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ABSTRACT

The development of biomaterials for scaffold and tissue engineering are in great advancement. Porous materials like bioceramic and polymer components for supporting bone tissue and cell growth are becoming an area of great interest in research [1]. Traditionally, biodegradable polymers have been used as scaffold material [2]. However, these materials are weak and non-osteoconductive. Polymer-based composite scaffolds containing bioceramics was then used to substitute the material. Thus, it is strongly believed that the bioceramic phase delivers the bioactivity and improves scaffolds strength. In addition to that, recently the engineering of biomaterial focused on the kind of material which can mimic both the mechanical and biological properties of real bone tissue matrix and this method known as biomimetic [3]. Other than that, there are also other recent challenges where scientists are also looking for biomaterials which can support the development of new blood vessels and large tissue formation. This paper was intended to demonstrate an overview of the current and potentially future development of composite bioceramic based scaffolds for bone tissue engineering.

Keywords: Scaffold, biomaterial, bioceramic

INTRODUCTION

The development of biomaterials for scaffold and tissue engineering are in great advancement. Porous materials like bioceramic and polymer components for supporting bone tissue and cell growth are becoming an area of great interest in research [1]. Previously materials were designed to be bioinert just to replace defected and injured hard tissue. However, with the development of technology the purpose of materials design nowadays has been shifted to be bioactive which combines with biological molecules or cells and stimulate tissues [1, 4].

An ideal scaffold for bone regeneration requires many criteria. The basic criterion of the scaffold material is that the materials should preferably be both osteoinductive and osteoconductive. Osteoinductive is the ability to promote the new osteoblast generation from the mother cell. Osteoconductive is to encourage bone growth and support the ingrowths of surrounding bone. They must also be osseointegration which means can integrate into surrounding bone [1].

The new challenge today is to design scaffolds which can mimic the composition and properties of the organ which they aim to replace such as bone which has a complicated hierarchical structure. Another challenge is to design scaffolds that can stimulate and facilitate full bone regeneration in three dimensions and then degrading simultaneously with the growth of the new tissue. The scaffolds must also mechanically capable to support the work loading during the forming of the new tissue until the new tissue bond is strong enough to accept the loading [5].

The most important consideration today is to determine the size of porosity of the scaffold so that it can assure the bone vascularization. This is because if the blood vessels does not reach the scaffold, the new formed tissues will fail to function. To date, the suggested porosity for successful bone ingrowths and sufficient oxygenation are 100 μm. Other than that, scaffolds material should also be compatible with the bonding environment and its requirement [1, 5].

There are several materials which have been designed for implantation that are therefore candidate materials for scaffolds development. In general, they consist of either synthetic polymers or bioactive materials, including bioactive glasses, bioactive glass-ceramics, bioactive calcium phosphate ceramics and bioactive composites and coatings. However to date there are still no such material that can fulfill all the criteria. Here, we present some of the materials which have been used in the tissue engineering and scaffolding for the past four decades.

TYPE OF SCAFFOLD MATERIALS

Polymers

Previously, biological polymers like collagen and hyaluronic acid and synthetic polymers like polyfumarates, polylactic acid (PLA), polyglycolic acid (PGA), copolymers of PLA and PGA (PLGA), and polycaprolactone has been used as bone implant. These polymers can attach well with cells and promote chemotactic responses. They have been accepted by medical-profession-accepted and the US Food and Drug Administration (FDA) as the suitable material for tissue substitute [1]. However the strength of these materials are very weak and will reduce further if porosity is applied to them. Furthermore the materials are also non-osteoconductive [2].

Recently bioactive bioceramics like tricalcium phosphate, Hydroxyapatite (HA), bioactive glasses, and their combinations have broadly been used for bone tissue engineering applications. These bioactive bioceramics is potentially use for bone tissue engineering and the development of scaffolds.

Bioactive Glass

One of the bioactive glass which often used to repair bone defects is synthetic hydroxyapatite (sHA,$Ca_{10}(PO_4)_6OH_2$) since its mineral, carbonated hydroxyapatite has the similarity with mineral of the natural bone. The bioactive glass also proven to be bioactive and osteoconductive. The weakness of this material is that it resorbtion rate is very slow. We can increase the resorbtion rate by adding silicon or carbonate substituted apatites. However the increasing rate is not much different with the previous. Thus, the bioactive glass can only be used as an implant of the damage bone but not for bone regeneration scaffold [6].

Bioglass®.
In 1971, Professor Larry Hench launched the alternative bioactive glass, the Bioglass® with the composition Na_2O-CaO-P_2O_5-SiO_2 system with B_2O_3 and CaF_2 additions. This bioglass formed a strong supporter for the bone bonding. [7] The advantages of this material are they are bioactive. In vitro tests showed that they form a carbonated apatite layer on their surface which is chemically and structurally similar to the mineral phase in bone thus enhancing the bonding of the bone [8]. In addition, they are osteoinductive since they can generate new bone to grow when they dissolve in the body. They discharge critical concentrations of active ions and inspire the genes with osteogenic cells [9]. However, this material resolve on sintering and form a glass-ceramic. Due to that, Bioglass cannot be made into a scaffold. [10]

A-W glass-ceramic
Kokubo et al. has developed a new glass-ceramic, Apatite-wollastonite (A-W) glass-ceramic in 1982. It has the highest bending strength, fracture toughness and Young's modulus among bioactive glass and glass ceramics. This criteria fulfills some major compression load bearing applications like vertebral prostheses and iliac crest replacement. It combines high bioactivity with suitable mechanical properties. [11]

Calcium Phosphate
Levitt et al. have discovered that calcium phosphate is a mineral component in the natural bone in 1969 [12]. Then, several researches were conducted on synthetic calcium phosphate ceramics, Hydroxyapatite (HA) between 1980 and 1990. Hence, it became the most popular synthetic ceramic for implantation. Calcium phosphates are now used for a variety of different applications covering all part of the bone such as spinal fusion, restoration of craniomaxillofacial, bone defects and breakage healing, substitution of total joint and revision surgery [4]. Calcium phosphate implants especially hydroxyapatite, also has been used in the form of coatings on metallic implants, as fillers in polymer matrices, as self setting bone cements, as granules or as larger, shaped structures.

