Biomaterials and its Applications in Tissue Engineering

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Abstract: ***Medical textiles are one the most rapidly growing sector in technical textile market. Medical Textile involves the combination of textile technology and medical sciences. Application of textiles in medicine includes extra corporeal, implantable, non-implantable, health and hygiene products. In implantable and extracorporeal devices, biomaterials are the base to produce the end products. Biomaterials can be Ceramics, Metals, and Polymers. In textile field, polymers are taken as a base material, from which woven/knitted/braided/nonwoven fabrics are produced for Medical applications. Tissue engineering is one of the emerging fields, in which biomaterial polymers are widely used. Mostly widely biodegradable polymers are used, and nanofibers are produced from that which is further converted into fabrics, to be used for tissue engineering applications. Nanofibers can be produced by both naturally occurring and synthetic polymers by various techniques like Rotary Jet Spinning method, Electrospinning, Centrifugal Spinning etc. When spun, the material stretches much like molten sugar does as it begins to dry into thin, silky ribbons.The most commonly used natural biopolymers for tissue engineering include silk, chitosan, collagen, etc. Synthetic polymers include degradable polymers such as, polymethylmethacrylate (PMMA), polylactic acid (PLA), polyurethane (PU) etc. The biodegradable nanofibers are used in the areas of tissue engineering such as neural, bone, cartilage, skeletal muscle, blood vessel, skin and ligament., Polymers possess great biocompatibility, good mechanical strength, good biodegradability, and it is used to replace diseased part, assists in healing, improves or corrects the function also assists in cell adhesion, growth, proliferation.***

Keywords: Biomaterials, Biocompatibility, Tissue Engineering, Proliferation

1. Introduction

Biomaterials acts as 3D frames, which can be scaffolds, matrices or constructs. These 3D frames due to their high surface area to volume and their micro porous structure areused in cell binding, growth and differentiation.And as biodegradable nanofibers are used as scaffolds it eliminates the necessity of surgical removal. Hence the applications of nanofibers as scaffolds playa vital role in tissue engineering. The potential of nanofibers are widely followed in biological and non-biological applications. This report deals with the fabrication and application of nanofibers in tissue engineering.Nanofibers have been used in all areas of tissue engineering such as bone, cartilage, ligament, skeletal muscle, vascular, neural and skin, and also it controls the delivery of drugs, proteins and DNA. Tissue engineering is an alternative method for organ transplantation, and its prime job is to (i) replace natural tissues characteristics, (ii) fill the space until damage tissue is regenerated, (iii) temporarily replace tissue function, (iv) to help in managing tissue growth. The main aim of tissue engineering is to repair or replace the damaged or diseased tissue.

2. Biomaterials

A natural or synthetic material (as a polymer or metal) that is suitable to introduce into living tissue especially as a part of medical device, to repair damaged or diseased parts.

2.1 Types of Biomaterials

1. Metals
2. Polymers
3. Ceramics

Polymers are classified into three types namely Natural and synthetic.

Natural Polymers

Natural polymers occur in nature and can be extracted. They are often water-based. Examples of naturally occurring polymers are Silk, Collagen, Chitosan, Alginate etc

Synthetic Polymers

Synthetic polymers are derived from petroleum oil, and made by scientists and engineers. Examples of synthetic polymers include PMMA, Polyethylene etc.

Biomaterials For Tissue Engineering

1) It has a good biodegradable property
2) It is used to replace diseased part
3) It assists in healing
4) It improves or corrects the function
5) It has a good biocompatibility and mechanical properties

2.2 Importance of Biomaterials

Toxicology

Biomaterial should not be toxic. Toxicology for biomaterials deals with the substance that migrates out of the biomaterials. It is reasonably to say that a biomaterial should not give off anything from its mass unless it is specifically designed to do so.

Biocompatibility

The ability of a material to perform with an appropriate host response in a specific application.Material should not bring out a prolonged inflammatory response.

Healing
Injury to tissue will stimulate an inflammatory reaction that leads to healing. When a foreign body is present in a wound site then it is known as foreign body reaction. Biomaterials assist for wound healing.

