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A BRIEF DESCRIPTION OF THE ELECTROSPINNING PROCESS UTILIZED TO CREATE DRUG-LOADED NANOFIBERS FOR PHARMACEUTICAL USES

Sanjivani S. Panditkar[1*], Prajakta U. Waghe[2], Wasudeo B. Gurnule[3]

[1*,2]Department of Chemistry, Yeshwantrao Chavan College of Engineering, Nagpur -441110, India.

[3]Department of Chemistry, Kamla Nehru Mahavidyalaya, Nagpur – 440024, India.

Corresponding Email: [1*]Panditkar.sanju@gmail.com

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ABSTRACT:

The electrospinning process can be employed to produce continuous fibers in the nanometer range from drug-polymer solution. Nanofibers so produced are gaining more attention as promising therapeutic carriers due to biocompatibility, bioavailability, biodegradability, and high loading capacity. Wide array of drugs and polymers had been used in preparing drug loaded nanofibers with high surface area, extreme porous structure, small pore size, surface morphologies that make them suitable for biomedical and bioengineering applications which can provide solution to current drug delivery issues of poorly water soluble drugs. The main theme of this paper is to throw light on the electrospinning technology for creating nanofibers embedded with drugs, types of electrospinning, the impact of various electrospinning process parameters, researcher's contributions, use of materials like polymers, pharmaceuticals and solvents, characterization tools, assessment of prepared nanofibers and drug delivery functions of electrospun nanofibers.

Keywords: Polymers, Drugs, Electrospinning, Drug Loaded Nanofibers, Drug delivery system.

1. INTRODUCTION

Drug delivery systems which allow drugs to enter the living body include liposomes, soluble polymers, microspheres, conjugated proteins, hydrogels, nanoparticles, and nanofibers. A nanofiber for drug delivery is the main focus of this paper. Different polymers can be utilized to create nanofibers, which have diameters in the nanometer range and have various physical and technical uses. A range of processes rely on them, including air filtration, lithium-air batteries, optical sensors, cancer diagnosis, drug administration, and tissue engineering. [1–6]. The popularity of nanofibers as potential therapeutic carriers is increasing due to their biocompatibility, bioavailability, biodegradability, and high loading capacity. The various methods had been used for its production were Self- assembly [7], template synthesis [8, 9], drawing [8, 9], phase separation [10, 11], electrospinning [10, 11] etc. Out of these methods electrospinning is a novel and sophisticated technique for the production of nanofibers with high surface area, extreme porous structure, small pore size and surface morphologies that make them suitable for biomedical and bioengineering applications, which can provide solutions to current drug delivery issues of poorly water-soluble drugs.
The main theme of this paper is the electrospinning technology for creating nanofibers embedded with drugs, types of electrospinning, the impact of various electrospinning process parameters, researcher's contributions, use of materials like polymers, pharmaceuticals and solvents, characterization tools, assessment of prepared nanofibers and drug delivery functions of electrospun nanofibers.

Electrospinning Process

The progress of changes in the Electrospinning has taken place since a long period of time. In the 16th century William Gilbert, reported the phenomenon of electrostatic interaction with liquids wherein they found out that if there is existence of a moderate amount of charge on a liquids droplet surface then it reshaped into a cone and then very finely drops started ejecting from the tip. They further revealed that the droplets converted into the mist when a suitable high electricity field is applied. Lord Rayleigh in 1885 concluded the required critical amount of charge for above droplet deformation. During the period of 1902 to 1960 many researchers in the field of electrospinning throw light on the process of electrospinning, some got patents. After period of 30 years, Reneker 1990 concluded an experiment to electrospinning using 20 different polymers enabling to fabricate fibers on the nanoscale giving a boost to develop inherent in the field of nanotechnology. In furtherance of above work Sun et al contributed much by performing and developing triaxial, new coaxial and near field electrospinning.
It would be interesting to go through the development of electrospinning. The development of electrospinning has gone through four stages:
1. Analysis of the spinnability of various polymers and the effects of spinning process parameters and environmental factors on fibre diameter and characteristics.
2. Research on the diversity of nanofiber components and diverse electrospun fibre architectures.
3. The third stage focused on the use of electrospun fibres in the sectors of medical, energy, optoelectronics and the environment.
4. The key focus of the fourth stage was the industrial manufacturing of electrospun fibres.
The electrospinning procedure requires the following four basic elements:

Syringe pump: which regulates polymer solution flow.
A voltage power source: It exerts pressure on the charged polymer solution to cause it to stretch into a fibre form.

Needle: This is necessary to move the solution into a strong electric field.
A collector: For collecting electrospun nanofibers, such as a metal screen, plate, or wheel, either stationary or rotating. One electrode is mounted on the polymer solution syringe needle and is wired to a metal collector. A liquid droplet becomes charged when exposed to a sufficient high voltage (1 to 30 kV).
When the applied electric field is high, the charged polymer forms a Taylor cone at the tip of the needle and a little jet is blasted from the droplet's surface. Nanofibers are created on the collector as a result of the solvent evaporating in the air when the polymer solution accelerates.

