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RESEARCH ARTICLE

Microwave assisted synthesis of ε-caprolactone: Effect of reaction conditions and PLA/PCL fabrications

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ABSTRACT

In competition with petrochemicals polymers, Polycaprolactone (PCL) is presented as the best bio-based polymer candidate for the future developments not only because these are biodegradable but also are produced from renewable resources. The most important biomedical applications of biodegradable polymers are in the areas of controlled drug delivery systems, in the form of implants devices for bone, skin and dental repairs, Microwave irradiation as a heating source for polymerization reactions is a rapidly growing branch in polymer science. Over the last decade, conventional heating has been widely applied in polymer synthesis but the current research shows that microwave synthesis is efficient alternative which takes less time for polymerization. With microwave synthesis polycondensation, free and controlled radical polymerization, and ring opening polymerization (ROP) can be done. The characterization of Polycaprolactone was done by Fourier Transform Infrared Spectrophotometer (FT-IR), scanning electron microscopy (SEM),. The polymer interactions were checked by Differential scanning calorimetric (DSC). and The XRD analysis was carried out to determine structural changes.PLC/PLA nanofabrication's done by electrospinning Technique for biomedical applications.

INTRODUCTION

In recent years bio-degradable polymer is most advance topic in polymer study due to its environmental effect and cost effectiveness. Polycaprolactone is biodegradable synthesis that is currently used in the number of biomedical application.3 Pcl is mainly important due to its mechanical property, miscibility with many other polymer and due to its biocompatibility. Pcl synthesis by two method : The polycondensation of hydroxycarboxylic acid and Ring opening polymerization of caprolactone(1) We use ring opening polymerization method for synthesis of Polycaprolactone by using stannous octoate as catalyst in microwave radiating system. Microwave system is more efficient than old heating method, it required less time and it's easy to process. The result of ring opening polymerization of Polycaprolactone (i.e. degree of conversion of caprolactone to Polycaprolactone) studied by Fourier-transform Infra Red spectroscopy (FTIR), Differential scanning calorimeter (DSC), X-ray diffraction patterns (XRD) and gel permeation chromatography (GPC)(2).In recent year biodegradable polymer have been extensively investigated for application such as tissue engineering scaffold, drug delivery system, as well as surgical sutures etc. A biomaterial is material intend to interphase with biological system to treat or replace any organ or tissue or function of body. Biomaterial only chooses due to their interfrance with living cell.

Natural polymer are expensive due to short supply and various form of batch to batch of production and may be cross contaminated from unknown virus or disease. On other hand, synthetic bio-degradable polymer has easy control on property and quality also modification is easy in lab synthesis product. Polycaprolactone was used extensively in the bio–material field for drug delivery system during 1970s and 1980s. Polycaprolactone has specific property of rheological and viscoelasticity behavior over many other polyesters. In 1970s, Food and Drug Administration (FDA) approved biomedical specific applications of Polycaprolactone for used in the human body as (for example) a drug delivery device. In recent years, Polycaprolactone is used for tissue engineering application by larger amount. Polycaprolactone is hydrophobic, slow-degrading synthesis biodegradable aliphatic polyester composed of hexanoate repeating unit. It has low melting point around 60^0c and glass transition temperature about -60^0C. It is a semi-crystalline polymer with 69% of degree of crystallinity.

Polycaprolactone have special property such as enhanced solubility in some organic solvent, ability to process at low temperature, and its non toxic byproduct after degradation. One of the most attractive property is controlling rate of degradation i.e. we can control rate of degradation by changing molecular weight and crystallinity of polymer product by simply modifying lab processing method. Co-polymerized Polycaprolactone is one of most important polymer due its low cost and help in increasing growth of cell. Polycaprolactone co-polymerized with polylacticacid, and some other polymer. Co-polymerization helps in reduce degradation rate of polymer. Pcl copolymer enhance the property for

example, an iodine bearing copolymer was synthesis by iodine fictionalized caprolactone monomer reacting with ε-caprolactone at 100^0C in toluene with methanol as initiator. The product used as temporary reconstruction or drug delivery system in more efficient way. The physical, chemical, thermal and mechanical property mainly depends upon its molecular weight and degree of crystallization. At room temperature, Polycaprolactone is highly soluble in chloroform, dichloromethane, benzene, toluene, and cyclohexanone; slightly soluble in acetone, 2-butanone, ethyl acetate, and acetonitrile; insoluble in alcohols, petroleum ether, diethyl ether and water. Polycaprolactone have good elastomeric and elongation property. Polycaprolactone miscible with polymer such as polyvinyl chloride, polystyrene acrylonitrile, poly acrylonitrile butadiene styrene, bisphonol-A and in some polycarbonates (1).