Functional Tissue Structure
Biomaterials are implanted into tissues and organs. The structure and role of biomaterial should mimic the natural one.

Biodegradability
The degraded products of the scaffold must have a safe route for removal from the host.

Mechanical And Performance Requirements
Biomaterials and devices must have mechanical and performance requirements that originate from the physical properties of the materials. The three categories of such requirements are mechanical performance, mechanical durability, and physical properties. The scaffold must be able to provide support to the forces applied to it and the surrounding tissues (especially true for the engineering of weight-bearing orthopaedic tissues).

3. Silk

Silk fibroin is a natural protein produced by the domestic silkworm. Biodegradability is the essential properties of biomaterial. Silk is popular for its luster and mechanic properties. It is a natural filament produced by silkworm. This contains fibrous protein termed as fibroin, and that forms sericin which helps to reinforce together. Removal of sericin from silk is done for biomedical, cosmetic, biotechnological, tissue engineering, drug delivery applications in order to prevent inflammatory. Silk has more mechanical strength and it has a very high strength and toughness.

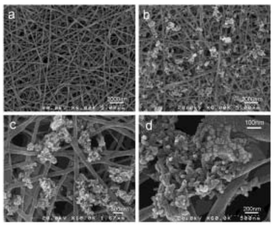


Figure 1: Silk Fibers

Properties of Silk
- Supports in cell adhesion, growth, proliferation
- Excellent luster and good texture
- Excellent temperature retain ability
- High mechanical properties, high strength and excellent elasticity
- Very good tensile strength
- Good degradability and biocompatibility

Chitin and Chitosan
Chitin is a white, hard, inelastic, nitrogenous polysaccharide found in the outer skeleton of insects, crabs, and shrimps. It is basically obtained from prawn/crab shells. Chitosan is produced by chemically treating chitin. They both are suitable material for wound healing. They are natural polymers and they have excellent biodegradability, biocompatibility, non-toxicity and adsorption. They are also antibacterial and act against fungi. They possess low mechanical strength. They are more suitable for wound dressing materials as they have a very good wound healing property.

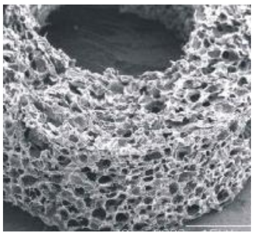


Figure 2: Chitosan

Collagen
Collagen is an important biomaterial in medical application for its excellent biocompatibility, biodegradability and weak antigenecity. Collagen makes up one quarter of all the total protein in the body. It possesses a fibrous structure and imparts strength to tissues such as tendons, ligament, and skin. It is very good to promote cell, tissue attachment and growth. It possesses low mechanical strength and has safety issues when derived from animals.

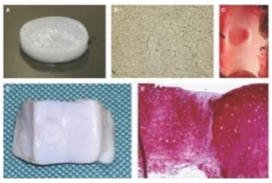


Figure 2: Collagen

Poly (Methylmethacrylate)
It is a light weight synthetic material. It is alternate to polycarbonate, where extreme strength is not necessary. It does not contain potentially harmful substance. It possesses moderate properties, easy handling, processing and low cost. It has a good degree of compatibility with human tissue. In cosmetic surgery, PMMA injected under the skin to reduce wrinkles or scars permanently. It is rresistant to inorganic solutions. It has excellent optical properties. It is suitable for Blood pump and reservoir, implantable ocular lenses, bone cement.

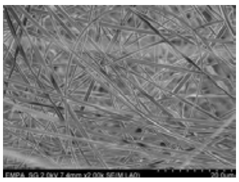


Figure 4: PMMA

Polyvinylchloride (PVC)
It is amorphous & rigid polymer, have high melt viscosity. It is made flexible and soft by the addition of plasticizers. It is suitable for blood and solution bag, surgical packaging.

Figure 5: PVC

Polyurethanes (PU)

They have excellent mechanical properties and good biocompatibility. They are used in the fabrication of medical implants such as vascular grafts. Polyurethanes can be designed o have chemical linkages that are degradable in biological environment. They are very much suitable for tissue engineering applications because of their mechanical properties and good biocompatibility.

