Manufacturing Sustainable PEO Fibres for Healthcare Applications

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ABSTRACT

The field of polymeric fibre production focuses heavily on morphology and application, overshadowing the sustainability aspects. The principles of green chemistry and sustainable manufacturing are incorporated to develop a sustainable framework for the manufacturing of polyethylene oxide (PEO) fibres through electrodynamic (EHD) technology. This study undertakes a methodical analysis of electrospinning PEO in different solvents, namely water, ethanol, acetone, acetic acid and glycerol, to study EHD phenomena. Solution properties and process parameters, centred around viscosity, solution concentration, flow rate and applied voltage are investigated. External variables, such as temperature and humidity were also explored to identify an optimal method of manufacturing fine PEO fibres. The obtained results, with fibre diameters ranging between 0.1 μm to 2 μm, are evaluated with literature reviews to discuss the potential medical applications for the polymeric fibres.

Keywords: Sustainable, Green Chemistry, Polyethylene oxide, Electrohydrodynamic, Healthcare

1. INTRODUCTION

Throughout the last decade, polymeric fibres gained popularity in the field of medical sciences due to their favourable properties of flexible manufacturing and enhanced miscibility of chemicals when absorbed in the body.

1.1 Green Chemistry

Figure 1: Principles of green chemistry [2]

Anastas et al. [1] defined the 12 principles of green chemistry, listed in figure 1. They act as a guideline for professionals to utilise sustainable methods of synthesis, which can be categorised into different areas of focus. This includes pollution and waste prevention (principles 1, 2, 8, 10 and 11), environmental protection (principles 4, 5 and 7), efficiency improvement (principles 6 and 9) and accident prevention (principles 3 and 12).

1.2 Sustainable Manufacturing Framework

Yusup et al. [3] developed 5 mediation aspects to improve sustainable performance, which involves design, process, quality, safety and competency. Saad et al. [4] listed quantitative and qualitative measures as criteria for sustainability assessment, considering economic development, social development and environmental protection aspects. Eslami et al. [5] conducted a survey and concluded that energy efficiency, emissions and waste management hold the greatest meaning of sustainability. Waltersmann et al. [6] developed a benchmark for industry sectors, identifying 146 indicators from established approaches and categorised into classifications of material, energy and emissions. Scharmer et al. [7] developed sustainability measures based on energy consumption, resource efficiency and waste production.

The objective of this research examines how green chemistry and sustainable practices can be further incorporated into electrohydrodynamic technology to manufacture uniform and fine PEO fibres for healthcare applications. In the light of the evaluated publications on green chemistry and sustainability, a holistic approach of sustainable criteria is developed, which includes pollution and waste reduction, energy efficiency and environmental protection.

2. LITERATURE REVIEW

2.1 Electrohydrodynamic

Existing polymer manufacturing techniques include drop-casting [8], inkjet printing [9], pressurised gyration [10], electrochemical polymerisation [11] and electrospinning [12], etc.
Electrohydrodynamic (EHD) in electrospinning is a phenomenon that produces high resolution polymer fibres through electric fields. This technology exhibits favourable properties, which is incorporated in diverse fields, such as food packaging [13], energy storage, catalysis [14] and, most notably, in biomedical applications. [15] EHD technique overshines other processes as it holds the ability to print fibres thinner than nozzle dimensions, made possible by jet diameter constriction during the formation of Taylor cones. As fibre diameter is independent of the nozzle diameter, the EHD jet nozzle is larger compared to other manufacturing processes. Thus, blockages are less likely to occur and liquids of higher range of viscosity can be employed. [16] Furthermore, its low manufacturing costs, greater flexibility and simplicity are reasons why this technique is heavily imposed in producing nanoparticles [17], ceramic materials [18], organic functional materials [19] and polymer fibres.

2.1.1 Electrohydrodynamic Set-up

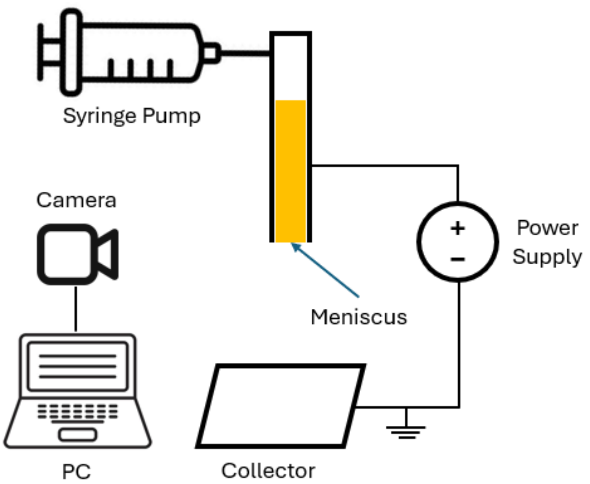

Figure 2: Conventional Set-up for EHD

Figure 2 illustrates the conventional set-up for single needle EHD printing. It composes of a high-voltage electrical supply, a syringe, a conducting needle connected to the syringe, a pump and an aluminium foil collector that is grounded.
The printing is predominantly completed at ambient temperatures, where the syringe emits the polymer solution through the needle onto the grounded collector at a given applied voltage.