Polycaprolactone degrades within several days to years depending upon its molecular weight, degree of crystallization of polymer and environmental condition. Microbes in nature are able to degrade Polycaprolactone completely. The amorphous phase degrades firstly, increasing the crystallinity of polymer. Polycaprolactone degrades by Firmicutes and proteobacteria. Aspergillus sp. degrades high density Polycaprolactone quickly than Penicillium sp. Polycaprolactone also degrade by clostridium under anaerobic condition.

Polycaprolactone is uses in different field such as scaffold in tissue engineering, in long term drug delivery system in packing, in microelectronics as adhesives. Polycaprolactone monomer is delivered from renewable recourses as well as its interesting property makes it widely acceptable (6).

The failure or damage of an organ or tissue is a major human health problem. To treat patients with such problems is routinely practiced by tissue or organ transplantation. However, the shortage of donor limits the present diagnosis method. The limitations enforced by the problem have made the researchers around the world to seek for suitable alternatives. Tissue engineering has emerged as a promising approach to create artificial organs and tissues, or to regenerate damaged tissues. The technique involves the culturing of the cells in temporary three-dimensional scaffolds to form the new organ or tissue by using the patient's own cells (8). A number of 3-D porous scaffolds fabricated from a wide range of materials have been developed and used for tissue engineering of various tissue and organs such as liver, skin, bladder, bone, cartilage, nerve etc (8). The key challenge to this technique is the design and fabrication of the scaffolds. Ideally, scaffolds for tissue engineering should meet several design criteria: (8) the surface of the material used for the preparation of scaffold should permit cell adhesion, promote cell growth, and allow the retention of differentiated cell functions; (9) it should be biocompatible, (10) it should be biodegradable; (11) it should possess high porosity to facilitate homogeneous tissue formation; (12) it should be reproducibly processable into three-dimensional structure, and (13) it should be mechanically strong (8). There are several methods for the synthesis of polymer nanofibers which includes electrospinning, melt-blown, phase separation, self-assembly, and

template synthesis. Among these, electrospinning is the most popular technique due to its advantage over the other methods. It is simple, cost-effective and can be employed to use various materials. In addition to this, this method can be used for large scale production of continuous nanofibers for industrial applications (10). Recent studies in our group shows the successful synthesis nanofibers of various polymers using electrospinning technique [10, 11]. In the present research work we are proposing the Synthesis of Polycaprolactone and development of biocompatible and biodegradable polymer nanofibers using electrospinning and their application for the preparation of scaffolds used for tissue engineering application.

EXPERIMENTAL SECTION

MATERIALS AND METHODS.

ε-Caprolactone (ε-CL) was Purchased from (Sigma Aldrich 99%), tin octoate (SnOct2) was purchased from Sigma Aldrich, and PLA (polylactide resin 3052D) with a molecular weight of 1,33,000 g/mol (analyzed by gel permeation chromatography) was acquired from Nature Works LLC (Minnetonka, MN), Tetra hydro furan (THF) HPLC grade, Acetone (lab reagent grade), DMF (Dimethyl Formaldehyde was purchased from Sigma Aldrich) The solutions were prepared at room temperature, The syringes used to pump the fluids were obtained from BD Medical, The syringe pumps was purchased from Yash Tech Ltd.

Phase 1

Synthesis of Polycaprolactone by Microwave Assisted Polymerizations:

Synthesis and characterization of Poly(Ɛ-caprolactone),Variation of watt power ,Variation of reaction time, Variation of reaction catalyst, Variation of temperature Synthesis and characterization of Poly(Ɛ-caprolactone)Polycaprolactone is synthesized by conventional heat induce polycondensation as well as microwave assisted ring opening polymerization.Figure1a,b use In current study, microwave synthesis of Polycaprolactone was carried out with stannous octoate as a catalyst and ε-caprolactone as a monomer. The effect of varying reaction temperature and microwave wattage capacity was studied on the synthesis Microwave method is used for the synthesis of Poly (Ɛ-caprolactone). Ɛ-caprolactone (Sigma Aldrich, India) was used as a monomer and stannous octoate (Sigma Aldrich, India) was used as a catalyst. Microwave synthesis of Poly (Ɛ-caprolactone) was done by adding calculated amount of catalyst to 5 mL monomer solution in Tetrahydrofuran as a solvent (THF, Sigma Aldrich, India) . The reaction conditions were varied and thereby synthesis was conducted in 4 different Runs. The synthesized polymer is characterized using Gel permeation chromatography (GPC). The results obtained shows that the polymer synthesized in Run 2 possess Mn = ~10000 and Mw = ~ 30000 which is well in agreement with the report available in literature. It is also observed that the polydispersity index (PDI) of the synthesized

polymer is 2.9 which is also in agreement with the reported values in literature. Therefore, it is concluded that the polymer is properly synthesized.

Effect of various parameters on the synthesis

The effect of various parameters on the synthesis of Polycaprolactone was studied. Following are the range of parameters selected for the study Table 3.