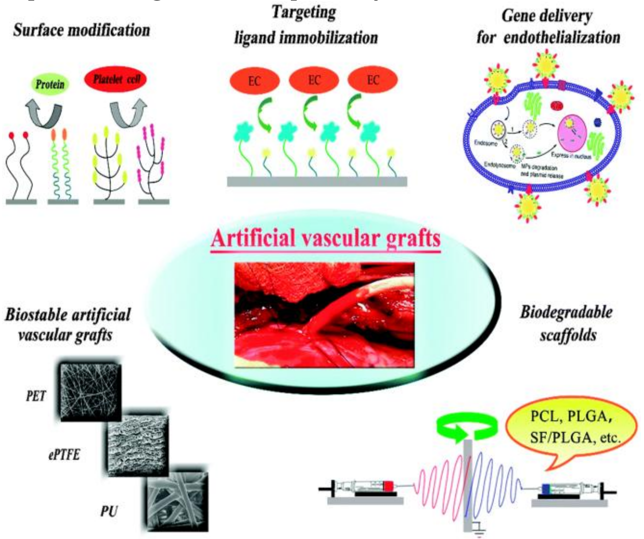


Figure 6: PU

4. Applications of Tissue Engineering

Tissue engineering is widely used in the fields as mentioned below.

4.1 Bone Tissue Engineering

It is based on physical properties of scaffolds such as mechanical strength, pore size, porosity, hardness and 3D architecture etc. Scaffolds with greater porosity are preferred for better cell/tissue-in-growth and enhanced bone regeneration. Studies have shown that PCL based nanofibrous scaffolds are potential candidates for skin tissue engineering.

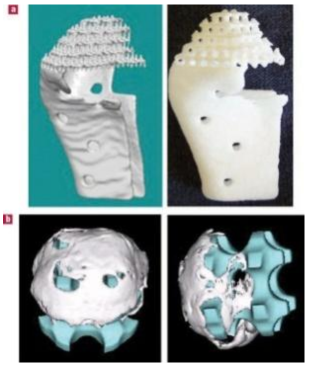


Figure 7: Bone tissue engineering

4.2 Cartilage Tissue Engineering

PCL based nanofibrous scaffolds by electrospinning are the most suitable one for this. It possesses very good mechanical properties. It has a good degradation, cell attachment and growth factor delivery.

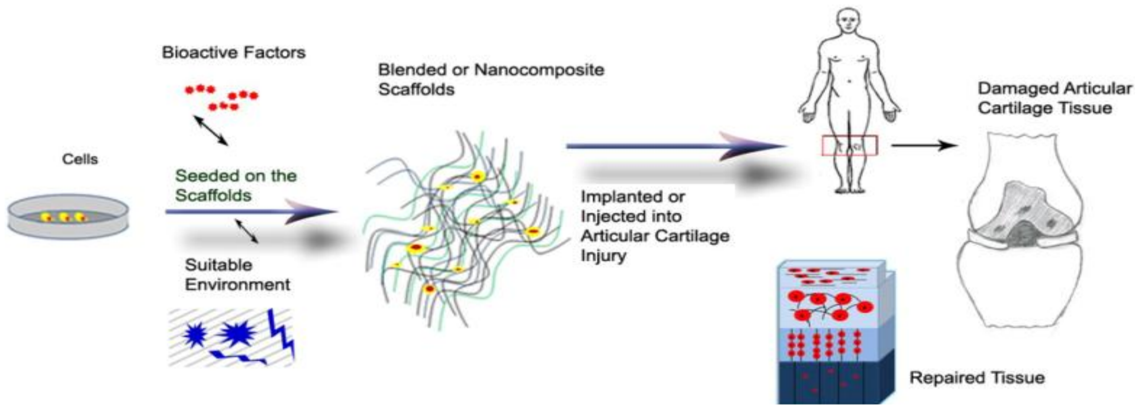


Figure 8: Cartilage tissue engineering

4.3 Ligament Tissue Engineering

They are connective tissue responsible for joint movement and stability. Ligament ruptures result in damage of connective tissues leading to tissue degenerative diseases, which do not heal naturally and cannot repair by clinical methods. PU nanofiber aligned tissue engineering successfully meet this challenge.

