

Nanocomposite materials in orthopedic applications

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Abstract This chapter is an introduction to nanocomposite materials and its classifications with emphasis on orthopedic application. It covers different types of matrix nanocomposites including ceramics, metal, polymer and natural-based nanocomposites with the main features and applications in the orthopedic. In addition, it presents structure, composition, and biomechanical features of bone as a natural nanocomposite. Finally, it deliberately presents developing methods for nanocomposites bone grafting.

Keywords nanocomposite materials, orthopedic applications, bone grafting nanocomposites, nanocomposites classification

1 Introduction

Nanocomposite materials are known as the materials of the 21st century owing to the unique design and properties which are not similar to the conventional composite materials [1]. They are defined as a new type of composites as they show excellent properties compare to the microscale materials. These new type of materials are considered as potential candidates to meet the emerging demand in advanced technologies [2]. There are many types of nanocomposite which are prepared in different processes, however, there is still a big challenge for the researchers to overcome the problems associated with nano size materials [3]. Therefore, there is a great opportunity and tremendous interest in investigation on nanocomposite materials in a wide range of areas [4]. Recently, there are growing needs for bone tissue substitutes due to the huge rise in the number of elderly populations and patients with trauma and bone cancer [5]. According to the statistical reports, about 6.3 million bone fractures occur in the

United States of America annually [6]. In addition, investigators predict that there will be about 6.3 million hip fractures in 2050 while it was 1.7 million in 1990 [7]. Over the past 25 years, different types of composite materials have been developed and applied to fulfill a broad diversity of orthopedic requirements. In all orthopedic implants, a variety of features such as physicochemical, mechanical, and biological properties is required as key factors to increase the success rate of implantation [8,9]. Recently, development in nanocomposites provides an excellent potential to enhance the performance of current orthopedic implants [10]. It is believed that nanocomposites and nanostructure materials play a key role in orthopedic applications since bone itself is an amazing and true nanocomposite [11].

2 What is nanocomposite?

Nanocomposites have been studied for more than 50 years [12]. However, the significance of nanocomposite materials in many applications have been revealed as early as 1990 [1]. Since then nanocomposite science and engineering have appeared in all field of materials such as biomaterials, ceramics and more. Nanocomposite is a heterogeneous combination of two or more materials with different properties in which at least one of the material is in the scale of nano (less than 100 nm) [13,14]. Developing nanocomposites is an effort to blend the best properties of materials to create an efficient material with unique properties and big design opportunities [15]. The unique characteristics of nanocomposites can be derived from the effective mixture of original components into a single material. The structure of nanocomposites consists the reinforcement in the form of nanoparticles, nanofibres, nanotubes plus the matrix material [16]. The applications of nanocomposite materials is expanding rapidly in many fields such as bone cement [17], solar cell [18], and filter membranes [19]. Due to the control of composition and

stoichiometry in the nanocomposite materials, it is believed that they can be applied as an alternative candidate to limit the restriction of microcomposite and monolithic materials [1,20]. The overall insight of nanocomposites properties has still considered as a big challenge for the researchers. It is indicated that changes in the properties of materials occur when the size is less than a certain level, which is called as critical level [1]. Moreover, with the decrease of dimension to the nano level, the interactions at phase interfaces become significantly enhanced which is important on the improvement of materials properties. In this regard, the surface area/volume ratio of reinforcement in nanocomposite materials is very critical in determining the structure-property relationships [1,21]. The properties of nanocomposites depend on different factors such as the matrix dimension, loading, shape, orientation, and degree of dispersion of the second phase [21]. To date, many nanocomposite materials have been developed and used in orthopedics application. For instance, it is known that tricalcium phosphate (TCP) is similar to the natural bone in terms of chemical properties therefore, is applied as a suitable candidate in bioresorbable bone healing devices [22]. However, it is not considered as good material for load-bearing sites due to the brittleness and low bending strength [23]. Swain et al. [24] developed a β -TCP-matrix nanocomposite containing 30 vol-% iron (Fe), with and without silver (Ag). Findings revealed that all the nanocomposites prepared in different concentrations have superior mechanical strength with several folds higher than that of pure β -TCP. Incorporation of Fe with Ag results in an increase in both strength and ductility [24]. In addition, owing to the antimicrobial properties of Ag [25], the developed β -TCP-FeAg nanocomposites provides the significant antibacterial effect.

2.1 Classification of nanocomposites

Nanocomposite materials used in orthopedic applications are classified into four different categories including ceramic, metal, polymer, and natural-based nanocompo-

sites. The details regarding structures and properties of these four types of nanocomposites with emphasis on the orthopedic application are discussed as follow.