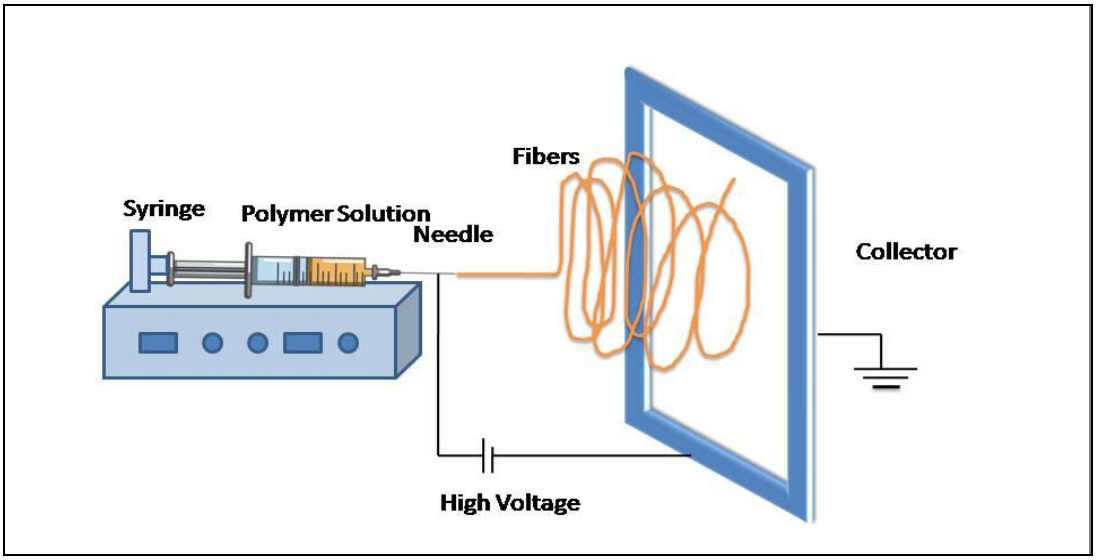

Fig.1. Electrospinning apparatus.

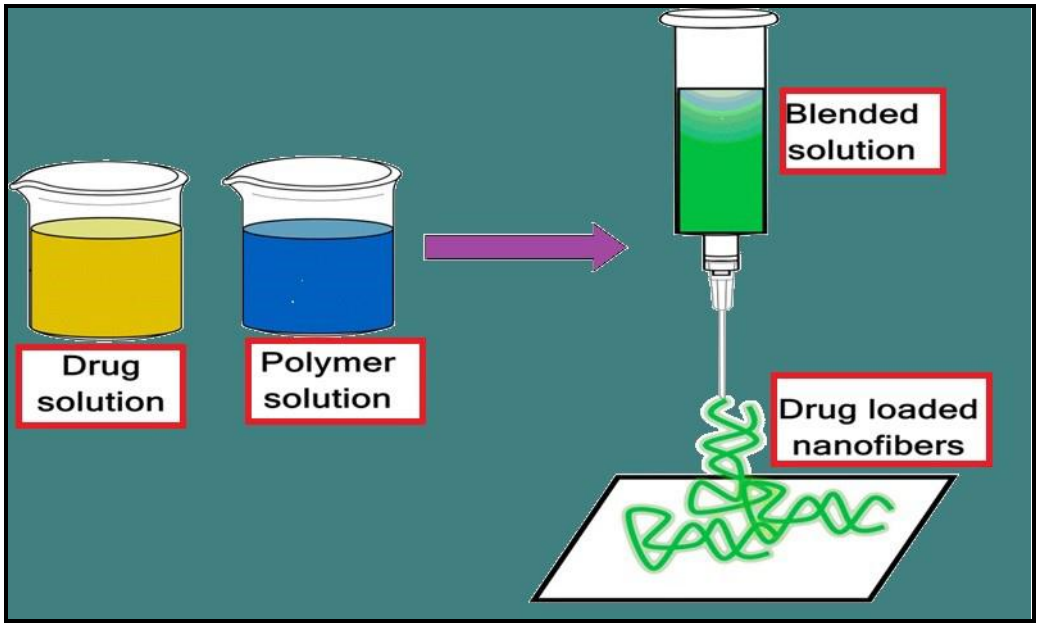

Fig.2. Schematic Representation of Electrospinning Process

Types of Electrospinning
Fabrication of nanofibers from the polymer solution can be carried out by two different types of electrospinning techniques mentioned below along with subtypes:

Table 1: Different Types of Electrospinning Techniques

Sr. No.	**Needle Based Electrospinning**	**Sr. No.**	**Needleless Electrospinning**
1.	Multi-axial Electrospinning	1.	Bubble Electrospinning
2.	Coaxial Electrospinning	2.	Two Layer Fluid Electrospinning
3.	Tri-axial Electrospinning	3.	Splashing Electrospinning
4.	Bi-component Electrospinning	4.	Melt Differential Electrospinning
5.	Multi-needle Electrospinning	5.	Gas Assisted Melt Differential Electrospinning
6.	Electro blowing /Gas-assisted/Gas JET Electrospinning	6.	Rotary Cone Electrospinning
7.	Magnetic Field Assisted Electrospinning	7.	Rotating Roller Electrospinning/ Nano Spider Technology
8.	Conjugate Electrospinning	8.	Edge Electrospinning
9.	Centrifugal Electrospinning	9.	Blown Bubble Electrospinning

Out of these several techniques only few from needle based Electrospinning are mentioned here which are mostly used methods.

Needle Based Electrospinning

The syringe pump is positioned across the syringe needle in the horizontal electrospinning configuration, parallel to the floor. When the resulting electrical field vector is perpendicular to the floor, the configuration is referred to as a vertical electrospinning setup, and when it is parallel to the floor, it is known as a horizontal electrospinning setup. The collector is positioned on the insulating floor in the vertical electrospinning configuration, and the syringe pump is positioned above the collector. Rotating drum and flat surface collectors are employed in both horizontal and vertical electrospinning installations. Generally, the main methods used for fabricating polymer drug delivery systems are- a) Blend electrospinning, b) Emulsion electrospinning, c) Co-axial electrospinning.

Blend Electrospinning

The foundation of blend electrospinning is the physical mixing of the medication and polymer solution before the electrospinning process. In order to encapsulate the medicine onto the polymer matrix for sustained release, the drug is finally softened or distributed in polymer resolution. Drugs often leave the polymer network either through erosion or diffusion. In situation of non-biodegradable polymers, the drug released by diffusion of polymeric layer, whereas biodegradable polymers decomposed and released the drug from the polymeric network. In this approach, the solvent enters the polymeric network, causing swelling and reorganisation of the polymeric chain to take place. The drug is entrapped mostly on the surface of the polymeric network. Either organised diffusion or organised erosion causes this kind of discharge.

