INFLUENCE OF SOLUTION PROPERTIES ON ELECTROSPINNING BEHAVIOUR OF BIOCOMPATIBLE POLYMERS

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INFLUENCE OF SOLUTION PROPERTIES ON ELECTROSPINNING BEHAVIOUR OF BIOCOMPATIBLE POLYMERS

by

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CERTIFICATE

This is to certify that the thesis entitled **'Influence of solution properties on electrospinning behaviour of biocompatible polymers'** being submitted by **Ms. Deepika Gupta** to the Indian Institute of Technology Delhi for the award of degree **Doctor of Philosophy**, is a record of bonafide research work carried out by her. She has worked under our guidance and supervision and fulfilled the requirements for the submission of thesis which has attained the standard required for a Ph.D. degree of this institute. The results contained in this thesis have not been submitted, in part or in full to any other university or institute for the awards of any degree or diploma.

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ABSTRACT

Nanofibres are indispensable for applications like tissue engineering, filtration, sensors etc., due to their unique properties. Electrospinning is an excellent technique for producing nanofibres from polymer solutions or melts using high electric field. Control of nanofibre morphology and quality are important to augment their utility for various applications. Spinnability and morphology of fibres are affected by solution, ambient and processing parameters.

Process parameters that include flow rate, spinning voltage and spinning distance were recently reported to not have any significant effect on the fibre diameter, if the spinning is carried out at minimum electrospinning voltage (MEV). It has been suggested that solution properties have a stronger influence on controlling the fibre diameter. However, the studies in this direction are limited. The rheological properties can be expressed in terms of viscosity and elasticity, which are affected by the type of polymer, its molecular weight, its concentration and the nature of solvent used.

To isolate the elastic effect from the viscous effect, Boger fluids of poly(vinyl alcohol) (PVA) were prepared by blending small amounts of high molecular weight PVA (HMW-PVA) with highly concentrated solutions of low molecular weight PVA (LMW-PVA). The resulting solutions with increase in HMW-PVA content showed increasing elasticity, while maintaining the same viscosity, thereby, separating the two effects. On electrospinning, the elasticity of the solution (expressed in terms of relaxation time (λ) and Deborah number (De)) was found to have a direct correlation with diameter of the electrospun fibres.

Nature of solvent is known to affect the solution rheology. Rheology and electrospinning behaviour of PVA in two different solvents, i.e. dimethyl sulfoxide

(DMSO) and water, was studied. The rheological properties for the same concentration of PVA were found to be significantly different in the two solvents. The viscosity, storage modulus and relaxation time (λ) were found to be higher in PVA-DMSO system. However, the fibre diameter obtained from PVA-DMSO system was lower than that from PVA-water system. Interestingly, still a linear correlation of the fibre diameter with λ could be established for the two solvents with two different slopes. On further investigation, a single linear equation could be drawn for the two systems between diameter and the number of entanglements per chain suggesting elasticity arising from chain entanglements was governing the fibre diameter.

Effect of solvent-solvent (DMSO-water) interaction on rheological properties and spinning behaviour of PVA solutions was also studied. Because of the strong interaction of water with DMSO, both the rheology and spinnability of PVA solutions were influenced by the composition of the binary solvent mixture. At the same concentration of PVA, the morphology of electrospun fibres changed from highly uniform thick fibres to very fine fibres with large number of beads or droplets.

Influence of incorporating small quantity (1-20 wt%) of non-solvent (1,4-dioxane) on rheology and spinning behaviour of PVA-water mixture was also studied. The spinning behaviour was dependent on the water-dioxane composition, where the diameter first decreased on addition of 1-3 wt% dioxane to 206 ± 21 nm and then it increased to 439 ± 21 nm on addition of 4 to 20 wt%. The diameter was found to have a better correlation with λ as both the fibre diameter and λ increased by 41 and 40%, respectively, compared to the viscosity, which increased by only 13% with the increase in dioxane content.

