrous scaffolds include A substantial surface area, biomimicry of the original ECM structure, and appropriate mechanical characteristics **[27].** PGA is a thermoplastic polymer with good resorbability and great application provides a matrix of support for the restoration of brain tissue or the creation of systems for regulated drug release. It decomposes to produce glycolic acid more quickly compared to PLA **[28].** Additionally, the enormous specific surface area and porosity of nanofibrous PGA scaffolds can speed up the rate of deterioration by facilitating the diffusion of degradation products **[28].**

Because PEO is highly susceptible to dissolving upon hydration, crosslinking is required during electrospinning. Nevertheless, PEO is a polymer that is hydrophilic and can be employed for programmes that need mechanics like soft tissue **[29].** Thus, it is crucial to create synthetic polymers that resemble this kind of biocomplexity behaviour to increase the likelihood of using artificial supports in this field **[30].**

NANOFIBERS COMPOSITES MADE OF MANY MATERIALS:

The drawbacks of mono-component systems can be addressed by combining several types of polymers. Using this method, novel tissue engineering scaffolds with the best possible mechanical and biological properties can be created. High mechanical strength is typically provided by synthetic polymers, while natural polymers on the scaffolds' exterior or inside allow for the signals for cell recognition that are essential for cell activity and development **[31].** The physicochemical, biomechanical, and biocompatibility features of gelatin mixed with natural or synthetic polymers made it an appealing option for scaffolds **[31,32].** Moreover, Chitosan and PVA biopolymer blends have been created as scaffolds made of nanofibers using electrospinning on a free surface method, and they have demonstrated promise for a variety of tissue engineering uses**.[32]**

PREPARATION OF FUNCTIONAL NANOFIBERS:

Electrospun nanofiber scaffolds have many benefits but they often require additional surface and structural modification to enhance their chemical, biological, as well as mechanical characteristics. The material properties of a scaffold strongly influence its interaction with cells. For example, a material may not be suitable for cell development due to its bulk or surface characteristics, but it may be a good option for scaffold creation. Researchers have investigated co-electrospinning with conductive components or biological molecules as additions, treating surface features after electrospinning, and adjusting the size and configuration of electrospun fibers to improve their functionality.

CO-ELECTROSPINNING WITH ADDITIVES:

Co-electrospinning, which involves incorporating biological components into a basic polymeric substance, is a well-known technique for enhancing a polymer's particular biological capability. The mixture that is produced effectively enhances cell adhesion, proliferation, viability, and differentiation **[33].** For instance, PCL nanofibrous scaffolds with functionality achieved by adding carbohydrate biomolecules. They showed that, on day 24, the meniscal cells' in vitro DNA content had grown more by about 1.6 times in a scaffold made of galactose, and that their collagen and glycosaminoglycan secretion had improved. Carbon nanotubes (CNTs) and gold are examples of conductive and biocompatible additions that have been used to increase scaffold conductivity **[33,34].** Composite nanofiber scaffolds made of Polyhydroxy butyrate grafted with electrospun carboxyl multi-walled carbon nanotubes (CMWCNT-g-PHB) was created. The activity of human osteoblast cells MG-63 about the enzyme alkaline phosphatase (ALP) rose by 260% when the composite nanofiber scaffolds' CMWCNT content rose **[34],** additionally, after culturing for 24 hours. **[34,35]** revealed that utilising PVDF as a composite scaffold and incorporating gold nanoparticles (AuNPs) caused cells to become longer and more dispersed, possibly due to the prepared scaffolds' improved piezoelectricity due to the high conductivity mediated by AuNP.