Effect of reaction temperature and wattage

At a fixed catalyst loading of 0.01 g, the effect of wattage and temperature were studied on the synthesis of Polycaprolactone (PCL) with a reaction time of 15 min. The results of the above experiments are shown in following figure. It was observed that by increasing the temperature the % yield of PCL increases till a particular temperature and the further increase in the temperature results in decreased yield. With 100 W and 150 C, the % yield of synthesis was observed to be 80%. Further increase in the reaction temperature from 150 till 190 C increased the yield from 80% to 86%. However, further increase in the temperature from 190 C to 230 C decreased the yield from 86% to 78%.

It is also observed that the effect of temperature on the synthesis remained same for any wattage value. It is observed the increasing wattage from 100 - 300 W improved the synthesis and higher yield values were obtained with a corresponding increase in wattage. However, at higher wattage values such as 400 W, the % yield reduced significantly. Therefore, from the above studies temperature of 190 C and wattage of 300 W are considered as optimum reaction conditions. For a fixed wattage of 300 W and at a reaction temperature of 190 C, the effect of reaction time in the range of 5 min -20 min was studied on the synthesis. It was observed when the solution was kept for 5 min and 10 min reaction time, there was no product formed. At 15 min the % yield was observed to be 90 %. When the reaction time was further increased to 20 min, % yield was 98%. Figure 2

RESULT AND DISSCUTION:

Gel permeation chromatography:

PCL was synthesized at various reaction parameters. Following table no.4 shows the reaction condition for different runs.

GPC result of Polycaprolactone

Gel permeation chromatography (GPC) is use for analysis of polymer that separates analytes on the basis of size. GPC used for the analysis of polymers. When characterizing polymers, polydispersity index (PDI) is important as well the molecular weight. Polymers can be characterized by molecular weight including the number average molecular weight (M_n), and the weight average molecular weight (M_w) the viscosity molecular weight (M_v),or the size average molecular weight (M_z), It was observed that, increasing the reaction temperature increases the formation of PCL and it is evident from the increase in the Mw and PD value. For optimum reaction parameters of 300 W, 190 C, 0.01 g catalyst and a reaction time of 20 min, Mw of the

synthesized PCL was observed as 31829 and PD as 2.9.

X-Ray diffraction (XRD)

The XRD analysis was carried out to determine structural changes. A normal focus diffractometer (Regaku Miniflex, Japan) source Cu target at 30 kV and was used with scan rate of 3°/min. The data recorded in the range 2o -50o and analyzed using Jade 6.0 software-ray diffraction patterns of synthesized PCL shows sharp crystalline peaks at 21.3° and 23.8° which can be attributed to the [110] and [200] crystallographic planes of the PCL crystal, respectively. The obtained results are in well agreement with the reported data (Gloria et al., 2013). Result of XRD Show in Figure 3.

Fourier Transform Infrared Spectrometry

Fig 4 shows Fourier Transmittance Infrared Spectroscopy (FTIR) was used for Identification of Polycaprolactone measuring Transmittance from 500 to 4000 cm-¹ Synthesis of Polycaprolactone was validated by FTIR spectroscopy. The FTIR spectroscopic graph of poly caprolactone is depicted in Figure no. 5. In FTIR spectra of Polycaprolactone, peaks at 1720, 2940, 2863 cm-¹ verified the presence of Polycaprolactone. All the measurements were carried out on recorded on a bruker –Alpha's Zn-Se ATR Model.

Differential scanning calorimetry

Determination of Tm, Tc and Tg of the aliphatic polyester which is grafted on to starch is calculated by DSC thermogram. We can conclude that the molecular weight of the PCL grafted is high enough to allow the polyester chain to crystallization. Figure 5 a,b,c shows.dsc melting temperature 64.7 .

Phase 2

Design of electrospinning Setup and Different Collectors.

Design of electrospinning apparatus and Formation of polymer Nanofibers Electrospinning is a very simple process. It can be used for the fabrication of continuous nanofibers. The electrospinning device consists of three main components:

1. syringe pump, collector and high voltage supply, Synthesis of Polymer nanofibers by electrospinning in Figure 6 a,b,c,d,e

Procedure:

- The polymer is first dissolved in solvents.
- Then the solution is inserted into a syringe.
- The tip of the syringe needle is connected to a high-voltage power supply.
- The solution acquires a charge when it is ejected through the needle, which causes it to gravitate toward the collecting plate.
- The collector acts as the template for the fibers to attach

Electrospinning apparatus for continuous production of fibers using by Electrospinning Setup with collector, Figure 7 shows roller collator flat plate collector.

<u>Controllable Parameters:</u>

Table 5, shows controllable parameters.

Optimized Parameters for Nanofiber Fabrication with PLA polymer:

Deposition height: 7cm from needle tip to receiving plate

Polymer Concentration: 5 %, 10% 15% PLA in DMF with Acetone

Voltage Applied: Varry as per conc. 10kv - 20kV

Deposition Patterning: Random Deposition (No patterning)

Flow Rate: 0.5 ml -5ml per hr.