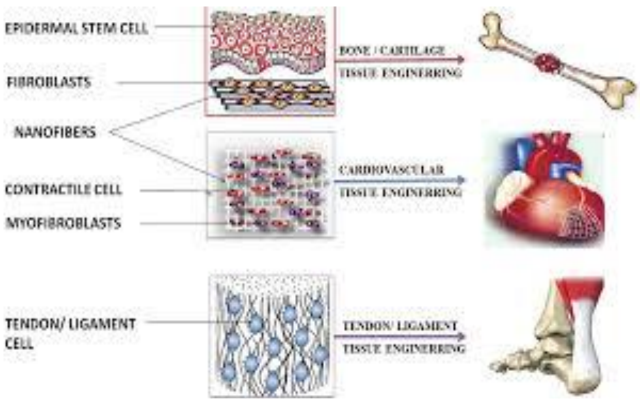


Figure 9: Ligament tissue engineering

4.4 Skin Tissue Engineering

Skin wounds heal naturally by formation by epithelialized scar tissue rather than by regeneration of full skin. Of the two of d layers of skin, epidermis and dermis, has less capacity to heal. But when large areas to be heal, normal regeneration is lacking, hence epidermis to be replaced. The scar tissue that forms in the absence of dermis lacks elasticity, flexibility and strength. Scar tissue causes pain, limit movements.

For this, skin tissue engineering is the very good alternative to stimulate the regeneration of dermis. Nonwoven based silk nanofibers by electrospinning method are much suitable for skin tissue engineering due to their high porosity and high surface area to volume. And also this coated with type I collagen is suitable to promote cell adhesion and spreading.

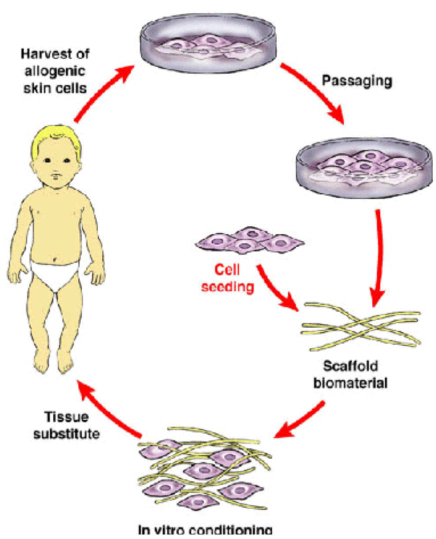


Figure 10: Skin tissue engineering

4.5 Blood Vessel Tissue Engineering

Conventional spinning method produces randomly oriented nanofibers. Biodegradable PLLA-CL nanofibers explored to fabricate tubular scaffolds that could be used for blood vessel. They mimic the natural ECM, provide mechanical properties and give a good architecture which helps for cell adhesion and proliferation.