2.1.2 Taylor Cone Formation

The solution in the nozzle is first adjusted to show a flat meniscus at the tip of the needle. When an applied voltage runs through the nozzle and grounded wire, a hemispherical droplet is created on the meniscus as shown in figure 3A. Raising the applied voltage, enlarges the electrostatic repulsion. Once the force from the repulsion of charges exceeds the surface tension of the pendant droplet, the hemispherical meniscus contorts into a cone-like shape known as the Taylor cone in figure 3B. The polymer solution is then ejected from the needle as a fine charged jet stream in the direction of the electric field. [20] The conical jet was first discovered by Sir Geoffrey Ingram Taylor in 1964, [21] and its formation is only possible under the absence of gas discharge. [22]

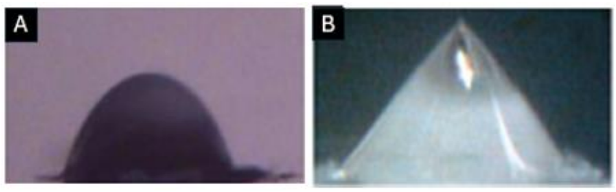

Figure 3: (A) Hemispherical Meniscus [23], (B) Conical Meniscus [24]

2.1.3 Cone-jet Transition

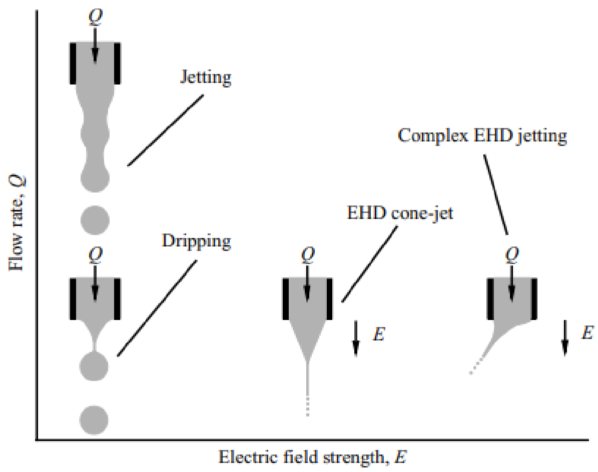

Figure 4: Effect of flow rate and electric field strength on polymer flow [25]

Figure 4 shows how flow transitions when the flow rate and/or the electric field strength is adjusted. At a low or non-existent applied voltage, the liquid drops out from the nozzle in the form of droplets as the gravitational force is greater than the surface tension. The Taylor cone forms once critical potential difference is reached. Once the applied voltage exceeds the optimal value, the cone starts to become unstable and a thin jet is discharged from the conical apex. [21] Complex jetting phenomenon occurs at even higher electric field strength, where the fluid flows at a tilted angle, hence they do not give precise deposition.

Under the cone-jet mode, a fine jet is created at the tip of the Taylor cone. The further increase of charge leads to instability in which its trajectory becomes unpredictable. Subsequently, if the applied voltage is too low, fluid exits as droplets due to varicose instability.

2.2 Sustainable Polymer Solute

Electrospinning creates fibres from different polymers, often used as a solution or melt. In the past, large quantities of plastics have accumulated in aquatic and terrestrial ecosystem, due to their high resistance to degradation in nature. [26, 27] Therefore, nowadays, polymers with biodegradable properties are favoured in the fields of biomedicine and engineering.