Needle Diameter: 16-20 gauge

RESULT AND DISSCUTIONS

Polylacticacid /Polycaprolactone Nanofibers 15%

Polylactic/Polycaprolactone nanofiber shown in Figure 8 a at 1000x,Figure 8 b at 5000x and Figure8c is confocal image.SEM image of a Randomly Oriented 15% Polylacticacid/Polycaprolactone nanofiber deposition. Electrospun 15% PLAPCL nanofiber diameter was 226nm ± 82.3 nm. Scale bar = 1000x, Figure8b SEM image of an Aligned 15% PLAPCL nanofiber deposition. Electrospun 15% PLAPCL, nanofiberScale bar = 5000 x, Figure 8c Confocal image of 15% PLAPCL nanofibers

Differential scanning calorimetry

Differential scanning calometry(DSC) To analyze the melting and crystallization behaviors of neat polymers and their blends, differential scanning calorimetry (TA Q100, USA) was used, determination of Tm, Tc and Tg of the aliphatic polyester which is grafted on to starch is calculated by DSC thermogram. We can conclude that the molecular weight of the PCL grafted is high enough to allow the polyester chain to crystallization show in Figure 9.

Gel permeation chromatography

Gel permeation chromatography (GPC) is use for analysis of polymer that separates analytes on the basis of size. GPC used for the analysis of polymers. When characterizing polymers, polydispersity index (PDI) is important as well the molecular weight. Polymers can be characterized by molecular weight including the number average molecular weight (M_n), and the weight average molecular weight (M_w) the viscosity molecular weight (M_v),or the size average molecular weight (M_z), I have taken Polylactic acid from natures works Bangalore and check molecular weight by gel permission chromatography was observed as 133418 and PD as 2.545.

CONCLUTION

The above study present preparation and characterization of Polycaprolactone by microwave heating method, Effect of irradiation time on molecular weight and conversion of polymers were investigated, Molecular weight of the synthesized polymer increases with microwave irradiation temperature up to a certain wattage power. However, further prolonged irradiation does not make anymore difference, Therefore, microwave heating is an efficient technique to

obtain polymers in reasonably less reaction time with similar conversion and molecular weight with PDI.Poly caprolactone having fixed molecular weight with varying concentration of solvent were successfully synthesized by Microwave Assisted Polymerizations, Effect of various parameters on the synthesis use stannous octane as a Catalyst. Effect of reaction temperature and wattage- At a fixed catalyst loading It was observed that by increasing the temperature the % yield of PCL increases till a particular temperature and the further increase in the temperature results in decreased yield. However, further increase in the temperature from 190°C to 230° C decreased the yield from 86% to 78%.Effect of reaction time: For a fixed wattage of 300 W and at a reaction temperature of 190°C, the effect of reaction time in the range of 5 min - 20 min was studied on as increases Reaction Time Increases in % Yield Polylacticacid/Polycaprolactone PCL nanofibers shows SEM image of a Random 15% PLA PCL nanofiber deposition. Electrospun 15% PLAPCL nanofiber diameter was 226nm ± 82.3 nm. Scale bar =1000x which we can be use for biomedical applications.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article**.**

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TABLES

Table 1: Property of Polycaprolactone

density	1.1 g/cc
Elastic modulus (youngs)	1.2GPa
Elongation at break	300%
Glass transition temperature	-60^0C
Heat of combution	24 MJ/Kg
Melting onset (solidus)	60^0C
Strenght to weight ratio	9.1 KNm/Kg
Tensile strength: ultimate (UTS)	10MPa
Melting point	$55\text{-}65^0$C

Table2: caparison between pla and pcl

Structure size	EP4	
Polymer	Polycaprolactum	Polylactic acid
Young's modulus (GPa)	0.7	2.7
Meltion point(℃)	55-65	170-180
Process condition	Extrusion condition	
Extruder screw, rpm	8.3	2.2

Table 3:Parameter for Caprolactone Synthesis

Sr. No	Parameter	Range
1	Wattage	100 - 400 W
2	Reaction time	5-20 min
3	Temperature	160- 200 C
4	Catalyst	0.001 - 0.1 g

Table 4: GPC result of Polycaprolactone

Run No.	Synthesis parameters				Molecular Weight		
	Temperature (C)	Reaction time (min)	Wattage (W)	Catalyst concentration (g)	Mnc	Mnw	PDI
1	120	20	300	0.01	9020	18905	2.09
2	150	20	300	0.01	10565	27493	2.602
3	190	20	300	0.01	10974	31829	2.9
4	200	20	300	0.01	12878	26816	2.80