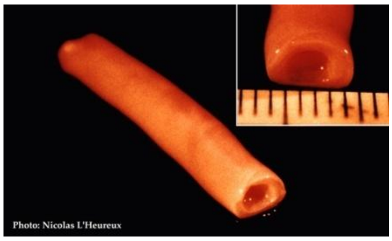


Figure 11: Blood vessel tissue engineering

5. Applications of Tissue Engineering With Suitable Polymers

Method	Polymers	Unique factors	Application
Biodegradable porous scaffold fabrication			
Solvent casting/salt leaching method [35–37]	Absorbable polymer (PLLA, PLGA, collagen, etc.)	Biodegradable controlled porous scaffolds	Bone and cartilage tissue engineering
Ice particle leaching method [38–40]	PLLA & PLGA	Control of pore structure and production of thicker scaffolds	Porous 3D scaffolds for bone tissue engineering
Gas foaming/salt leaching method [41–43]	PLLA, PLGA & PDLLA	Controlled porosity and pore structure sponge	Drug delivery and tissue engineering
Microsphere fabrication			
Solvent evaporation technique [44–46]	PLGA, PLAGA	High-density cell culture, due to the extended surface area	Bone repair
Particle aggregated scaffold [47–49]	Chitosan, HAP	High mechanical stability	Bone, cartilage, or osteochondral tissue engineering
Freeze drying method [50–52]	PLGA, PLLA, PGA, PLGA/PPF, Collagen, and Chitosan	3D porous sponge structure, durable and flexible	Tissue engineering scaffolds
Thermally induced phase separation [53, 54]	PEG, PLLA	Highly porous scaffold for cellular transplantation	Complicated shapes for tissue engineering applications
Injectable gel scaffold fabrication			
Ceramic-based injectable scaffolds [55–57]	CP ceramics, HAp, TCP, BCP, and BG	Porosity and bioresorbability	Cartilage tissue engineering
Hydrogel-basedinjectable scaffolds [58–60]	Hydrophilic/hydrophobic diblock and triblock copolymer combinations of PLA, PGA, PLGA, and PEG. Copolymers of PEO and PPO and polyoxamer. alginates, collagen, chitosan, HA, and fibroin	Biomimetically, exhibit biocompatibility and cause minimal inflammatory responses, thrombosis, and tissue damage	Cartilage, bone tissue engineering, and drug delivery

Hydrogel scaffold fabrication			
Micromolding [61–63]	Alginate, PMMA, HA, PEG	Microgels, biologically degradable, mechanical and physical Complexity	Insulin delivery, gene therapy, bioreactor, and immunoisolation
Photolithography [64–66]	Chitosan, fibronectin, HA, PEG, PNIAAm, PAA, PMMA, PAam, and PDMAEM	Microwells, microarrays, controlled size and shape	Microdevices, biosensors, growth factors, matrix components, forces, and cell-cell interactions
Microfluidics [67–69]	PGS, PEG, calcium alginate, silicon and PDMS	Microbeads, microrods, valves, and pumps	Sensing, cell separation, cell-based microreactors, and controlled microreactors,
Emulsification [70–72]	Gelatin, HA, and collagen	Microgels, microsensors, cell-based diagnostics	Sustainable and controllable drug delivery therapies
Acellular scaffold fabrication			
Decellularisation process [73–75]	Biological tissues	Retain anatomical structure, native ECM, and similar biomechanical properties	Tissue engineering
Keratin scaffold fabrication			
Self-assembled process [76–78]	Keratin	Biocompatibility	Drug delivery, wound healing, soft tissue augmentation, synthetic skin, coatings for implants, and scaffolds for tissue engineering

Method	Polymers	Unique factors	Application
Fibrous scaffold fabrication			
Nanofiber electrospinning process [79–81]	PGA, PLA, PLGA, PCL copolymers, collagen, elastin, and so forth	High surface area, biomechanical, and biocompatibility	Drug delivery, wound healing, soft tissue synthetic skin, and scaffolds for tissue engineering
Microfiber wet-spinning process [82–84]	PLGA, PLA, chitosan, and PCL	Biocompatible fibres with good mechanical properties	Solar sails, reinforcement, vascular grafts, nonwetting textile surfaces, and scaffolds for tissue
Nonwoven fibre by melt-blown process [85–87]	Polyesters, PGA, and PDO	Submicron fiber size, highly porous scaffold	Filtration, membrane separation, protective military clothing, biosensors, wound dressings, and scaffolds for tissue engineering
Functional scaffold fabrication			
Growth factor's release process [88–90]	Collagen, gelatin, alginate, chitosan, fibrin, PLGA, PLA, and PEG	Membranes, hydrogels, foams, microsphere, and particles	Angiogenesis, bone regeneration, and wound healing
Ceramic scaffold fabrication			
Sponge replication method [91–93]	PU sponge, PVA, TCP, BCP or calcium sulfate	Interconnected porous ceramic scaffolds	Bone tissue engineering
Simple calcium phosphate coating method [94–96]	Coating on: metals, glasses, inorganic ceramics and organic polymers (PLGA, PS, PP, silicone, and PTFE), collagens, fibres of silk, and hairs	Improve biocompatibility or enhance the bioreactivity	Orthopedic application
Automation and direct organ fabrication			
Inkjet printing process [97–100]	Sodium alginate	To build complex tissues composed of multiple cell types (Hydrogel scaffold)	Biosensor development, microdeposition of active proteins on cellulose, biochips and acellular polymeric scaffolds
Melt-based rapid prototyping process [101, 102]	Biodegradeable polymers or blends	Complex 3D solid object, good mechanical strength	Honey comb structure scaffold, hard-tissue scaffolds
Computer-aided design (CAD) data manipulation techniques [103–105]		Design and fabrication of patient-specific scaffolds and automated scaffold assembly algorithm	Develop a program algorithm that can be used to design scaffold internal architectures
Organ printing [106, 107]	Tubular collagen gel	Layer by layer deposition of cells or matrix	To print complex 3D organs with computer-controlled,