Co-axial electrospinning

Co-axial electrospinning relies on the simultaneous spinning of medication solution and polymeric liquids that are delivered using two independent syringe pumps or two interconnected needles. Co-axial manufacturing techniques are widely known for creating drug-releasing nanofibers. A comprehensive method based on the coaxial positioning of two needles is utilised to produce core-shell nanofibers. The inner needle was used to pump the core material, which was typically a medication, and the outside needle was used to pump the shell material, which was typically polymers. When a powerful electric field is applied, combined electrospinning jet which additional extended to the formation core shell nanofibers.

Emulsion electrospinning

The emulsion electrospinning technique was created to address the drawbacks of both blend and co-axial electrospinning in terms of drug release. The use of an emulsification technique incorporates both approaches. In this method, two separate immiscible solvents that can be blended to create an emulsion was used to dissolve two immiscible polymer mixtures or polymers with drugs. With the help of this emulsion, core-shell structured nanofibers can be made utilising a single nozzle electrospinning method. The electrospinning system manages the electrospinning of stable emulsions of two or more phases that are not mixed together during the electrospinning process, nor the organization's core shell structure. These two phases are often stabilised by certain surfactants and are more likely to be immiscible [13]. In emulsion electrospinning, a polymer solution was combined with the medication that had been dissolved in oil to create a water-oil emulsion. After electrospinning, the active drug molecule either forms a core-shell shaped nanofiber mat or is spread within the nanofibers depending on whether a low molecular weight medication was utilized. When opposed to traditional mix electrospinning, the fundamental benefit of emulsion electrospinning is that the medicine and polymer are liquefied in proper solvents, reducing the requirement for a common solvent for both the drug and polymer. This technique allows for the loading of hydrophobic pharmaceuticals into hydrophilic polymers and vice versa.

Factors Affecting Electrospinning

Table 2. Various Factors Affecting Electrospinning Process

<table>
<tr><th>Solution properties</th><th>Process parameters</th><th>Environmental conditions</th></tr>
<tr><td>1. Dielectric Property of Solvent.</td><td>1. Flow rate</td><td>1. Relative Humidity</td></tr>
<tr><td>2. Surface Charge Density.</td><td>2. Applied voltage,</td><td>2. Temperature</td></tr>
<tr><td>3. Surface Tension</td><td rowspan="2">3. Geometry of the Collector.</td><td rowspan="5">3. Air pressure</td></tr>
<tr><td>4.Viscosity of Solution</td></tr>
<tr><td>5. Molecular Weight</td><td rowspan="2">4. Distance between the Tip of the Needle and Collector</td></tr>
<tr><td>6. Concentration</td></tr>
<tr><td>7. Volatility</td><td>5. Needle Diameter,</td></tr>
</table>

Consequence of dielectric property of solvent

Generally, the solution with the higher dielectric property reduces the propensity of the creation of beads and the diameter of the produced fibre during electrospinning. Tetrahydrofuran, Toluene, Acetone, Chloroform, Acetic acid, Ethyl Acetate, m-Cresol, Dichloromethane, Dimethyl formamide, Ethanol, Acetonitrile and other solvents might be used to enrich the dielectric property of the solution that will be electrospun. A rise in the solvent's dielectric constant produces a rise in the bending instability of the electrospinning jets, which increases the area where fibres are deposited. Additionally, the final fibre diameter is smaller as a result of the expanded jet path. When electrospinning a charged jet with a solvent that has a significantly higher dielectric constant, the charged jet is subjected to greater elongation forces because the solvent often has a larger net charge density.

Effect of surface charge density.

The electrospinning jet is influenced by surface charge density toward transmit additional charges, and the adding ions can affect the jet's development. The consequence of NaH_2PO_4, KH_2PO_4 and NaCl on poly (d,l-lactic acid) was studied by Zong et al. They discovered that the

fibres formed from dissolved NaCl solution had the shortest diameter and the highest diameter, respectively. The smaller atomic radius of sodium and chloride ions makes them more mobile under the applied voltage than potassium and phosphate ions. As a result, sodium ion-containing jets experience stronger elongation forces, which reduce fibre diameter. Researchers discovered that solutions with low surface charge density can form beads, while solutions with zero surface charge density cannot produce any fibres. Electrospinning jets from solutions with low surface charge densities have lower mobility and, as a result, experience less elongation force than is necessary, resulting in the formation of beads. Conversely, electrospinning jets from solutions with high surface charge densities lack the necessary dipole moment to form jets, and as a result, no fibers is formed.

Consequence of Surface tension

In the process of electrospinning, the investigation of the solution's surface tension is crucial. In order to start the electrospinning process, surface tension in the solution must be overcome. Beadles fibres can reportedly be created by lowering the solution's surface tension; conversely, raising the solution's surface tension results in the instability of the jets. In order to create a beadles fibre, at lower surface tension, where there is more contact among the solvent molecules and the polymer molecules, the solvent particles attempt to blowout above the entwined polymer molecules. On the other hand, when there is a lot of surface tension, the solvent molecules tend to group together into a sphere, which is where beads are supposed to develop. However, a solution's lower surface tension does not always favour electrospinning. When all other elements are held constant, the solution's surface tension often helps in identifying the upper and bottom borders of the electrospinning window. A low surface tension solvent or surfactant can be added to the solution to reduce surface tension.

Impact of viscosity of solution

One of the utmost significant parameters aimed at a fruitful electrospinning technique is the choice of the proper solution viscosity. This is because of the fact that low viscosity solutions cannot build continuous fibres, and at high solution viscosities, electrical charges were unable to produce the necessary strength to attenuate the solution and create fibres. The amount of polymer chains entangled in the solution increases along with viscosity, and before making smooth fibre, the beads' shape transforms from spherical to spindle-like. According to research, the ideal range for spinning viscosities is between 1 and 200 poises, while consistent nanofibers can be created at viscosity levels between 1 and 20.

Effect of molecular weight

The molecular weight of the polymer solution for electrospinning must be sufficient. However, in some unique situations, such as oligomer-sized phospholipids nonwoven from lecithin solution, electrospinning can occur if sufficient intermolecular connections can be given by chain entanglements. Additionally, other elements including surface charge density, viscosity, dielectric strength and surface tension are influenced by molecular weight. If the concentration of the solution does not change while electrospinning, decreasing the molecular weight of the polymer causes the development of more beads, increasing it causes the creation of smooth fibre, and extra swelling it causes the formation of micro-ribbon.