Mn^c – Number average molecular weight by GPC,

Mn^w -Weight average molecular weight determined by GPC

Molecular Weight	
Mw	PD
133418	2.254

Table 5: Parameters electrospinning nanofiber Formation

Parameters	High	Low
Deposition height	no fiber deposition	chance of arching
Polymer Concentration	viscosity will not allow fiber formation	globules of polymer will form.
Voltage Applied	chance of arching	not enough pull to form fibers
Flow Rate	globules form	inconsistent fiber deposition
Needle Diameter	diameter of nanofibers increase with gauge	Low Diameter

FIGURES

Figure 1a: Synthesis of Polycaprolactone by ring-opening polymerization (ROP) of ε- caprolactone

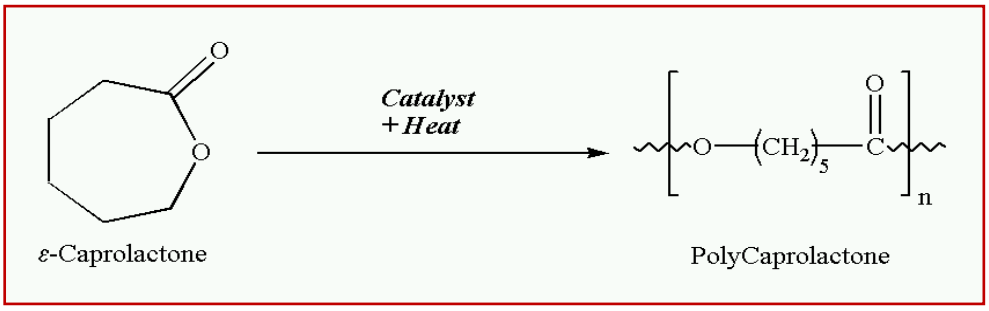

Figure 1b: Microwave Apparatus

Figure 2: Effect of reaction temperature and wattage on the synthesis of PCL

Effect of reaction time:

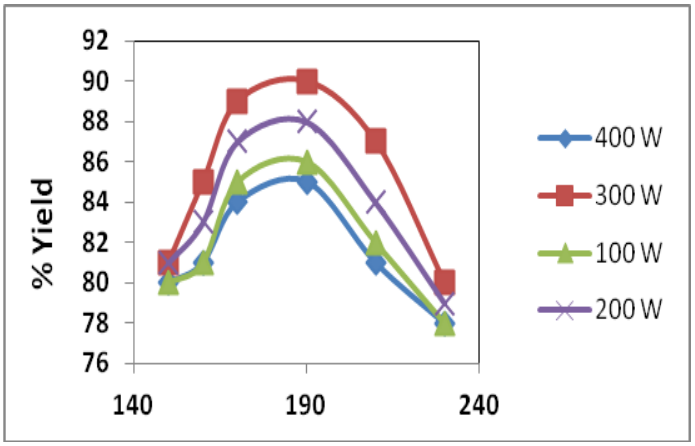

Figure 3: X-Ray diffraction (XRD)