Polyethylene oxide (PEO), polycaprolactone (PCL), polylactic acid (PLA) and polyvinylpyrrolidone (PVP) are all synthetic polymers commonly used in electrospinning, each having its unique advantages. PLA is often used in the bioplastic market as it has great processibility, industrial composability and is relatively cheap, yet the material shows brittle properties, which may not be best suited in certain medical applications. [28] The manufacturing of PLA is done through converting corn into resin. Although the green biopolymer is easily recyclable, the fertilisers bring adverse effects to the environment. [29]

PEO is widely used in medical fields due to its biocompatibility, hydrophilicity, low toxicity, high viscosity and tendency to form hydrogen bonds (H-bonds) with oxygen of ether. PEO is used EHD technology due to its unique set of properties. Firstly, solvents with hydroxyl groups or groups containing lone pair of electrons can readily form H-bonds with the oxygen in PEO. [30] For this reason, PEO is highly soluble in water and most organic solvents compared to other common polymers, such as PCL and PVP. [31, 32] This property is beneficial when used in aqueous environments in the human body, especially in drug delivery and tissue engineering applications. Secondly, the high viscosity of PEO gives it resistance to deformation, keeping its shape during injection and facilitates the formation of uniform patterns. [33] Furthermore, PEO is biodegradable [34] and is approved by the Food and Drug Administration as a safe material in drug delivery systems. [35] Its biodegradable nature allows the polymer to be decomposed into smaller innocuous products by living microorganisms, which avoids pollution and reduces waste products.

Additionally, PEO has great ionic mobility due to its electrolytic properties. It can readily dissolve ionic salts, [36] allowing easy migration of cations and anions. [37] Once dissolved in a solvent, the dipole moment in PEO solution modulates the flow of ions allowing the a smooth Taylor cone formation when a voltage is applied.

PEO is also widely used as a complementary solute along with other natural or synthetic polymers during electrospinning due to its easy spinnability. [38] Polymeric materials, such as poly (N-isopropylacrylamide) [39], chitosan [40], keratin [41] and pectin [42], are unable to be electrospun in their pure form. Therefore, PEO is often added in the solution during production of fibres.

The morphology and the sustainability and biocompatibility factors of PEO gives it a competitive edge over other polymers; hence it is chosen as the solvent for this research.

2.3 Sustainable Polymer Solvent

The solvent for PEO must have suitable boiling points, volatility and viscosity, whilst meeting the requirements as a green solvent. Avossa et al. [43] defined a green solvent as a solvent that minimises the environmental impact of chemical production until the safe disposal of solvents. Capello et al. [44] developed environmental, health and safety indicators as criteria for sustainability, which corresponds to the ideology of green chemistry. Common solvents for electrospinning are listed under solvent name in figure 5.

GSK’s solvent selection guide is an award-winning Eco-Design toolkit, offering clear guidance and ranking on sustainability for solvent selection [45], as shown in figure 5. While benzene and chloroform are strong solvents, they are labelled red due to its toxic nature. Benzene is radiomimetic and long exposures can lead to aplastic anaemia, leukaemia and multiple myeloma. [46] Similarly, chloroform is a toxic reagent, which can cause nervous system renal and hepatic failures, anaesthesia and arrhythmia. [47] Chloroform poisoning can also occur after ingestion causing abdominal pain, nausea and vomiting. [48] While methanol is listed as yellow under composite colour, long exposures can lead to severe metabolic acidosis, visual disturbance and neurological deficit. [49] In the light of the toxic nature of benzene, chloroform and methanol, the accident prevention criteria of green chemistry is not satisfied, hence both solvents will not be chosen.

On the other hand, water, acetic acid, ethanol, glycerol and acetone show promising characteristics in terms of environmental impacts, health and safety. Therefore, these five solvents are selected based on the environmental protection and the accident prevention criteria satisfied in green chemistry.

Classification	Solvent Name	Composite Colour	Boiling Point (°C)	Incineration	Recycling	Biotreatment	VOC Emission	Aquatic Impact	Air Impact	Health Hazard	Exposure Potential	Flammability & Explosion	Reactivity and Stability	Life Cycle Analysis
Water and Acid	Water		100	4	2	4	6	10	8	10	9	8	10	10
	Acetic Acid		118	3	5	4	7	8	4	7	5	8	6	8
Alcohol	Ethanol		78	5	5	3	4	9	5	10	8	6	10	9
	Methanol		65	4	7	3	3	10	7	4	6	5	10	9
Esters	Glycerol		187	5	6	6	10	6	8	10	8	10	10	-
Ketones	Acetone		56	5	6	2	2	10	6	10	6	4	9	7
Aromatics	Benzene		80	9	6	6	4	7	5	1	1	3	10	7
Chlorinated	Chloroform		61	3	9	5	1	7	5	4	1	5	10	6

Composite Colour Key
- Few Known Issues
- Some Known Issues
- Major Known Issues

Column Heading Colour Key
- Waste
- Environment
- Human Health
- Safety

Figure 5: GSK's Solvent Selection Guide [45]