Effect of concentration

By extending the charged jets in uniaxial directions, fibre is created during electrospinning. of higher surface tension and little viscosity lead the charged jets to mislay their intermolecular attractions at low concentrations, which causes them to disperse in precipitations after the Taylor cone. The production of beads and fibres will mix as the concentration rises. While employing a suitable solution concentration and a not too high solution concentration, on the other hand, smooth fibre can be created, after a certain point micro ribbons in the shape of helixes will form.

Effect of processing parameters

Effect of voltage

Jet starts frequently need applied voltages more than 6 kV. At high voltage, more polymer solution may be ejected because of the heightened electrostatic interaction in the charged solution, there is a potential for greater stretching and the generation of stronger repulsive forces on the fluid jets, which leads to the development of fibre with a small diameter. The applied voltage also affects how fibre molecules are arranged. Electrostatic attenuation, which occurs at high voltage, causes the polymer molecules to become more organised, improving the fiber's crystallinity. However, because of the jets' decreased flight period after a certain generated voltage, crystallinity might be reduced.

Effect of flow rate

The drift velocity of the solution to be electrospun have a noteworthy impact on the diameter, porosity, and shape of the electrospun nanofiber. Researchers recommend a modest flow rate for creating beadles uniform fibres because the polymer solution needs time to polarise; yet, electrospinning requires a minimum flow rate. A higher flow rate increases the potential to generate beaded fibres, but it also correlates with an increase in pore size and diameter.

Consequences of diverse forms of collector

In the collector, charged jets quickly form whether a conducting material collector is present or not, which limits the amount of fibre deposited and results in the production of beaded fibres. According to Deitzel et al., 3D fibre structures arise in the case of non-conducting collectors as a result of the repelling pressures of charges. Repulsion between the succeeding fibres causes the construction of honey comb structures as long as there is a sufficient density of charges on the fibre mesh. As the fibres have more time to evaporate, a rotating collector aids in obtaining dry fibres. Getting aligned fibres also benefits from rotating collectors. By utilising revolving collectors, Boland et al. and Matthews et al. were effective in obtaining type I collagen and poly (glycolic acid) fibres that were aligned. The collector should revolve at a specific speed, known as alignment speed, as the charged jets move during electrospinning at a high rate of speed. More fibres are collected in the collector if the speed is less than that particular value, where the assembly of charges may reject the incoming fibre leading to less oriented fibres.

Effect of distance among collector and needle tip.

Generally speaking, changing the distance among the collector and needle tip can have an impact on the fiber’s size and shape. The influence, nevertheless, is not as strong as the other factors. The creation of defective fiber’s is caused by the needle's close proximity to the fibre collector. A few inter- and intra-layer linkages form at the joints of the fibres because the charged jet must travel a shorter distance, allowing beaded fibre to solidify more quickly. Conversely, if the separation between these two widens, the average fibre diameter can contract. There are some exceptions, though. For example, Lee et al. applied less electrostatic force across a larger area to produce PVA nano-fibers with a larger diameter.

Effect of electrospinning setup

The polymer droplet and Taylor cone's shapes are affected by gravitational force. A larger flow rate is needed with a horizontal configuration than a vertical one to produce beadles continuous fibres. Rodoplu and Mutlu demonstrated that 1.6 mL/h of feed rate is needed for a horizontal setup and 4 mL/h for a vertical setup in order to electrospin a 10 wt% PVA solution to produce beadless fibre.

Consequence of ambient parameters

Consequence of humidity

Changes in humidity when electrospinning have an impact on how the fibres are shaped. When the humidity level rises, electrospinning causes the surface of the fibre to grow tiny, rounded pores, according to study by Casper et al. These are produced by the solvent's

evaporative cooling as it travels from the needle tip to the collector during the electrospinning procedure. Additional humidity increases may result in the synthesis of fibre with asymmetrical structures. Megelski et al. claimed that at high humidity levels, polymer-based fibres made from volatile solvent-dissolved polymers may form condensed water on their surface. According to Li and Xia's notion, excessive humidity may make electrospinning more conducive to fibre discharge. According to Baumgarten, electrospinning stops when the solvent is extracted from the needle tip more slowly than it evaporates in low humidity conditions.

Marta Cavo et al. in their study, on the use of electrospun nanofibers in cancer research had been given a brief overview of the procedure involved, the majority of the materials used in it, and impact of altering the process parameters on the conformations and assemblies of the fibres. Electrospinning was used for creating three-dimensional fibrous materials for in vitro pre-clinical cancer models; and to create patches that contain anticancer medications for in vivo delivery [15].

Significant information about electrospinning technologies including detailed about the numerous environmentally friendly and sustainable composite nanofibers and membranes, as well as applications for these nanomaterials were covered by Hao Liu et al. There was also discussion of the variables affecting the characteristics and quality of these materials. They contended that issues with electrospinning technology still need to be resolved. Finding alternatives that are favorable to the environment is necessary due to the toxicity of the majority of the solvents utilized. To make electrospinning equipment more appropriate for extensive industrial uses, it must also be enhanced. They had been predicted that in the near future, with the help of numerous new electrospinning techniques, more unique, finer, and uniform nanofiber composites might be upgraded and optimized for usage outside of the engineering but they are also extensively applicable in a variety of sustainable disciplines. For instance, recent studies have indicated that electrospinning technology may offer creative solutions to foods' ephemeral bioactive components, improving food preservation throughout transportation. All of the recent advancements suggest that electrospinning technology will be crucial to the development of sustainable science and engineering [16].

Donepezil HCl loaded nanofibers were created by Zs. K. Nagy and colleagues using the electrostatic spinning method as a viable oral dosage form. For patients with dysphagia, the elderly, and other disorders, the new PVA-based nanofibrous orally dissolving web (ODW) formulation offers a potential technique for developing palatable and effective dose forms[17].