In 1980s de Groot et al introduced the hip prostheses femoral stems which was plasma sprayed with hydroxyapatite [13]. The plasma-sprayed stems were first implanted in patients by Furlong and Osborn [14]. This Hydroxyapatite-coated implant was clinically proved to have much longer life times after implantation than uncoated devices. It was also found that, this implantation is better on young patients [15].

The prospect of calcium phosphate as a filler in polymer-matrix composites was done by Dr. Bonfield's research group. The material was successfully developed as middle ear implants and marketed under the name HAPEX® [16]. The advantage of using this polymer-ceramic composites is that we can set desirable mechanical properties such as the strength via the ceramic phase and the toughness via the polymer phase. Another advantage of the materials is that they can easily can be shaped due to their softness and flexibility [17].

The potential of calcium phosphate for in situ molding and instill bone cements was also being discussed in 1980s. These bone cements is formulated based on different combinations of calcium compounds like tricalcium phosphate and dicalcium phosphate. However the final output is always calcium deficient hydroxyapatite [18, 19].

The development of chemically synthesized materials with reproducible structures and chemical composition has become important to replace natural bone for bone grafting. This is due to the limited availability of the natural bone. Bonfield, Best and co-workers has studied on the development of silicate-substituted hydroxyapatites (Si-HA) as the potential bone graft materials [20]. Proteins and cells is included into the HA implant in order to improve its integration with bone. In vivo studies, comparing the rates of bone apposition to HA and Si-HA ceramic implants, demonstrated a significant increase in amount of bone apposition and organization to around silicon substituted HA (Si-HA) implants.

Bioctive Composites and Coatings

Bioglasses, glass-ceramics and calcium phosphate ceramics is said to have outstanding bioactivity since the bond from these materials is generally stronger or equal to the host bone. The drawback of these bioactive ceramics is that they are less elastic and have weaker fracture toughness compared to bone. Hence, they are not biomechanically compatible for load bearing applications. In order to overcome this problem, structural tailoring of bioactive composites or coatings is applied [21].

A bioactive composite is a mixing of the polymer toughness and the inorganic strength to produce the kind of material which can mimic both the mechanical and biological properties of real bone tissue matrix and this method known as biomimetic. The composite also neutralizes the acidity of the polymer with alkalinity of the inorganic stuff [3]. Other than that, there are also other recent challenges where scientists are also looking for strong porosity biomaterials which can support the development of new blood vessels and large tissue formation.

Applying these materials as a coating on a mechanically tough substrate is the other method to overcome the load-bearing applications weakness. The bioactive coating materials have the excellent bioactivity of the bioactive glasses or ceramics, as well as the advantageous mechanical properties of metals or alumina. The bone-bonding capacity of these coating may help provide cementless fixation of orthopedic prostheses, especially in short term stabilization of the implants. But in long term implantation, the bioactive coating materials have deficiencies with respect to reliability of the coating/implant interface.

Sol-gel Glasses

Sol-gel glasses are derived from the early bioactive glasses. The sol-gel route can generate high purity glasses, which are more homogeneous than the early bioactive glasses. They have the strength which is similar to cancellous bone. They demonstrate higher surface area and porosity than the dense melt-derived glasses. They fulfill requirement of the osteogenic properties. Furthermore, their nanoporosity elements serve a controlled degradation and provide area for the cell to attach and the adsorption of the protein. In addition, the porosity is suitable for vascularised bone ingrowths.

The sol-gel can be composed with functionalised biodegradable polymers to produce inorganic-organic hybrid nanoscale composites. Hence, we can have the material which blend the bone bonding and bioactive ion release with toughness and controlled degradation. However, the chemistry and materials processing routes are complex, so the ideal materials are yet to be developed.

DISCUSSION AND CONCLUSSION

We have discussed some dramatic improvement in the engineering of biomaterial for medical usage especially in the numerous bioceramics being used in clinical application and also the quality of bone engineering they have delivered. However, the design criteria for an ideal scaffold for bone regeneration have not been fulfilled sufficiently. There is still potential development to be made in this field. Scientists and engineers are still required to research the ideal material that combines all the criteria of an excellent scaffold and at the same time need to determine the matrix of the scaffold. From our finding, we can list down the excellent criteria as follows:

1. Porosity size supports bone vascularization, bone ingrowths and sufficient oxygenation and degrading simultaneously with the growth of the new tissue
2. Mimic the composition and properties of real bone
3. Have the osteoinductive, osteoconductive and bioactive quality
4. Have the mechanical strength to support the work loading during the bone bonding.

Finally, the advancement of the scaffolding material technology is drifting and we hope to see forward more new composition materials which potentially could demonstrate the quality of the real bone in the future.

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