2.4 Medical Applications of Electrospun Materials

The World Health Organisation reported a million deaths from organ failure in the United States alone, whilst the Global Observatory of Donation and Transplantation approximated over 126 thousand annual organ transplants. [50] The scarcity in organ donation led to patients having to opt for alternative treatment options, such as surgical repair or chemotherapy, but they are unable to fully recuperate the morphology and practicality of defected organs or tissues. Over recent years, electrospun polymers used in tissue engineering and drug delivery have emerged as solutions to mitigate transplant rejection and disease transmission. This intricate field of engineering designs tissue composite systems to imitate the shape and design of the target tissue, improving the efficacy of body organs. [51] Tissue engineering implements cells and the regulatory factors into scaffolds, which gives structural integrity to the development of cells. [52, 53] The scaffolds are mainly developed from natural and synthetic polymers. [54] Although natural polymers show better hydrophilicity and bioactivity, [55] they show inefficient mechanical properties. [56] Synthetic polymers, on the other hand, show strong mechanical strength and promising fibre reproducibility. [56]

3. EXPERIMENT

3.1 Materials

Polyethylene oxide (PEO, Mv ~ 200,000, CAS: 25322-68-3), deionised water (Mw ~ 18.02, CAS: 7732-18-5), acetic acid (Mw ~ 60.05, CAS: 64-19-7) and glycerol (Mw ~ 92.09, CAS: 56-81-5) were purchased from Sigma-Aldrich (UK) and used as received. Ethanol absolute (Mw ~ 46.07, density ρ=0.79kg/L, CAS: 64-17-5) and acetone (Mw ~ 58.08, CAS: 67-64-1) was purchased from VWR Chemicals (UK) and LP Chemicals Limited (UK) respectively.

3.2 Solution Preparation and Characterisation

PEO samples are weighted and dissolved in the following solvents separately.

Table 1: *Solution Preparation*

Solvent(s)	PEO weight to volume ratio
Deionised water	10% w/v
Acetic acid	10% w/v
Glycerol	10% w/v

Acetone	10% w/v
Ethanol	10% w/v
Deionised water/Ethanol (1:1)	10% w/v
Deionised water/Ethanol (3:1)	10% w/v
Acetone/Ethanol (1:1)	10% w/v
Acetone/Deionised water (2:1)	8% w/v
Acetone/Deionised water (2:1)	10% w/v
Acetone/Deionised water (2:1)	12% w/v
Acetone/Deionised water (2:1)	16% w/v

The dissolution of PEO was done at (20±0.1)ºC with a vortex shaker and a laboratory magnetic stirrer for 24 hours, ensuring homogenous solutions were acquired for EHD electrospinning. The prepared solutions were stored in a seal container to prevent solvent evaporation and the potential of contamination.

3.3 Fibre Production

The EHD device shown in figure 2 was set up. The process parameters of flow rate and applied voltage were adjusted during the experiment and was kept constant once the Taylor cone is formed.
After inserting the solution into the syringe and attaching the syringe pump, the flow rate was set at 5 µm/min and is amended at increments of 1 µm/min until the solution can exit the needle nozzle as droplets. The voltage was set at 15 kV initially, which was gradually increased at 0.5 kV increments until the Taylor cone was formed.
The samples were electrospun with a needle to collector distance of (10±0.1) cm, and under ambient temperature and humidity of (20±0.1)ºC and (40±0.1)% respectively. Both environmental parameters were measured with a room thermometer and a humidity incubator meter. The power supply was kept on, and each sample was collected for 10 minutes. After adequate during of the fibres, they were carefully stored in petri dishes.

3.4 Data Processing

The scanning electron microscope (SEM) produces high-resolution fibre images. The dried samples were trimmed from the aluminium foil and attached on SEM specimen stubs with double-sided tape, which were then inserted into the SEM.
The measurements were conducted on a SEM (Jeol JSM-6480LV high-performance, variable pressure analytical SEM) equipped with an energy dispersive system (EDS) and an electron backscatter diffraction (EBSD) using the Oxford Link system. The SEM can operate under the low vacuum mode or high vacuum mode. The low vacuum mode is suitable for specimens with excessive water and non-conductive samples. Therefore, the high vacuum mode is chosen due to the absence of moisture and the utilisation of an aluminium conductor.
A sample of 100 diameters are measured for each fibre image using the scale bar calibration in ImageJ and the distribution of data is plotted in OriginPro as histograms.

4. RESULTS AND DISCUSSION

4.1 Polyethylene Oxide Solubility

All samples achieved homogeneity after 24 hours, except for the solutions with PEO/acetone and PEO/ethanol, where a proportion of PEO was suspended on the bottom of the test tube.