Jeffrey Thompson created nanofibers through the capability to load acetylsalicylic acid (ASA) as a model drug at a 10 weight percent concentration out of mixtures of polylactocaprone (PCL) and chitosan (CHI). With or without the addition of ASA, PCL/CHI fibres displayed smooth surface morphology at polymer compositions ranging from 100/0 to 40/60. Mechanical characteristics pointed to a brittle failure mechanism for drug-loaded fibres. A regulated release profile of ASA for up to 48 hours was seen in an in vitro drug release investigation. Research work was focused on the interactions between drugs and polymers and how these interactions affect the mechanical characteristics, fibre structure, and drug release profile. According to their findings, the drug's inclusion changed the fibres mechanical characteristics and revealed the capability to maintain the discharge of ASA from the fibres. Their research advances our understanding of how hydrophilic small molecule medications mechanical characteristics and controlled release are affected by interactions between pharmaceuticals and polymers[18]

Naveen Nagiah and colleagues utilised altered electrospinning techniques to produce novel, robust Tripolymeric scaffolds with a triaxial fiber structure. These scaffolds can deliver two separate medications, with a polycaprolactone core layer, a 50:50 poly outer layer and a gelatin inner layer. The sheath and intermediate layers of triaxial fibres concurrently released

the model small molecule rhodamine B and the model protein fluorescein isothiocyanate. Due to the fact that they lessened the shrinkage of the fibres generally seen in conventional electrospun systems, tripolymeric, and triaxial electrospun systems were shown to be the most effective at fostering mesenchymal stem cell growth. These tripolymeric triaxial electrospun fibres are intended for application in regenerative engineering and drug delivery. They are biomechanically sound and biocompatible and have two drug-releasing fibres. Loading the intermediate and sheath layers included models of large (BSA-FITC) and small molecules. The triaxially electrospun tripolymeric matrices, which have been mechanically enhanced, are required for use in regenerative engineering and drug delivery applications[19].

Hadi Samadian and colleagues aimed to develop and produce a Cellulose Acetate/Gelatin electrospun mat infused with berberine as a targeted dressing for diabetic foot ulcers. Electrospun nanofibrous dressings are ideal for wound dressing due to their small nanometer size, high surface area to volume ratio, adjustable porosity, and capacity to carry various medications and bioactive compounds. The electrospinning technique was used in the study at hand to produce a berberine-containing CA/Gel nanofibrous dressing, which was then characterised and used as a DFU dressing material. From the results they had shown that the produced CA/Gel/Beri dressing is an effective dressing for promoting DFU healing and preventing the invasion of dangerous bacteria at the wound site [20].

Genturki et al. investigated the effects of polyvinylpyrrolidone (PVP) and ethyl cellulose on the morphological features and drug release properties of PU nanofibers obtained through electrospinning. Electrospinning mixtures of PU with EC or PVP in various ratios, nanofibers were created. In order to examine the drug release characteristics of both PU/PVP and PU/EC electrospun nanofibers, donepezil hydrochloride (DNP) was selected as a model drug. The SEM images showed that EC or PVP did not influence the growth of nanofibers in PU solutions, and any nanofibers that formed had a smooth surface without small beads. According to the ATR-FTIR spectra, EC and PVP were individually added to the PU matrix. Data from in vitro releases showed that EC or PVP were present in PU. The Korsmeyer-Peppas drug release kinetic mechanism enabled PU/EC nanofibers (F4) to release drugs in a sustained manner, with the release rate being regulated by drug diffusion.

Arthanari Saravanakumar and colleagues developed composite nanofibers made of gatifloxacin-loaded polyvinyl alcohol (PVA) and sodium alginate (SA) for controlled drug release through the electrospinning process. Due to their controlled continuous release of the drug over 6 hours, as shown by the in vitro release profile, the drug-loaded PVA-SA composite nanofibers were determined to be a good choice for a drug delivery system [22].

Pattama Taepaiboon and colleagues have successfully engineered PVA nanofiber mats for the purpose of transdermal drug delivery. The four separate model medications, sodium salicylate, diclofenac sodium, naproxen and indomethacin,which are non-steroidal anti-inflammatory pharmaceuticals with differing water solubility properties were chosen. According to the findings, sodium salicylate and diclofenac sodium, were found to hasten the thermal decomposition of the PVA framework, whereas naproxen and indomethacin seemed to delay it [23].

Marziyeh Jannesari et al. successfully electrospun PVAc, PVA, and a combination of these polymers were formed into uniform, continuous nanofibers by adding Cip HCl. When utilising PVAc (50:50) blend nanofiber mats, the behaviour of drug release was significantly altered; in comparison to PVA nanofiber mats, it lowered the amount of drug released at early stages and delayed the drug release profile. However, due to a very noticeable increase in edoema compared to PVAc, mixing PVAc with PVA solution made mix nanofiber mats more flexible and comfortable for use as a wound dressing. The ability of the mix nanofiber mats to control medication release at both the initial and rate levels while also promoting edoema makes them suitable for the treatment of serious wounds [24].

Alvarez-Suarez et al. claim that because ulcers and skin burning are regarded to be hard to rebuild injuries because of the elevated hazard of infection, there is an increasing demand for the development of novel treatments for wound dressings. Because of this, they investigated the properties of PCL/PVP microfibers electrospun with sorbents containing Ag-Si/Al2O3-loaded Argovit silver nanoparticles as component parts for composite wound dressings. Based on the results, it was concluded that a wound dressing made of a PCL/PVP 85:15 scaffold and sorbent Ag-Si/Al2O3 would result in an efficient wound healing [25].

Spironolactone was used as a model drug in the work by E. Szabo et al., and they had prepared and examined polymer-based electrospun amorphous solid dispersions (ASDs). They mixed SPIR in a variety of concentrations with various polymers, including vinylpyrrolidone-vinyl acetate copolymer, polyvinyl pyrrolidone, and hydroxypropyl methyl cellulose. DSC, XRPD, and SEM techniques were used to evaluate the electrospun amorphous solid dispersions. It was found that all electrospun products were entirely amorphous, and the micro-sized fibres were helpful for enhancing dissolution. High-speed electrospinning was shown to be the most effective method for improving dissolution, while PVPVA64 with 40% drug loading was found to be the best composition (HSES). The research of HSES makes it possible to use ASD more effectively in practise following fibre preparation and makes it possible to produce electrospun fiber-based tablets continuously.[26]

The fabrication of biodegradable progesterone-incorporated nanofiber for estrus synchronisation was the main focus of Chitra Karuppannan et al. They had created three different concentrations of progesterone-impregnated nanofibers using electrospinning, and the results demonstrated that these fibres are an excellent means of progesterone delivery for the synchronisation of bovine estrus[27].