Polymers that spin electrically can be Aimed to produce scaffolds with improved osteoconductive qualities and mechanical characteristics. This process involves incorporating bioactive inorganic nanoparticles into the polymers. The resulting scaffolds have physicochemical similarities in substance and structure to hydroxyapatite (HA) and calcium phosphate (CaP), which are organic nanocrystals found inside bone tissue. This technique has shown promise in creating scaffolds that mimic the properties of natural bone tissue**.[35]** Human mesenchymal stem cells (hMSCs) were driven to become osteoblasts in vitro and to promote the production of bone in vivo investigations due to the composite scaffold's increased osteoconductivity and elastic modulus **[36].** In a different in this investigation, butylene adipate-co-terephthalate (HA/poly) nanofibers were created. The inclusion of HA guaranteed the Changes in human adipose stem cell differentiation (hADSCs) and increased the elongation at break by 52%, the elastic modulus by 12.7%, and the stress at break by 25.7%. **[37].** they created scaffolds made of electrospun silk fibroin nanofibrous that were functionalized in both cases with HA the both external and internal regions, significantly enhancing the mechanical characteristics (The Young's modulus, nearly 5 kPa).

SURFACE MODIFICATION OF ELECTROSPUN NANOFIBERS:

Human mesenchymal stem cells (hMSCs) were driven to become osteoblasts in vitro and to promote the production of bone in vivo investigations due to the Tuning the surface qualities of synthetic polymers (hydrophilicity, wettability, and cell adhesion) is still challenging because of their relatively inert chemical makeup. Because it increases their compatibility with tissue engineering, altering the surface of the nanofiber following electrospinning is crucial **[38].** Bioactive chemicals and ligands that recognize Cells are used to both chemically and physically modify the characteristics of nanofibers' surfaces. Altering the electrospun nanofibers' surface made from artificial polymers has often been accomplished through plasma treatment **[38].** "Nanofibers electrospun" surface can be made useful by introducing carbon species with higher oxidation states that contain carbonyl, ether, and alcohol collectives. As a result of the ensuing functional groups' modifications to the surface's wettability, polarity, protein adsorption, and the activity of cells is improved because of the increased polar interactions that the polar functional groups cause **[39].** A coating called poly(dopamine) can be applied to the surface of electrospun fibers as a modification technique, which takes inspiration from mussels. Studies have found that dopamine is present in catechol and alkylamine units capable of self-polymerization in an alkaline environment to produce PDA. **[40]**

It is expected that PDA layers will form on polymeric materials such as PCL and PLLA due to Van der Waals interactions, π–π stacking, and hydrogen bonding. The PDA stratum can also enable covalent connections involving various functional groups, possibly through Michael's and Schiff's basic reaction addition with thiols and amine functional groups**. [41]** Consequently, PDA chemistry could readily alter the roughness, mechanical properties, hydrophilicity, and chemical functionality characteristics of the electrospun nanofibers' surfaces **[40,41].** A dopamine solution was applied to electrospun Composite nanofibers of PLA and cellulose nanofibril (CNF) in a different investigation. The PDA coating layer's surface deposition rate on the composite nanofiber was aided by the bonding of hydrogen that formed between PDA and CNF molecule chains. In addition to having higher mechanical qualities and hydrophilicity than the pristine PLA/CNF scaffold, the PDA-coated PLA/CNF scaffolds performed superior in hMSC growth and multiplication **[42].**

Anionic and cationic triple-helical collagen was coated on polyacrylonitrile and PLGA using the LBL technique. The collagen's original triple helix shape was preserved, which improved the adhesion and dissemination of lung fibroblasts in L929 mice **[42].** In an alternative investigation, Adsorbed laminin (LN),

poly (ethylene imine) (PEI), and chitosan were applied to the PLLA ultrafine fibre surfaces via LBL assembly. An advantageous charge was produced on PLLA electrospun ultrafine fibres' surface using amine etching, which was caused by an interaction between the ester group of PLLA and the amine assemblage of PEI. This was Subsequently, the alternating attachment of positively billed chitosan and negatively billed LN. Compared to unmodified PLLA nanofibers, the modified PLLA ultrafine fibers demonstrated increased dorsal root ganglia neuronal development and neurite outgrowth **[43].**

STRUCTURE MODIFICATION OF ELECTROSPUN NANOFIBERS:

Creating a well-defined structure is crucial for scaffolds to accurately replicate the native extracellular matrix (ECM) and effectively direct cell development or tissue regeneration. However, designing scaffolds designed to resemble the buildings of genuine Nanoscale human tissues is a significant challenge. Electrospinning has gained significant attention due to its ability to produce fibers that resemble the fibrous architecture of the native extracellular matrix. Nanofibers can also become electrospun in different designs to achieve optimal reconstruction, depending on the tissue's intended structure, once the biological and structural characteristics of the natural tissues are recognised. **[44]**

Injecting fibers onto a collector while travelling at a fast rate (over 1500 rpm). can orient them in one direction and create aligned electrospun nanofibers easily. For tissue engineering, it is important to have nanofibers that are organized because some tissues like heart tissue, blood arteries, and tendons have highly structured and anisotropic arrangements **[45].**

Electrospun nanofibrous scaffolds that are properly aligned are highly effective in guiding cell migration, controlling behaviour at different levels, and altering cell shape. This is because when cardiomyocytes are cultivated using electrospun PCL nanofibers that are oriented, the scaffold's cellular elongation and alignment lead to more mature growth. The collagen fibre arrangement at the point where tendons connect to bones can be replicated by a nanofibrous scaffold that has parts that are both aligned and random. The aligned part would be similar to the collagen strands present in a typical tendon, while the haphazard component would be similar to those present in bones. When tested on the parallel section of the nanofiber framework, tendon fibroblasts showed a well- morphology that is organised, as opposed to those on the random part had a disorganized anatomy **[45].**

ELECTROSPUN NANOFIBER APPLICATION IN TISSUE ENGINEERING

MEDICAL TEXTURE ENGINEERING:

Numerous techniques have been employed to create completely functional vascular tissue in vitro, which can interact at the nanoscale with cells to promote the creation of blood vessels**.[46]** For instance, keratin and PCL were electrospun to create nanofibrous mats that might be used as vascular tissue. Because keratin contains cell adhesion moieties like LDV (Leu-Asp-Val) and RGD (Arg-Gly-Asp), as well as the higher hydrophilous characteristics of the keratin/PCL matting, These resources were more advantageous for NIH 3T3 cell adhesion as opposed to virgin PCL. Furthermore, the nanofibers showed a decreased rate of hemolysis in red blood cells and a reduced period of activation of thromboplastin when contrasted to the plasma control group with low platelets **[47].**

THE ENGINEERING OF NEURAL TISSUE:

Both synthetic nerve grafts and autografting are two methods that have been used to treat peripheral nerve injuries. However, autografting has limitations due to the limited number of eligible donors, and synthetic nerve grafts are not very effective in reconstructing nerve deficits. An alternative approach to treating peripheral nerve damage is to use scaffolds made of electrospun nanofibers**.[48]** Electrospun nanofibers have been found to improve neurite outgrowth and can be utilized to create artificial nerve grafts based on nanofibers. These synthetic nerve transplants can provide biochemical and mechanical signals for stem cell differentiation**.[48]**

Electrical stimulation may be a useful stimulus to improve neurite and axonal expansion as well as nerve cell growth and differentiation. To create a substrate with the right electrical conductivity, biodegradable polymers, electrically conductive CNTs, or less cytotoxic polyaniline could be combined with them or given electrospun nanofiber scaffold treatment. **[49]**

BONE TISSUE ENGINEERING:

The recovery process of bones is intricate. and incorporates several osteogenic mechanisms. Therefore, it is necessary to create synthetic tissues using scaffolds, cells, and mechanical or soluble components for the engineering of bone tissue. Biomimetic scaffolds for the creation of bone tissue should possess the following characteristics: resistance to tissue mechanical stress regeneration, increased porosity to promote cell growth

and rebuilding, as well as the differentiation of the nanofibrous collagen in the extracellular matrix. Scaffolds for bone regeneration made of electrospun nanofibrous have been created Using biodegradable polymers, bioactive inorganic materials, and their composites. This has resulted in strand-like nanocomposites using ingredients and structures similar to the fundamental components of naturally Collagen nanofibers with mineralization **[50,51].**