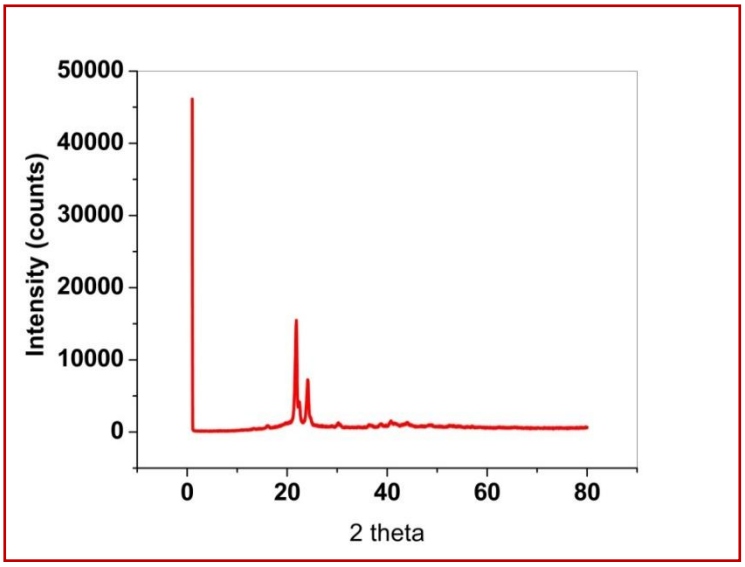

Figure 4 : Fourier Transform Infrared Spectrometry

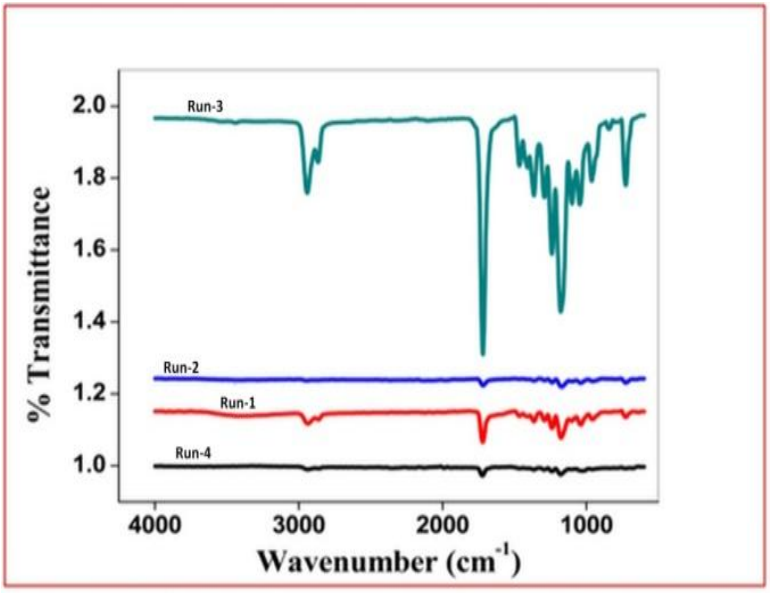

Figure 5a : Differential scanning calorimetry

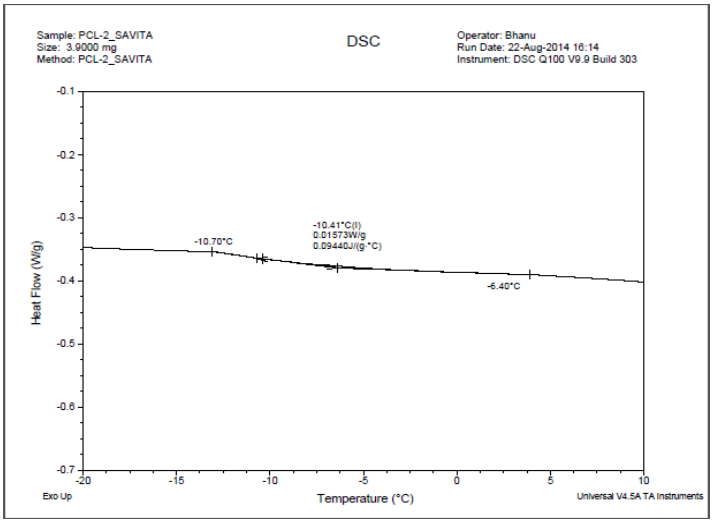

Fig 5 b: Differential scanning calorimetry

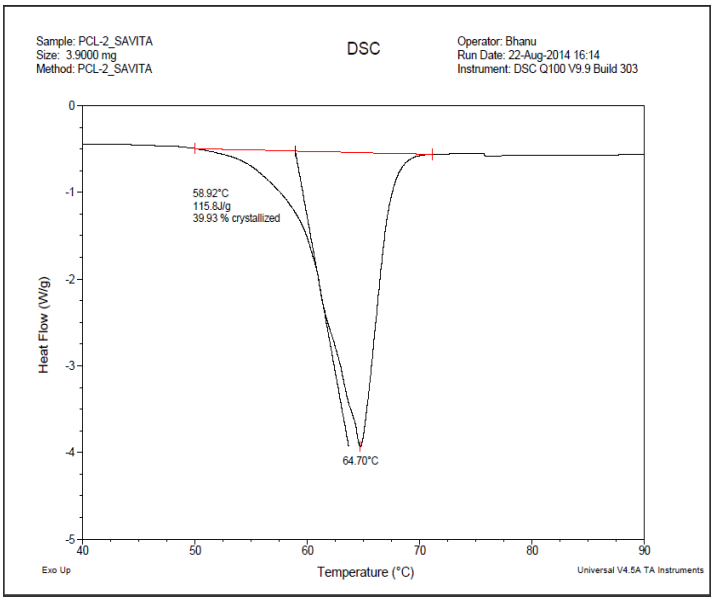

Fig 5 c: Differential scanning calorimetry

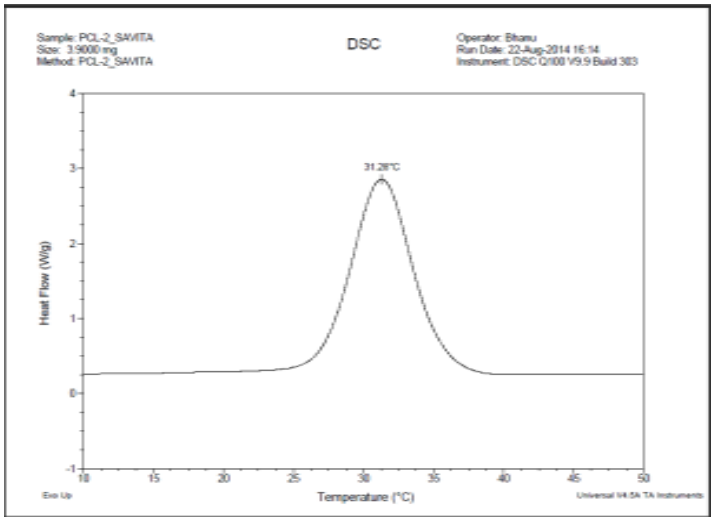

Figure 6 a : Design Electrospinning Setup(Roller plate)

figure 6 b: Design Electrospinning Setup(Flat Plate)

figure 6 c: Design Electrospinning Setup (Neddle less)