F. Mohammadian and A. Eatemadi proposed a variety of methods, like emulsion approaches, mixing, coaxial process, surface modification, and for incorporating biomolecules and drugs into electrospun nanofiber skeletons in their study work. Additionally, the application of nanofibers in drug delivery systems for cancer treatment, the administration of growth factors, the transportation of nucleic acids, and the transport of stem cells were reviewed, with the proper use of examples from transdermal systems and wound dressings.

Nicotinamide is encapsulated in an electrospun, water-soluble matrix that has been chemically crosslinked in order to control its release. A biocompatible nano-fibrous mat was made by electrospinning hydroxyethyl cellulose and poly vinyl alcohol together. Nicotinamide was successfully encapsulated using electrospun fibers after examining the parameters of the spinning solutions and process.

Hazim J. Haroosh et al. experimentally characterised electrospun poly (lactic acid): poly (□-caprolactone) drug carriers at five blends in varying ratios. Then, these electrospun fibres' morphological features, crystallinity levels, and thermal properties are evaluated. A popular antibiotic known as tetracycline hydrochloride was applied to prepared fibre mats at quantities of 1 and 5 weight percent. Better agreement between the experimental release data and the first order and Zeng drug release kinetics models showed that tetracycline hydrochloride release accelerated with rising TCH concentration [29].

Idris Cerkez and associates described electrospinning in preparing a fibrous membrane made of poly (e-caprolactone) that contained silver chloride particles which were characterized using TGA, DSC, SEM, and mechanical studies and concluded from their research that PCL fibrous membranes containing silver chloride showed enormous promise for a diversity of biomedical applications comprising as medical transplants, drug distribution, tissue skeletons, and wound plasters [36].

Nanohydoxyapatite (nHA) was integrated into an electrospun polycaprolactone (PCL) membrane by Mohd Izzat Hassan and Naznin Sultana. They also displayed good antibacterial

properties against bacterial growth by displaying inhibitory zones for E. coli and B. cereus after successfully loading a model drug, tetracycline hydrochloride, in the membrane [31].
Soroush Karimi et al. used chitosan for the electrospinning method to create a mucoadhesive non-woven fibre mat utilising pharmaceuticals (6% Wt), cysteine (4% Wt), polyethylene oxide (10% Wt), respectively, due to its non-toxicity, biocompatibility, and biodegradability. VAN and AMB were the medicines utilised for loading in mat. A comparison investigation was also done to see how medicines and mucoadhesive agents affected the production of nanofibers. By using the zone inhibition approach, they have looked into the antibacterial properties of CS/PEO nanofibrous layers both with and without VAN/AMB within the sight of gram-positive streptococcus. New mucoadhesive nanofiber mats based on chitosan were suggested for the RAS test in the study that was presented[32].
Erick Jose etal. synthesised PVA and PVP submicron fibre scaffolds by electrospinning, and they were then loaded with sildenafil citrate SC for quick drug dissolution and potential usage in the treatment of pulmonary arterial hypertension (PAH). In comparison to drug-loaded PVA fibres, the drug-loaded PVP fibres demonstrated improved quality in terms of size and uniformity. Various doses of the medication were electrospun onto PVA and PVP. The resulting loaded nanofibers have quick periods of dissolution, which are suitable for drug delivery through the mouth. This technique can help administer SC to paediatric patients who would otherwise require numerous doses of syrup formulations, which is cumbersome for both the patients and the caregivers [33].
Alven, S. et al. in their review article proposed that, silver nanoparticle-loaded nanofibrous scaffolds have excellent antibacterial, antioxidant, and anti-inflammatory capabilities as well as the ability to stimulate cell development, making them a vital bioactive component of wound dressings [34].

2. MATERIALS AND METHODS

Materials

1. Polymers used

The choice of polymer for producing nanofibers using the electrospinning method is crucial owing to interactions among drug, polymer, and solvent, which can impact the nanofiber formation, physicochemical properties, morphology, mechanical properties, drug release, and biocompatibility of the resulting nanofibers. This approach is suitable for producing nanofibers from a diverse range of polymer categories, including natural polymers like cellulose derivatives, chitosan, and alginate, as well as synthetic polymers such as polyvinyl pyrrolidone, polyvinyl alcohol, poly-L-lactic acid, poly-ε-caprolactone, and their blends. Hydrophobic polymers such as poly-ε-caprolactone and polyurethane are easily electrospun and demonstrate high mechanical strength and elasticity post-electrospinning. Nonetheless, the hydrophobic nature of electrospun nanofibers may not be conducive to cell attachment, necessitating additional modifications to enhance hydrophilicity. Natural polymers exhibit hydrophilicity, facilitating cell adhesion sites, while synthetic polymers offer superior mechanical properties and a slower degradation rate.

Table 3 :Different Types of Polymers Used for electrospinning.