Researchers were able to achieve bone regeneration in a lab setting using SF/PLCL nanofibrous scaffolds electrospun, which were grown using hADSCs. The 50/50 SF/PLCL scaffold exhibited an ideal tensile strength of 6 MPa. Moreover, SF was found to stimulate the osteogenic differentiation of hADSCs by increasing their ALP activity, which was measured at 150 absorbance index, compared to just 80 for pure PLCL **[52].**

CARTILAGE TISSUE ENGINEERING:

In articular cartilage tissue, which is made up of the presence of highly specialised chondrocytes with varying qualities in various places, the structure and function are complex, making treatment of cartilage defects a difficult task for orthopaedic surgeons**.[53]** The concentrations of collagen type II and proteoglycan, for instance, influence the spatial variation of cartilage extracellular matrix (ECM) proteins from the superficial to the deep areas. Hydrogel scaffolds, sponges made of collagen, and microspheres based on gelatin have all been used in numerous tissue engineering techniques to promote cartilage replacement. Additionally, due to their structure resembling the same as the extracellular matrix electrospun nanofibers in natural cartilage are derived derived from synthetic, natural, and hybrid polymers **[54].**

Electrospun nanofibers can enhance the biological characteristics of scaffolds, including chondrogenic differentiation and cell-matrix interaction. Additionally, they can increase the stiffness of the matrix**. [55]** found wherein PCL scaffolds electrospun with a large increased surface area chondrocyte development without the need for growth factors, while also enhancing the cell-matrix interaction.

THE CLINICAL VIEWPOINTS ABOUT ELECTROSPUN NANOFIBERS:

A type of electrospinning technique for creating nanoscale fibrous scaffolds that are well-known, easy to use, affordable, and adaptable. It has a lot of promise for producing multifunctional materials for tissue manipulation. However, its clinical use is still in its early stages. reached its potential within the marketplace. Despite notable technological advancements achieved by some businesses in this area, the FDA has not yet approved any of the items **[56,57].** At present, it is challenging to use an electrospinning setup to produce commercial items in large quantities continuously. However, if the issues with this process are resolved, the immense Electrospun nanofibers' promise in tissue technical can come to pass, leading to positive therapeutic outcomes **[58].**

FUTURE PERSPECTIVES:

In this study, we have examined the use of electrospinning technology for creating nanofibrous scaffolds. We focused on the techniques used for preparation, the types of materials used (including natural, synthetic, and composite polymers), and the changes in surface structure. The way the nanofibers are assembled can be significantly influenced by factors like voltage, flow rate, spinneret form, and the separation between the needle as well as the gatherer. The solution's characteristics, such as conductivity, solvent type, and polymer concentration, can also affect the shape of the nanofibers produced. The ideal nanofibers must have a porous structure with a sizable specific surface area and closely resemble the inherent characteristics within the in vivo native microenvironment.

The components used in creating the nanofibers are equally important to the electrospinning process. The primary drawbacks of scaffolds made of natural polymers are their poor structural integrity and low mechanical strength. Conversely, synthetic polymers have strong mechanical qualities, but because of their poor biological compatibility, they are not appropriate for cell attachment. As a result, numerous There have been attempts to create innovative composite materials that blend the benefits of the two categories above polymers. Extensive research has been conducted to enhance the biocompatibility of scaffolds by blending synthetic and organic polymers, incorporating non-living nanoparticles, and using conductive components.

Methods of surface modification like PDA coating, wet chemical treatments, and plasma therapy have all been utilized to improve the performance of scaffolds made of nanofiber. framework modifications made to the tiny fibres have a significant impact on the lengthening, multiplying, and changing of cells. Precise nanofiber Orientation is crucial for replicating the arrangement of biological tissues, including blood and tendons arteries, and trepidation.

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