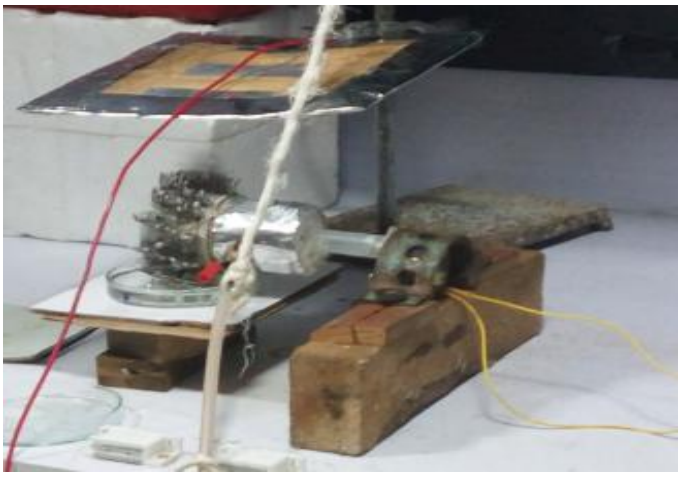

Figure 6d: Design Electrospinning Setup (niddle collector)

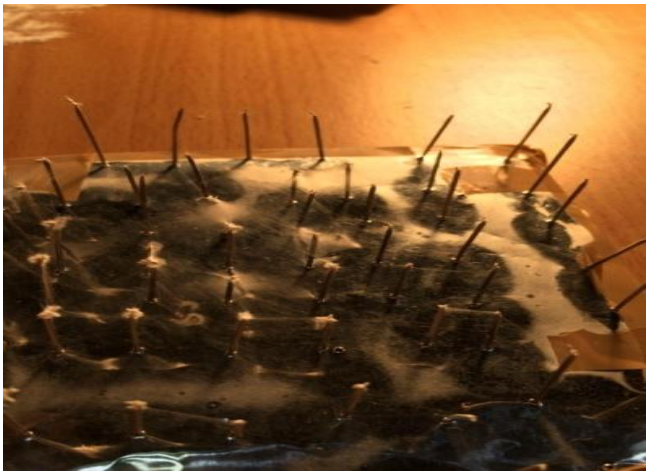

Figure 6e: Design Electrospinning Setup (zigzag aluminum collector)

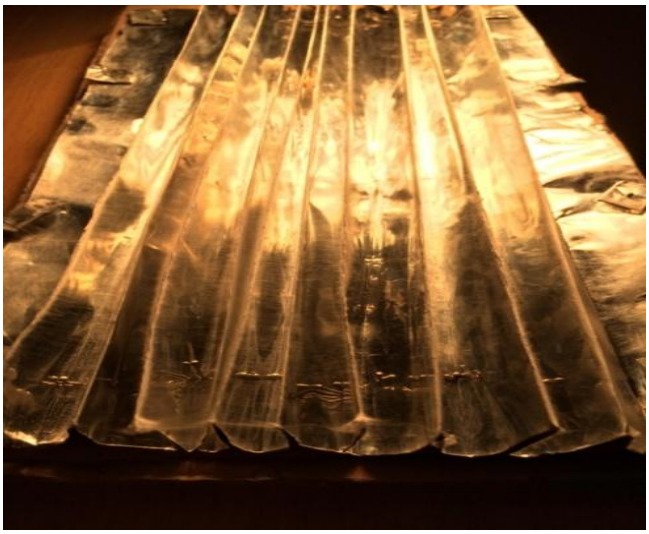

Figure 7a :Electrospinning Setup

figure 7 b: Electrospining Setup

Figure 8 a:Scanning Electro Microscopy(SEM) .