Natural	Synthetic	Blended
Collagen	Poly(lactic acid) (PLA),	Chitosan/PLA
Cellulose	Polycaprolactone (PCL),	PLGA/Chitin
Silk fibroin	Polyurethane (PU),	Collagen/PLA
Gelatine	Poly(lactic-co-glycolic acid) (PLGA),	Glucan/PLGA

Chitosan	Poly(3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV),	PCL/collagen
Alginate	Poly(ethylene-co-vinyl acetate) (PEVA)	Glucan/PVA

2. Drugs Loaded into Electrospun Nanofibers

Many kinds of drugs, including anticancer agents, proteins, antibiotics, ribonucleic acid, and deoxyribonucleic acid, have been loaded on electrospun nanofibers, some of them are listed below:

Table 4: Drugs Loaded into Electrospun Nanofibers

Sr.No.	Category of drugs used	Examples
1.	**Anti-inflammatory Drugs**	Ibuprofen; Sumatriptan, Naproxen; Indomethacin; Meloxicam; Ketoprofen; Acetaminophen, Aceclofenac etc.
2.	**Antimicrobial Drugs**	Griseofulvin, Ciprofloxacin, Glycerol Monolaurate, Tetracycline, Amoxicillin, Tenofovir disoproxil fumarate, Acyclovir.
3.	**Anticancer Drugs**	Docetaxel, Cisplatin, Paclitaxel etc.
4.	**Cardiovascular Drugs**	Carvedilol, Nicorandil, Spirolactone etc.
5.	**Gastrointestinal Drugs**	Metoclopramide hydrochloride
6.	**Antihistamine Drugs**	Chlorpheniramine maleate, Diphenhydramine
7.	**Palliative Drugs**	Donepezil hydrochloride
8.	**Contraceptive Drugs**	Progestin levonorgestrel
9.	**Miscellaneous**	Caffeine; Riboflavin

3. Solvents Used in Nanofiber Production

Water is the most commonly used solvent due to its safety and biocompatibility. Organic solvents like Acetone, dichloromethane, methanol, ethanol, acetic acid, dimethylformamide, ethyl acetate , trifluoroethanol, tetrahydrofuran, formic acid can also be used in electrospinning. The major disadvantages of organic solvents are their toxicity, price, and often too high volatility. A combination of two or more solvents is often used.

Method: Fabrication of Electrospun nanofibers

The nanofibers were prepared with an electrospinning apparatus. Polymer solutions were prepared by dissolving the known amount of precursor in distilled water. Polymeric blends were prepared in various ratios, and the mixture was stirred to get a homogenous solution. Drug was dissolved in suitable solvent by heating to get a final concentration of 1 mg/ ml, and then cooled before use. Drug solution was added to the mixture of polymers with constant stirring to get an emulsion. The emulsion was then drawn into a syringe with a blunt-end needle and fixed in a syringe pump at a feeding rate 0.5 to 2.0 ml/h, fixed tip-to-collector distance of 15 to 20 cm and applied voltage of 15 to 30 kV. The electrospinning process was carried out to obtain a nanofiber mat that was deposited onto the collector plate covered with Aluminium foil. The nanofiber was removed from the collector plate and kept in a vacuum oven overnight at 40^{o} C.

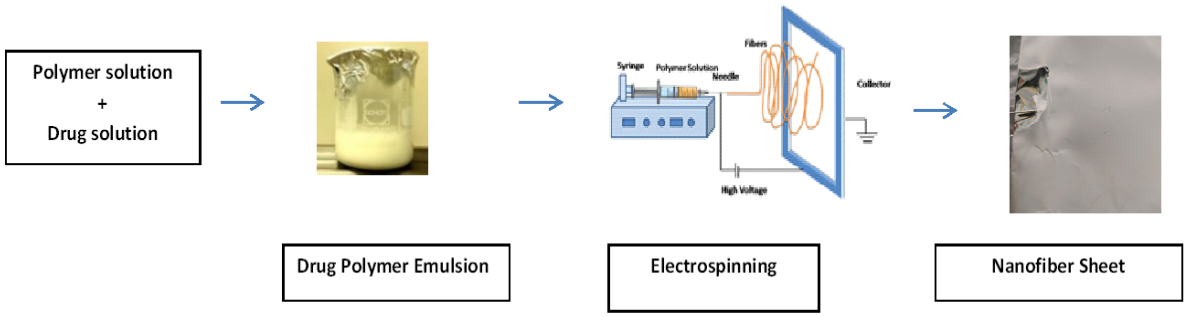

Fig.3. Production of Drug Loaded Polymeric Electrospun Nanofiber

3. RESULT AND DISCUSSION

Characterization of Drug Eluting Nanofibers

The prepared dug loaded nanofibers were characterized by using various techniques like elemental analysis, molecular weight determination, gel permeation chromatography, UV-visible, FTIR, XRD, and thermal (TGA) methods etc. to determined their structural makeup. The specific applications of each technique in this regards are mentioned in the following table.

Table 5. Various techniques used for Characterization of Drug Eluting Nanofibers

Sr. No.	Method	Specific Application
1	Scanning Electron Microscopy (SEM)	To examine the surface morphology of dug incorporated nanofibers.
2	Transmission Electron Microscope (TEM)	For investigating a sample specimen's interior structure.
3	Fourier transform infra-red spectroscopy (FTIR)	Used to identify the nature of chemical bonds in the molecules. Molecular interaction between the polymeric chain and entrapment of drug in polymeric matrix can be determined.
4	Differential Scanning Calorimetry (DSC)	Used to study the phase transition, glass transition, exothermic decomposition as a function of temperature.
5	Thermogravimetric analysis(TGA)	Used to measure the physical and chemical properties of nanofiber samples also to investigate thermal degradation.
6	Microscopic studies- Employing SEM, TEM, and BET analyzer techniques.	To examine the unique drug-eluting nanofibers under a microscope.

Assessment of drug loaded nanofibers

After successful preparation of drug eluted nanofibers it can be tested for various parameters including Antibacterial and Antifungal Activity of Nanofibers, Cytotoxicity Assessment, Contact Angle and Water Uptake Measurements, Degree of Crosslinking, Encapsulation

Efficiency, Friability, In vitro Release and kinetic Studies, Measurement of the Drug Solubility, Mechanical Testing, Mucoadhesive Properties, MTT Viability Assay, Powder Characterization and Tableting, Physical stability, Porosity, Statistical Analysis, Surface Roughness, Tablet Uniformity, Tensile Testing, Viscosity and Conductivity and may more.

Applications: Electrospun Nanofibers as Drug Delivery Carriers.