4.2 Amendments to Process Parameters

Figure 6 shows the critical flow rate and applied voltage of each solution. PEO/glycerol has the highest critical flow rate, whilst PEO/water has the highest critical applied voltage. Thus, 15 µm/min and 18 kV were applied for the entirety of the experiment.

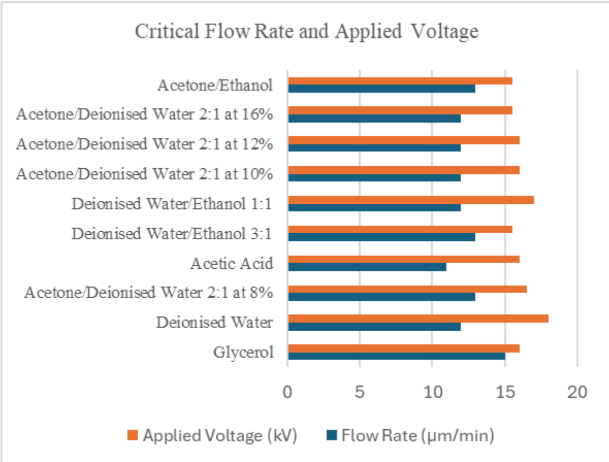

Figure 6: Critical process parameters of samples

4.3 Fibre Diameters

Table 2: *Fibre Diameters*

Solvent	Mean (µm)	Standard Deviation (µm)
Glycerol	0.21750	0.045962
Deionised Water	0.39235	0.029698
Acetone/Deionised Water 2:1 at 8% w/v	0.38899	0.055720
Acetic Acid	0.39600	0.110309
Deionised Water/Ethanol 3:1	0.40500	0.060811
Deionised Water/Ethanol 1:1	0.43066	0.097857
Acetone/Deionised Water 2:1 at 10% w/v	0.47500	0.031113

Acetone/Deionised Water 2:1 at 12% w/v	0.53750	0.152931
Acetone/Deionised Water 2:1 at 16% w/v	0.64376	0.150243
Acetone/Ethanol	0.81275	0.217126

4.4 Effect of Viscosity and Surface Tension on Fibre Morphology

Table 3: *Viscosity and surface tension of solvents*

Solvent	Viscosity (cP)	Surface Tension (mN/m)
Acetone	0.32	23.7
Deionised water	0.8949	71.97
Acetic Acid	1.056	27.10
Ethanol	1.074	21.97
Glycerol	934	63.4

Table 3 shows the viscosities and surface tension of all five solvents at 25°C according to PubChem. In general, a lower solvent viscosity generates thicker and smoother fibres, except for deionised water, where its high surface tension causes the formation of beads.

Thicker fibres are predominantly formed when a solvent of a higher molecular weight is used, except for glycerol. Its fibres are extremely sparse as shown in figure 7. The high viscosity of glycerol created frequent blockage to the needle during electrospinning, which in addition to a high boiling point, resulted in poor generation of fibres.

4.5 Effect of Solution Concentration on Fibre Morphology

The solution concentration is a significant factor of electrospinning. An inadequate PEO quantity weakens the fibrous structure, whilst a surplus of PEO quantity clogs the needle nozzle. An increase in solution concentration increases beading, fibre diameter and the separation between fibres. In figure 8, when the PEO concentration increases from 8% w/v to 16% w/v, there is a gradual shift from thin and fine defect-free fibres to thicker non-uniform fibres.

4.6 Effect of Solvent on Fibre Morphology

By changing the solvent of the PEO solution, fibres with a variation of diameters and shapes were generated.

In figure 9, acetone/ethanol and water/acetone, both 1:1, are used as solvents at 10% w/v. The lower boiling point of the acetone-ethanol mixture increases the diameter as the evaporation of the solvent is sped up during the spinning process. Water and acetic acid have two of the highest boiling points amongst the solvents test, showing large amounts of beading in fibres.

Fong et al. [57] examined the change in fibre structure with different solvent mixtures. PEO with distilled water, PEO with distilled water and NaCl, and PEO with distilled water and ethanol were prepared. The fibres utilising a water/ethanol mixture showed smoother fibres with larger diameters than with only distilled water. This is influenced by several factors, such as the viscoelasticity of the solution, charge density of the jet and the surface tension of the solution. Similarly, Song et al. [58] investigated the effects of different ratios of water and ethanol compositions on the electrospinning of PEO. The results showed that a higher ethanol content, increased the diameter, whereas the molecular chain orientation and crystallinity degree decreased.

