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SYNTHETIC BONE SCAFFOLDS IN TISSUE ENGINEERING

Bavithra P.S.*, Monisha M., Swathi G. and Arun P.

Department of Biotechnology, Dr. N.G.P. Arts and Science College (Autonomous), Coimbatore – 48, Tamil Nadu, India.

***Corresponding Author: Bavithra P.S.**

Department of Biotechnology, Dr. N.G.P. Arts and Science College (Autonomous), Coimbatore - 48, Tamil Nadu, India.

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ABSTRACT

The bone scaffolds play major role in regeneration of fractured bones. They can either be natural or artificial scaffolds. Traditionally, bone grafts were used for replacing the fractures, now it has widely been replaced by synthetic scaffolds. Synthetic scaffolds have been studied on a greater extent especially for their biocompatibility, biodegradability, mechanical strength and non-toxic nature. Later studies were concentrated on engineering the scaffolds to be more bioactive or more bioresorbable to enhance tissue growth. The bone scaffolds are designed to induce bone formation and vascularization, and hence are often porous and harbor growth factors, drug, genes or stem cells. The scaffolds are crucial in healing and it must be appropriate and must not bring any other new ailments while healing. There are several studies on the scaffolds used in tissue engineering but this study focuses on the wide range of the scaffolds, particularly those being used for bones.

KEYWORDS: Bone Scaffolds, Biocompatibility, Biodegradation, Osteogenesis, Bioglass, Polymers.

INTRODUCTION

Autografts are the gold standard for treatment of bone defects but limited supply and donor site morbidity are significant problems. Bone allografts are alternatives to autografts but they are expensive, and suffer from potential risks such as disease transmission and adverse host immune response. Synthetic biomaterials would be ideal bone substitutes, but the clinical success of procedures performed with available synthetic biomaterials does not currently approach that for autologous bone. Allografts and xenografts may raise other concerns in pathogen transmission and immunorejection, respectively.

Metallic implants have well-documented fixation problems, and unlike natural bone, cannot self-repair or adapt to changing physiological conditions. They are stronger and stiffer than bone and promote bone resorption by shielding the surrounding skeleton from its normal stress levels. Therefore, they tend to become unconstrained as time passes.

Therefore, the event of using artificial materials for system tissue engineering is predominant so as to satisfy the booming demand of orthopedical implantations. Scaffolds are used to replace the damaged organs or organ systems due to an injury or disease. The tissue engineering has opened a wide scope for the replacement of damaged organs through the use of polymeric scaffolds and their biodegradability is greatly enhanced to support the regeneration of the cells on their own.

The biopolymers especially are biocompatible, highly biodegradable, and less toxic and also maintain a great degree of flexibility. These scaffold implants are not tended to be permanent and hence, biodegradable scaffolds are used and it provides the regeneration of the tissue during its due time. This has greatly changed the face of surgery for damaged organs and has brought new hope for the patients undergoing treatment for affected/damaged organs.

Bone scaffolds have been of interest because it relieves the patient of the pain of double surgery for insertion and removal of plate that supports in the regeneration of the bones. The natural scaffolds like collagen, chitosan, alginate, silk fibroin, hyaluronic acid and peptide hydrogels are the most commonly used ones.

Bone Properties

Bone can be seen as an open cell composite material composed of osteogenic cells Extracellular Matrix (ECM) proteins, growth factors, mineral calcium in the form of Calcium hydroxyapatite, and a complex vascular system. The cells that make up the bone represent about 10% of the total volume and include osteoprogenitor cells of mesenchymal origin, i.e., osteoblasts and osteocytes and bone-resorptive cells of hematopoietic origin, i.e., osteoclast. The bones are composed of collagen, minerals, proteins and water.

Osteoblast differentiation occurs in three stages: (1) cell proliferation, (2) matrix maturation, and (3) matrix mineralization. During the proliferation stage ECM proteins are expressed and secreted by osteoblasts forming the non-mineralized bone matrix or osteoid. Following this, the proteins of the osteoid are cross-linked during matrix maturation that forms a stronger and more stable structure. Osteoclasts are giant, multinucleated cells that attach to bone matrix through a brush border, which on acidification causes the solubilization of its mineral content.