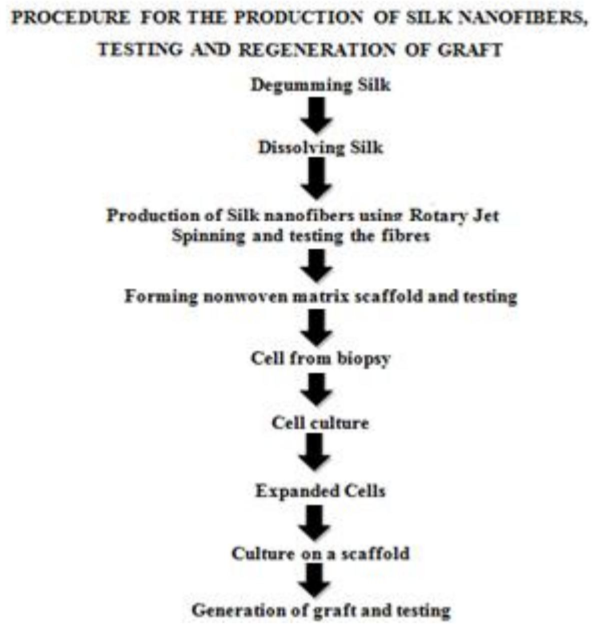
Scaffold sterilization		
Ethylene oxide gas (EOG) [108–110]	For degradable polymers and porous scaffolds, high penetration ability, and compatibility	Absolute freedom from biological contamination in scaffolds
Gamma-radiation sterilization [111–113]	Proven process is safe, reliable, and highly effective at treating single-use medical devices	Surgical disposables: surgical sutures, bandages, dressings, gauge pads, implants
Electron beam radiation [114–116]	Compatibility, low penetration, in line sterilization of thin products	Commercially successful technology for sterilizing a variety of disposable medical devices with a wide range of densities
Dry-heat sterilization [117, 118]	Efficacy, speed, process simplicity, and lack of toxic residues	Heat is absorbed by the exterior surface of scaffold and then passed inward to the next layer
Steam sterilization [119, 120]	Removal of all contamination, and scaffold can be reused	Porous scaffold for living cell immobilization

6. Research and Trends

Research in tissue engineering has revealed the design rules for joining cells with materials and for understanding the mechanism by which cellular functions can be influenced or interrogated by materials. Development of cell based micro-systems outside tissue engineering will in the long term provide technologies that will be applied to tissue engineering. The technology developed to integrate the functions of cells with electrical or mechanical processes in materials will have important benefits to the growth of tissue for transplantation and for prosthetic interfaces between indwelling devices and natural tissue.