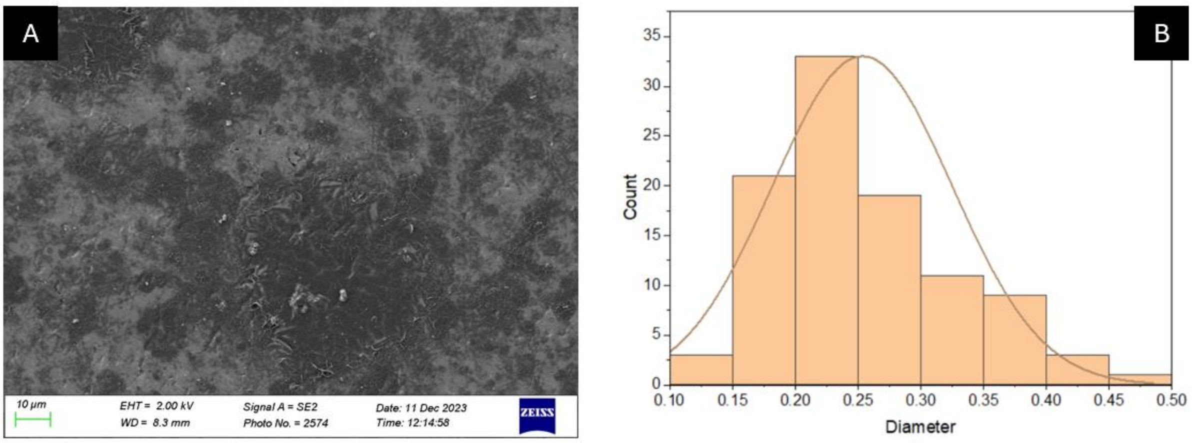

Figure 7: (A) SEM micrographs of PEO fibres spun with glycerol at 10% w/v, (B) histogram of diameters of PEO fibres spun with glycerol at 10% w/v