This process is tightly regulated via the paracrine co-regulation between osteoclasts and osteoblasts in a process called bone remodeling. The main recognized functions of bone transforming embody preservation of bone mechanical strength by substituting older, microdamaged bone, with newer, healthier bone and calcium and phosphate homeostasis.

The mechanical properties of bone vary with its anatomical location in the body and can be considered as anisotropic material. For instance, there is great variability in Young's modulus of elasticity, tensile and compressive strengths between the longitudinal and transverse loadings. In contrast, cancellous bone does not show a consistent mechanical strength and varies both longitudinally and from one bone to another. Therefore, as a result, on comparison with cortical bone, the cancellous bone exhibits much broader mechanical properties. The trabeculae of cancellate bone follow the lines of stress that may be realigned by changes within the direction of stress.

Artificial Bone Scaffolds

Metallic implants like stainless steel have long been used in the medical field as support for the bone repair. Artificial bone scaffolds vary from metals, ceramics to polymers, bioglass and composites. The synthetic polymers used in bone scaffolds are of significance due to their strength, toughness and reliability. The most commonly used aliphatic polymers are poly (lactic-acid), poly (glycolic-acid) and poly (caprolactone) and their copolymers. They are biocompatible, biodegradable, and can be easily fabricated into any shape. They have mechanical strength as well that serves a wide application in orthopedics. Other synthetic polymers in bone tissue engineering includes poly (methyl methacrylate), poly (e-caprolactone), poly hydroxyl butyrate, polyethylene, polypropylene, polyurethane, poly (-ethylene terephthalate), poly ether ketone, and poly sulfone.

Polymers

Synthetic polymers represent the most important category of biomaterials that are helpful in applications for soft as well as arduous tissue. Poly (methyl methacrylate), commonly known as PMMA, is widely used as bone cement while porous PMMA are utilized as bone scaffolds.

Aliphatic polyesters such as polyglycolic acid, polylactic acid, and polycaprolactone are the most commonly used polyesters for tissue engineering applications. These on degradation produce products that are similar to the own metabolic products and therefore are capable of removal by our own metabolic pathways. 3D scaffolds from these materials can be fabricated through various techniques, and tuning the molar ratios of these polymers can influence mechanical properties and degradation rates.

The porous scaffolds composed of Poly (L-lactide-co-ε-caprolactone (poly(LLA-co-CL)) and poly(L-lactide-co-1,5-dioxepan-2-one), (poly(LLA-co-DXO)) were evaluated and compared for potential use in bone tissue engineering constructs.

The polymer scaffold degradation is required for the regeneration of a natural tissue implant. The four stages of scaffold degradation are (i) hydration, (ii) loss of tensile strength, (iii) loss of mass, and (iv) solubilization.

Copolymers generally are enticed for tissue engineering applications due to their highly controllable physicochemical properties. Gel formation dynamics, crosslinking density, and material mechanical and degradation properties can be controlled by regulating molecular weights, block structures, degradable linkages, and crosslinking modes.

Hydrogels are the new addition to the polymers that are novel and popular. As an associate example for their degradable water containing substances they are injectable and thereby consist of different water contents and may even consist of Poly-(ethylene glycol), or gelatin.

Ceramics

Ceramics are an oversized family of inorganic/non-metallic compositions with a wide range of characteristics that vary with their processing technique. They can be dense, porous or non-porous and resorbable like tricalcium-phosphate, porous, inert and lead to bone ingrowth like hydroxyapatite-coated porous metals, or dense, non-porous, surface active materials, and are capable of attachment just like hydroxyapatite to our bone by chemical bonding.

Calcium phosphates represent a cluster of materials, whose properties depend on the ratio of calcium-phosphate and modification of crystallinity and porosity. They are biocompatible, osteoconductive and degradable. Based on the type of material, the degradation time varies from a few months to years.

Calcium phosphate ceramic blocks are brittle, extremely prone to fatigue fractures and hence their use is limited to simple bone replacements rather than complex weight bearing locations. Calcium phosphate cements can overcome this problem partially as they can be administered in paste form and injected into bone defects, which makes adaptation to local requirements very easy. They can also be administered through injections to the tissues without the need of operating. They harden without elevation of temperature. The cement setting results vary as either brushite-cement (pH ≤ 4, 2) or hydroxyapatite (pH > 4, 2) depending on their individual composition and pH.