Cell based engineering addresses the development of hybrid devices that combine cellular and tissue components with conventional materials and processes found in micro-fabrication. Research and development activities span a broad range of topics including technical development of methods and fabrication routes to join cells with materials, exploratory and discovery research to identify strategies for matching cellular processes with materials processes, and engineering of complete systems that exploit the unique realization that combining man made devices and biological systems.
Many consolidated findings that stem have enhanced the comprehension of molecular and process related to various diseases and physiological properties. Knowledge been applied to various types of medical treatments, such as creating intelligent biological drug system, and also helpful to better medical systems such as apoptosis and carcinogenesis. It must help us from mechanisms of aging, human development, and prevent from cancer, heart disease, mental illness, as well as several conditions. Hopefully it may help to successfully treat malignant disease in future.

Silk



Degumming of Silk
Silk is degummed with 1g/L of Na_2Co_3 for 45 minutes and 80^o C and washed.

Recipe
MLR – 1:50
Na_2Co_3 - 1g/L
Soap – 5g/L

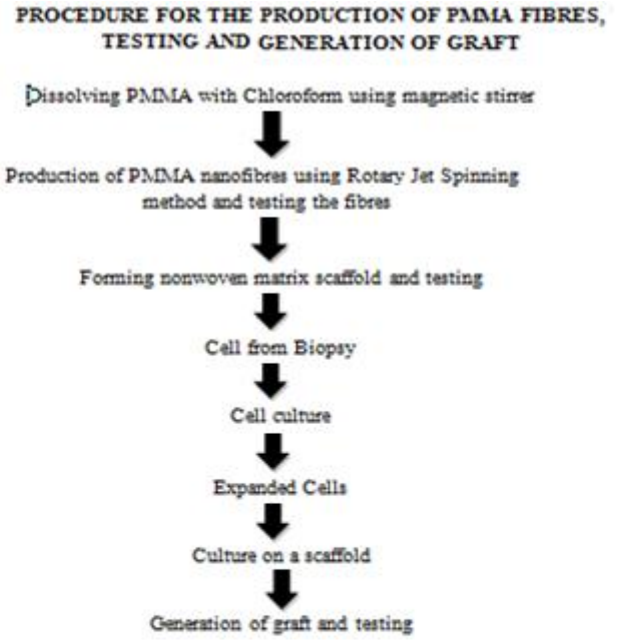
Dissolving Silk In Libr
50 ml of LiBr solution at 9.3M concentration, calculated amount of LiBr powder is 40.4 grams, which is dissolved in 32-33ml water. Then 2 grams of Silk is dissolved in 10 ml of 9.3M LiBr solution at 60^oC for 4 hours in a closed container.

Stirring Silk Using Magnetic Stirrer
Silk solution is stirred using magnetic stirrer till it reaches the gel state.

Silk Spinning Using Rotary Jet Spinning Method
The prepared polymer solution gel is poured into the reservoir of the RJS machine. As soon as the machine is switched on, with the help of the controllable motor, reservoir starts to rotate. There is a hole made in the

reservoir. Due to the centrifugal force, polymer inside the reservoir ejects out and forms a thin ribbon like fibre structure, which is collected in the collector. The fibre forms it own path during rotation.

PMMA



Stirring PMMA Using Magnetic Stirrer

2 grams of PMMA is taken with 10ml of Chloroform in a beaker. And it is stirred using magnetic stirrer till the polymers are completely dissolved in Chloroform and homogeneous mixture of solution is formed. The process is carried out till it reaches the gel state.

PMMA Spinning Using Rotary Jet Spinning Method

The prepared polymer solution gel is poured into the reservoir of the RJS machine. As soon as the machine is switched on, with the help of the controllable motor, reservoir starts to rotate. There is a hole made in the reservoir. Due to the centrifugal force, polymer inside the reservoir ejects out and forms a thin ribbon like fibre structure, which is collected in the collector. The fibre forms it own path during rotation.

7. Conclusion

Thus Silk has a very good biocompatibility, biodegradability, high surface area to volume, improved mechanical properties and hence very much suitable for skin tissue engineering. PMMA are light weight, which does not contain potentially harmful substance, moderate properties, easy handling, easy processing and low cost, good degree of compatibility with human tissue. Hence it is very much suitable for craniofacial and bone tissue engineering. In cosmetic surgery, PMMA injected under the skin to reduce wrinkles or scars permanently.

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