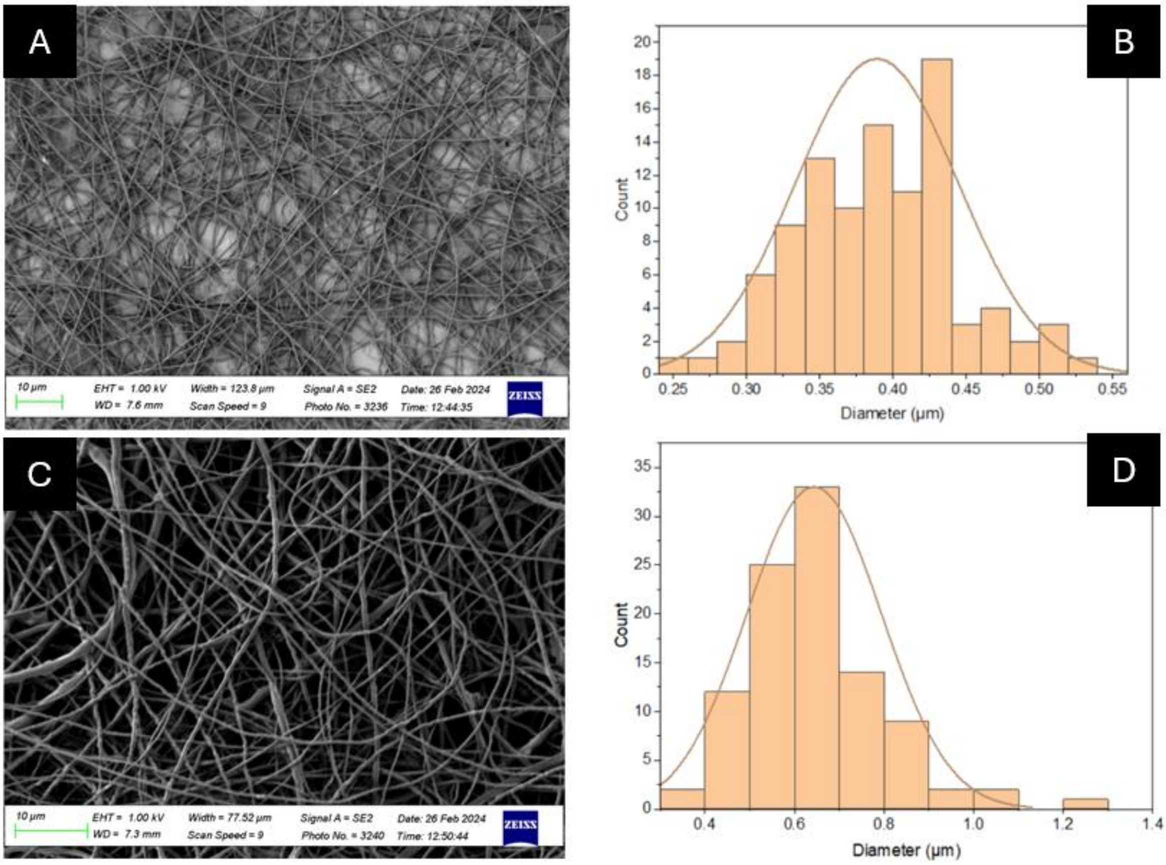

Figure 8: (A) SEM micrographs of PEO fibres spun with acetone/water (1:1) at 8% w/v, (B) histogram of diameters of PEO fibres spun with acetone/water (1:1) at 8% w/v, (C) SEM micrographs of PEO fibres spun with acetone/water (1:1) at 16% w/v, (D) histogram of diameters of PEO fibres spun with acetone/water (1:1) at 16% w/v

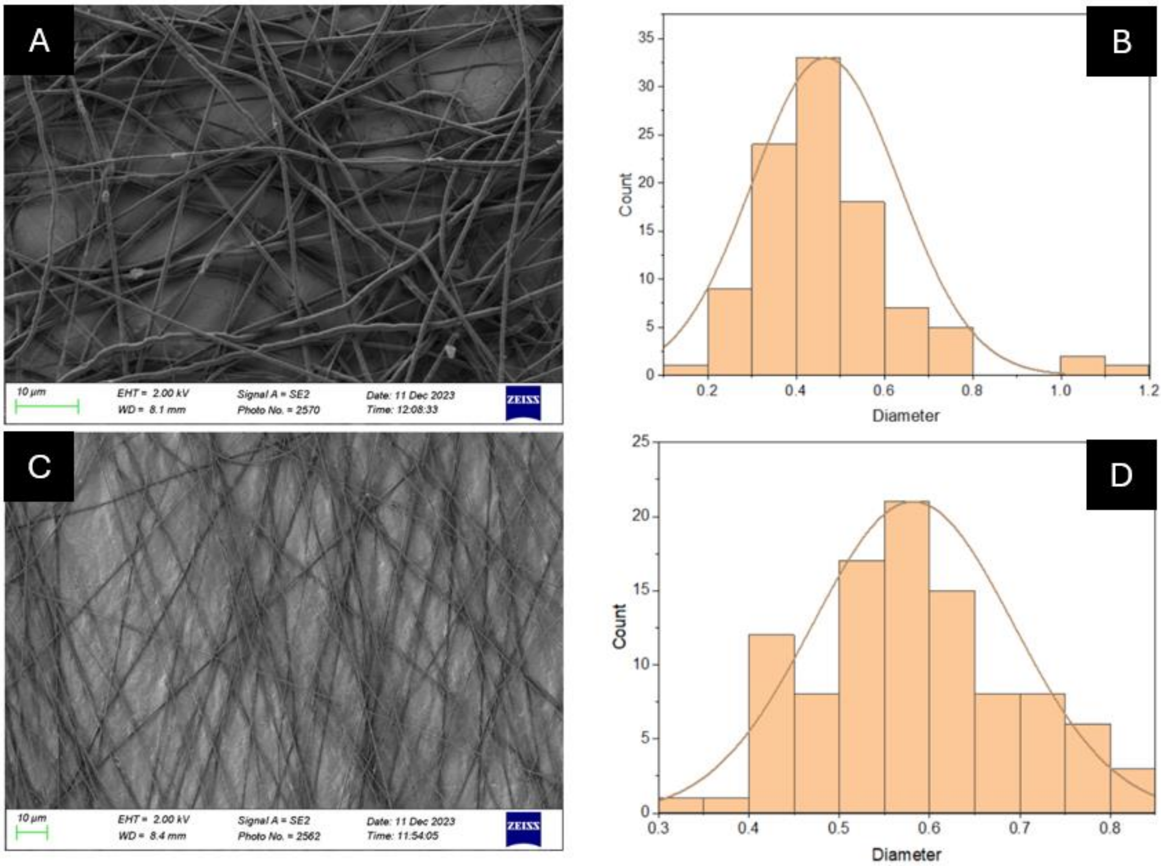

Figure 9: (A) SEM micrographs of PEO fibres spun with acetone/ethanol (1:1) at 10% w/v, (B) histogram of diameters of PEO fibres spun with acetone/ethanol (1:1) at 10% w/v, (C) SEM micrographs of PEO fibres spun with acetone/water (1:1) at 10% w/v, (D) histogram of diameters of PEO fibres spun with acetone/water (1:1) at 10% w/v