The calcium orthophosphate cements are broadly classified into four major classes, viz., dicalciumphosphate dihydrate, calcium and magnesium phosphates, octocalciumphosphate and non-stoichiometric apatite cements.

Hydroxyapatite is used as implant coating, granules and in block structure. It easily attaches close to a bone as their chemical compositions are similar. They even stimulate bone growth in osteoporotic bones and are able to fill gaps between bone and implants up to 2mm. Therefore, the implants coated with hydroxyapaite integrate with the bone healing process. Hence, this osteophilic characteristic feature of the implant acts as a good substrate for osteoblasts. Considering all these, the hydroxyapatite is quite commonly used as a coating of implants.

A few scientists have found that such use may lead to osteolysis when the implant used is in close proximity with bone marrow as well as soft tissues. There, the hydroxyapatite wear debris is thought as the main cause for implant failure as its phagocytosis stimulates the release of cytokines. As a result, these implants are to be held responsible for (granulomatous) inflammation that causes disturbance during bone remodelling and in local osteolysis.

Bioglass

Since the discovery of 45S5 bioactive glasses by Hench, they have been frequently considered as scaffold materials for bone repair. Bioglasses have a widely recognized ability to foster the growth of bone cells, and to bond strongly with hard and soft tissue. Upon implantation, bioglasses undergo specific reactions, leading to the formation of an amorphous calcium phosphate (ACP) or crystalline hydroxyapatite (HA) phase on the surface of the glass that mediates bonding with the host tissue. Bioactive glasses are also reported to release ions that activate expression of osteogenic genes, and to stimulate angiogenesis.

The advantages of the glasses are ease in controlling chemical composition and, thus, the rate of degradation which make them attractive as scaffold materials. The structure and chemistry of glasses can be tailored over a wide range by changing either composition, or thermal or environmental processing history. Therefore, it is possible to design glass scaffolds with variable degradation rates to match that of bone ingrowth and remodeling.

A limiting factor in the use of bioactive glass scaffolds for the repair of defects in load-bearing bones has been their low strength. Recent work has shown that by optimizing the composition, processing and sintering conditions, bioactive glass scaffolds can be created with predesigned pore architectures and with strength comparable to human trabecular and cortical bones. Another limiting factor of bioactive glass scaffolds has been the brittleness. This limitation has received little interest in the scientific community, judging from the paucity of publications that report on properties such as fracture toughness, reliability, or work of fracture of glass scaffolds.

Issues in Bone Scaffolds

Many studies have shown excellent biocompatibility, biodegradability and mechanical strength. Apart from these there remain a few key challenges in regards to the bone scaffolds which are: (i) biocompatibility and biomechanical strength in polymeric scaffolds, (ii) metal ion release, limited bioactivity and biodegradation for metallic scaffolds, and (iii) toughness as well as reliable and reproducible manufacturing techniques for ceramic scaffolds.

The Scaffolds are usually composed with porous nature to facilitate the seeded cells to grow, in essence there are also osteogenic and angiogenic agents added. However, organization of porosity in the scaffolds can play a significant role in the quality of bone formation. Understanding associated with the effects of pore orientation on quality and the amount of bone formation is required for designing the optimal performance of bone scaffolds.

CONCLUSION

Scaffolds being the emerging trend in treating bone related issues have drastically improved in the recent years. Traditional autograft and allografts have been greatly replaced by synthetic scaffolds for the greater control that can be exerted by the designers. The scaffolds are greatly managed by varying the mixtures and finding the right proportion to be effective in their own way. According to each patient and the depth of damage the design and fabrication of scaffolds vary.

The scaffolds must be biocompatible, biodegradable and non-toxic and at the same time, they must have high mechanical strength to support the bones. Also, their porosity must also be considered accounting to their ability to help in enhancement of the regeneration of the damaged tissues. The porosity also helps in the development of the cells seeded in the scaffolds.

The polymers, copolymers, bioglass and ceramics are in their own way helpful in making the scaffolds which vary according to their usage and the region of bone that is damaged. The mixtures of the scaffolds used could also be influenced according to their need.

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