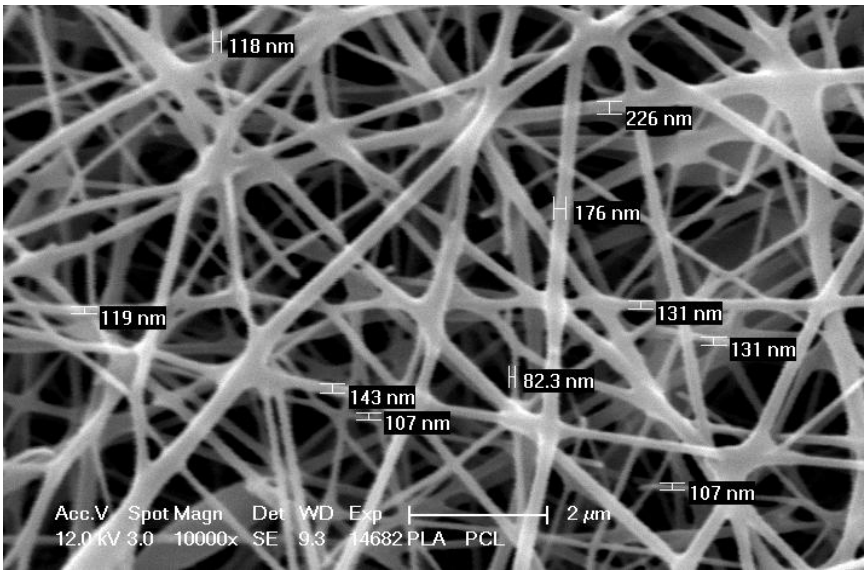

Figure 8b: Scanning Electron Microscopy(SEM) .

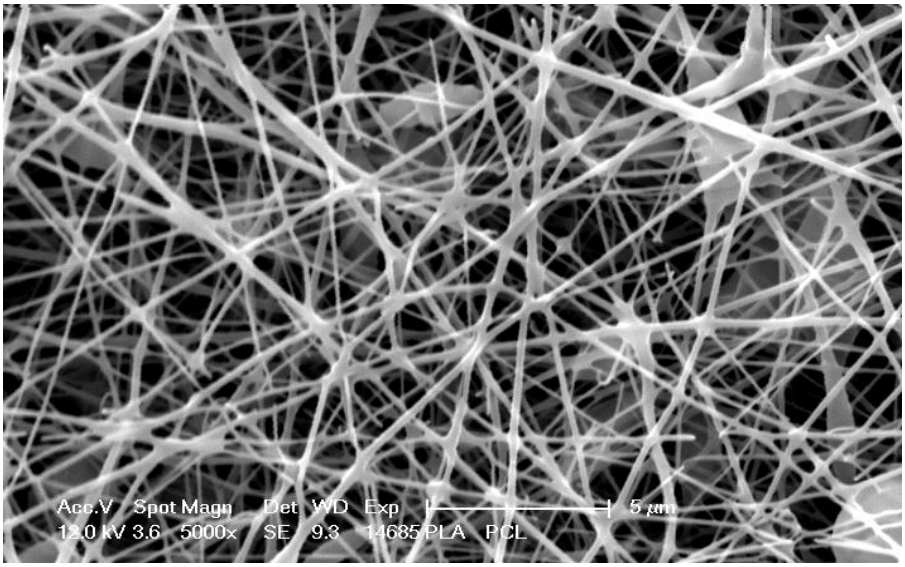

Figure 8 c: Confocal image of Nano Fibers.

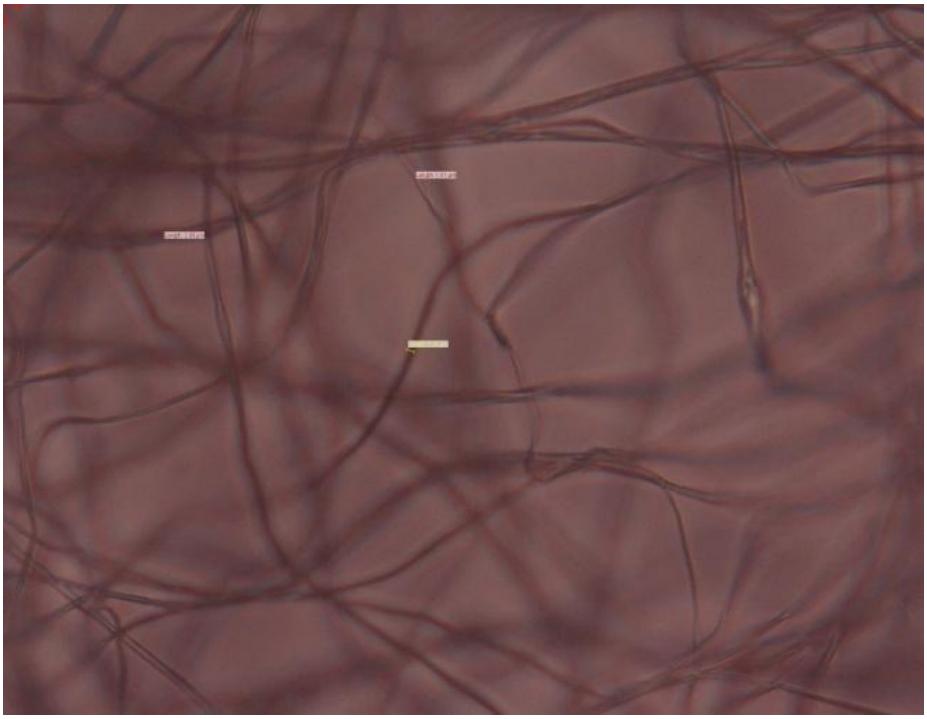

Figure 9: Differntial Scanning Calorimetry