Poly(galacturonic acid) (PGuA) is an important natural biopolymer, however it has not been processed into fine films and fibres due to its anionic nature and rigid structure. This study aimed at modifying the solution properties of PGuA in aq. sodium hydroxide to enable their conversion into electrospun nanofibres. Addition of anionic surfactants, helped in individualizing the PGuA chains that led to formation of small spindle shaped fibres of length ranging from 2-10 µm and diameter from 287 to 997 nm. However, continuous fibres could not be formed. Using the understanding developed from the PVA Boger fluids, a small amount (1-3 wt% in solution) of high molecular weight PVA was added to modify the rheology of the PGuA solutions. This resulted in formation of continuous fibres. Correlation of fibre diameters of PGuA/PVA with the rheological properties suggested a strong dependence of diameter with the elasticity of the blend solutions.

Applicability and suitability of electrospun PGuA/PVA nanofibres as biocompatible substrates for tissue engineering was also investigated. PGuA based nanofibrous substrates obtained from 70:30 blends of PGuA and PVA were compared with conventionally used PGuA based films for bone tissue engineering. The crosslinked samples of PGuA/PVA nanofibres showed enhanced differentiation and mineralization of hMSCs (human mesenchymal stem cells) as compared to the films. Results indicated that PGuA/PVA based nanofibres facilitated better cell migration and boosted cell adhesion.

The present study was able to develop an understanding of the importance of elasticity, which is expected to facilitate better control of the fibre diameter in electrospinning process. Also, utilising the understanding obtained from this study, spinning of non-spinnable polymers can be achieved.

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LIST OF SYMBOLS AND ABBREVIATIONS

Symbol/Abbreviation	**Meaning**
ω	angular frequency
η	apparent viscosity
G^*	complex modulus
η^*	complex viscosity
J'	compliance
c	concentration
c^*	critical concentration
α	dilution coefficient
η'	dynamic viscosity
G	gauge
χ	interaction parameter
$[\eta]$	intrinsic viscosity
kV	kilovolt
G''	loss modulus
MPa	mega pascal
M	molar
Pa	pascal
Φ	polymer volume fraction
rad	radian
λ	relaxation time
γ°	shear strain
τ	shear stress
G'	storage modulus
wt%	weight percentage
η_0	zero shear viscosity
HFIP	1,1,1,3,3,3-hexafluoro-2-propanol
TFA	2,2,2-trifluoroethanoic acid

TFE	2,2,2-trifluoroethanol
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
ARS	alizarin red s
ALP	alkaline phosphatase
BSA	bovine serum albumin
CV	collector voltage
De	Deborah number
DH	degree of hydrolysis
DI	de-ionized
dia	diameter
DCM	dichloromethane
DMSO	dimethyl sulfoxide
DMEM	Dulbecco's modified Eagle's medium
EV	effective voltage
C_e	entanglement concentration
$(n_e)_{soln}$	entanglement number of solution
ECM	extra cellular matrix
FBS	fetal bovine serum
Gel	gelatin
GAGs	glycosaminoglycans
HMW	high molecular weight
hMSCs	human mesenchymal stem cells
HA	hydroxyapatite
LG	low glucose
LMW	low molecular weight
M_e	melt entanglement molecular weight
MSCs	mesenchymal stem cells
MEV	minimum electrospinning voltage
DMAc	*N*,*N*-dimethylacetamide
DMF	*N*,*N*-dimethylformamide
NV	needle voltage

NBF	neutral buffered formalin
NMP	*N*-methyl-2-pyrrolidone
NMMO	*N*-methylmorpholine *N*-oxide
PBS	phosphate-buffered saline
PVDF	poly(1,1-difluoroethene)
PAN	poly(1-acrylonitrile)
PANI	poly(aniline)
PCL	poly(carprolactone)
PEG	poly(ethylene glycol)
PEO	poly(ethylene oxide)
PGuA	poly(galacturonic acid)
PHB	poly(hydroxyl butyrate)
PLA-PGA	poly(lactic-co-glycolic acid)
PGA	poly(L-glycolic acid)
PLA	poly(L-lactic acid)
PMA	poly(methacrylate)
PVP	poly(*N*-vinyl pyrollidone)
PS	poly(styrene)
PVA	poly(vinyl alcohol)
RH	relative humidity
SDS	sodium dodecyl sulphate
$M_{e(soln)}$	solution entanglement molecular weight
THF	tetrahydrofuran
3-D	three dimentional
TE	tissue engineering
2-D	two dimentional
UV	ultraviolet
TCP	β-tricalcium bis(phosphate)