Delivering pharmaceutical substances in the most viable physiological manner holds paramount significance within the realm of medicine. The provision of a medication characterized by reduced dimensions and an appropriate coating material serves to augment its capacity for digestion or absorption at the designated site. The strategy of targeted drug administration through electrospun nanofibers is predicated on the premise that the rate of drug dissolution escalates in tandem with an expansion in both the surface area of the carrier and the drug itself. A multitude of publications have underscored the advantages associated with employing electrospun nanofibers as a conduit for drug delivery. Through meticulous control over the temporal aspects, velocity, and specific region of drug discharge, electrospun nanofibers laden with pharmaceutical compounds can be harnessed for the purpose of introducing biomolecules into the biological organism, thereby heightening both its effectiveness and safety. As compared to bulk materials, electrospun nanofibers have a higher specific surface area and shorter diffusion route length, making them better drug delivery devices. Also by modulating the shape, porosity, and content of nanofibers it is possible to control the drug release rate more precisely making them more suitable for drug delivery applications. Electrospun nanofibers are widely employed in the administration of a variety of pharmaceuticals, comprising anticancer, antibiotics treatments and other medications. Electrospun nanofibers encapsulate the therapeutic agent to preserve the bioactivity and integrity of the medication molecules during drug delivery.

4. CONCLUSION

Overall, research on drug-loaded electrospun nanofiber shows its usefulness for delivering pharmaceuticals at a controlled rate that can enhance the therapeutic qualities of the drug and make it safer, more reliable, and most effective. The medicine's efficacy and selectivity can be improved, its longevity can be extended, and its toxicity can be decreased by administering it at a regulated rate. Therefore, it can be suggested to build a drug delivery system in which electrospun nanofibers can be created by combining a medication with polymer solutions, followed by electrospinning, in a straightforward and affordable manner. In order to make considerable progress, more work can be put into creating drug-loaded nanofibers with distinct physiochemical and biological features.

5. REFERENCES

1. Vasita R, Katti D.S. Int. J. Nanomedicine, (I), 15–30, (2006).
2. Ahn SY, Mun CH, Lee SH RSC Adv. 5, 15172- 15181, (2015).
3. Garg T, Rath G, Goyal AK J. Drug Targeting, 23, 202–21, (2015).
4. Yang X, He P, Xia Y Electrochem Commun. 11, 1127–1130, (2009).
5. Zhang B, Kang F, Tarascon J.M, Kim J. K . Prog Mater Sci. 76, 319–380, (2016).
6. Scholten E, Bromberg L, Rutledge GC, Hatton TA. ACS Applied Mater & Interfaces. 3, 3902–9, (2011).
7. Naik S, Chiang AST, Thompson RW, Huang FC. Chem Mater. 15, 787–792, (2003).
8. Guarino V, Cirillo V, Altobelli R, Ambrosio L. Exp. Rev Med Devices. 12, 113–129, (2014).
9. Zhong S, Zhang Y, Lim CT. Tissue Eng Part B Rev. 18, 77–87 (2011).

10. Ma Z, He W, Yong T, Ramakrishna S. Tissue Eng. 11, 1149–1158, (2005).
11. Widmer M.S, Gupta P.K, Lu L, Meszlenyi RK, Evans GR, Brandt K, et al. Biomaterials 19, 1945–1955, (1998).
12. N. Sasithorn, L. Martinová, J. Nanomater.,2014, 1–9, (2014).
13. F. Yener, O. Jirsak, J. Nanomater., 2012, 1–6, (2012).
14. Esenturk I., Erdal S. M. and Gungor S., J. Fac. Pharm. Istan. 46, 49-69, (2016).
15. Marta Cavo and et al Biomater. Sci., 2020, 8, 4887–4905
16. Hao Liu and et al Int. J. Mol. Sci. 2020, 21, 4019; doi:10.3390/ijms21114019. http://www.mdpi.com/journal/ijms
17. Nagy Zs. K. , Nyúl K., Wagner I., Molnár K. and Marosi Gy., eXPRESS Polymer Letters Vol.4,No.12 (2010),763–772
18. Thompson J., Gizaw M. and Chou S. F., Proc. ASEE Gulf-SW Sec. An. Conf. Uni. Texas Austin April 4-6, (2018).
19. Nagiah N., Christopher J. Murdock , Bhattacharjee M., Nair L. & Laurencin C. T., Scientific Reports (2020) 10:609
20. Hadi Samadian and et al Scientific Reports (2020) 10:8312 | https://doi.org/10.1038/s41598- 020-65268-7
21. Genturck A., Kahraman E, Gungor S., ozsoy Y., A. Sarac S., Turk J Pharm Sci 2020;17(6):638-644
22. Arthanari S. and et al Biotechnology, 44:3, 847-852, DOI: 10.3109/21691401.2014.986676
23. Taepaiboon P., Rungsardthong U. and Supaphol P., Nanotechnology 17 (2006) 2317-2329.
24. Jannesari M., Varshosaz J. and Zamani M. M. M., International Journal of Nanomedicine 2011:6
25. Álvarez-Suárez A.S.,Dastager, S. G., and Bogdanchikova N., Micromachines 2020, 11, 441;
26. Szabo E., and et al Nagy, eXPRESS Poly. Lett.12, No.5 (2018) 436–45.
27. Karuppannan C., Sivaraj M., Kumar J. G., Seerangan R., Balasubramanian S. and Gopal D. R. Nano. Res. Let. 112-116, (2017).
28. Mohammadiana F. and Eatemadib A. Arti. Cells nano.biotech, 45, 881–888, (2017).
29. Haroosh H. J., Dong Y., Lau K. T., J. Mater. Sci. 49, 6270-6281,(2014).
30. CerkezI I., Sezer A., and Bhullar S. K., R. Soc. Open sci. 4:16091, (2017).
31. Hassan M. I. and Sultana N., Springer 3 Biotech, 7:249, (2017).
32. Karimi S., Moradipour P., Azandaryani A. H. and Arkan E., Braz. J. Pharm. Sci. 55 (2019) 17115.
33. José E. Martínez T. and Lizeth G. J Pharm PharmSci (www.cspsCanada.org) 22, 313 - 331, 2019.
34. Alven, S.; Buyana, B., Feketshane, Z., and Aderibigbe, B.A. Mate. Pharma.13 (2021) 964.