4.7 Electrohydrodynamic Limitations

Despite the heavy implementation of electrospinning in fibre production, there remains concerns regarding the production efficiency and how EHD technology can be further innovated to further enhance its sustainability aspects.
Single-needle EHD technology was used for this experiment, which has limited production capacity of 0.01 – 0.1 g/h. [59] Nozzle-free electrospinning offers greater efficiency on an industrial scale. Multiple Taylor cones are generated on the surface simultaneously in this method, along with the absence of the nozzle avoids clogging, hence improving the production efficiency. [60] However, nozzle-free methodology produces fibres with nonuniform diameters and is incompatible with volatile solvents. Despite the favourable attributes needle-free electrospinning carries, as most of the solvents investigated are volatile, it still requires further development and innovation to be suitable for industrialised medical applications.
Emulsion electrospinning utilises homogenous mixtures of two or more immiscible liquids. This was carried out by mixing combinations of deionised water, ethanol and acetone in pairs as a solvent for PEO. This methodology is similar to single-needle electrospinning; however, the fibres produced are reported to have a core-cell structure. [61] This nature enables the protection of the biologically active material in the core.

5. HEALTHCARE IMPLICATIONS

5.1 Hard Tisssue Engineering

Hard tissue engineering includes the production of bone and dental tissues. Currently, PEO fibres are predominantly used in targeting cartilage tissue. [62]
The hierarchical organisation of nano-sized and micro-sized structure of the bone provides the ability to weight bear and prevent fractures, which is achieved through mechanical energy dissipation. [63] The PEO fibres produced with acetone/ethanol as solvents are suitable for bone tissue repair, as their variation in fibre diameters imitate their natural microstructure. [64]
Dental cavity and periodontal diseases are causes to a decrease in the pulp-dentin complex and tissue destruction, which will ultimately lead to the loss of the tooth. [65] Chen et al. [66] studied the smooth nanofibrous morphology of polymer fibres in dental tissue engineering. The fibres produced was cocultured with human periodontal ligament cells. Once experimented on rats, high bone density, cementum-esque tissue and mineralisation was observed, showing great potential of electrospun polymer scaffold in the regeneration of the cementum.

5.2 Soft Tissue Engineering

Soft tissue engineering includes the production of skin, cardiac and neural tissues.
The smooth and uniform fibres acetone/deionised water at 8% w/v and 10% w/v shown, can be utilised in the regeneration of heart and nerve tissues. Gnavi et al. [67] reported that regularity in fibre diameters is necessary to facilitate proper cell development.
Vigani et al. [68] examined the neuroprotection and neuroregeneration of tissues for treatment of spinal cord injury. A PEO scaffold was created by electrospinning and it was tested to have cell viability and scaffold biocompatibility.
Overall, the usage of polymeric fibres show great potential in the field of healthcare, as polymeric fibres can be easily customised, based on the tissue type needed to be regenerated on its scaffold.

5.3 Drug Delivery

Calvo et al. studied that hydrophilic nanoparticulate carriers are extremely compatible for therapeutic molecules when organic solvents are used during electrospinning [69], while Xue et al. discovered that the biocompatibility, biodegradability and high therapeutic payload capacity is important therapeutic delivery. [70] Therefore, PEO fibres would be ideal for therapeutic delivery applications.
The mouth is the most common and suitable drug delivery route. PEO electrospun fibres offer great versatility in fibre diameter, giving it the ability to deliver both micro and macromolecules. [71] Additionally, electrospun fibres can be easily tailored to portray any desirable properties, such as controlled [72], quick [73] and delayed [74] releases of drugs in capsules. As the structures of PEO fibres are easily adjusted through changing processing parameters, they are heavily used when designing oral drug delivery systems. [74]

6. CONCLUSIONS

The findings of this study shows discrepancies in fibre diameters, uniformity and presence of beading by adjusting solution concentrations and solvents sued in EHD electrospinning process. Overall, these

variations portray the versatility of EHD printing technology, whilst emphasizing the significance of selecting specific parameters and an appropriate polymer solution composition for different medical applications.
Despite the popular use of EHD printing technology in healthcare manufacturing, such as tissue engineering and drug delivery, there may be potential for further innovation and development of the sustainability aspects of EHD processes. Although incorporating all 12 principles of Green Chemistry is exceptionally challenging, this embraces the vision of a more sustainable future.

7. DECLARATIONS

7.1 Acknowledgements

The author would like to thank his Supervisor and PGTA for guidance and assistance throughout the research. The author would also wish to thank UCL Faculty of Engineering Sciences for supplying the resources and equipment for the experiment.

7.2 Use of AI

No artificial intelligence was used for this research.

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