2.1.1 Ceramic nanocomposites

Ceramic matrix nanocomposites (CMNC) are a subgroup of nanocomposite materials which have been shown to be extremely important materials for future application [16]. Due to the enhanced mechanical properties, excellent wear resistance and chemical stability, CMNC have been attracted considerable attention in many fields of study [26]. One of the main application of CMNC is in thin films. A solid layer consists of few nm to some tens of μm thickness coated on a substrate is called thin film [27]. Over the past half-century hydroxyapatite (HA) as a bioceramic material has received significant attention particularly in orthopedics owing to its desirable attributes such as high biocompatibility and osseointegration rate, as well as similar structure and composition to the bone [28,29]. Hydroxyapatite ($\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$), is a suitable coating layer for orthopedic implants, however, brittleness and poor mechanical features such as fracture toughness and micro-hardness and make it an unsuitable candidate in many load bearing applications [30–33]. To overcome these problems different reinforcements in nanoscales such as alumina nanoparticles, TiO_2 nanoparticles and nanotubes, and carbon nanotubes have been incorporated into the HA matrix [34–36] to create HA-based nanocomposites. In a study conducted by Shirdar et al. [37], TiO_2 nanotubes was incorporated into the matrix of HA coating layer to improve the mechanical properties including micro-hardness and adhesion strength. Field emission scanning electron microscopes images of pure HA and HA- TiO_2 nanotubes coating layer on the metallic implant is illustrated in Fig. 1. It is obvious that the HA- TiO_2 nanotubes coating layer has a denser structure as compared to the pure HA coating layer. This study indicated that TiO_2 nanotubes filled up the micro porous of pure HA layer and create a crack-free nanocomposite coating layer with enhanced mechanical properties.

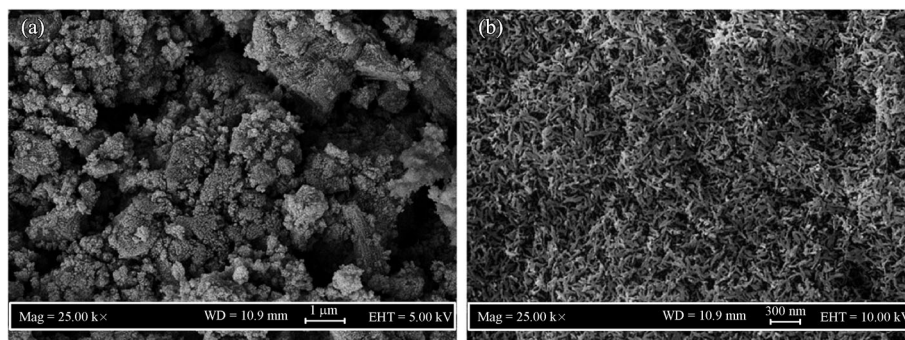


Fig. 1 Field emission scanning electron microscopes images of (a) Pure HA and (b) HA- TiO_2 nanocomposite coated layer on Co-Cr-based alloy [37]

2.1.2 Metal nanocomposites

Metal matrix nanocomposites (MMNC) are the materials consist of a ductile metal or alloy matrix with some implanted nanosized reinforcement [38]. MMNC are promising candidates for production of materials such as orthopedic implants in which adequate mechanical properties are required [39]. Metal matrix nanocomposites are classified as continuous and non-continuous reinforced materials [27]. Carbon nanotube metal matrix composite is one of the important continuous nanocomposite which is an emerging new material with high tensile strength [40,41]. In the field of orthopedics, metal nanocomposite materials have attracted fundamental research. For example, magnesium (Mg) has known for its high biocompatibility and comparable mechanical properties to the natural bone [42]. Therefore, it is widely used in orthopedic implants over traditional metallic materials [43]. However, two major drawbacks of Mg which are initial fast degradation and low level of bioactivity, limit its application in this area [44]. Recently, incorporation of nano-HA and nano-TiO₂ as reinforcement materials in Mg matrix have been reported [45]. Results indicated that MgO coated Mg-HA-TiO₂ nanocomposite remarkably enhanced the ductility and corrosion resistance of Mg-based nanocomposite [45]. Figure 2 presents the schematic illustration of Mg-HA-TiO₂ nanocomposite and surface field-emission scanning electron microscopy (FESEM) of MgO coated Mg-HA-TiO₂ nanocomposite. In another study conducted by Zhu et al. titanium/silicon carbide (Ti/SiC) MMNC was fabricated by friction stir processing. Findings revealed that the developed nanocomposite not only have superior mechanical properties under stress-bearing conditions but also provide improved surface and

physicochemical properties for cell attachment and osseointegration [46]. In addition, in order to enhance surface mechanical properties as well as osteogenic capacity, a novel Ti-6V-4V/zinc surface nanocomposite was developed using friction stir processing. Results suggested that this novel nanocomposite has significantly improved mechanical properties and biocompatibility, in addition to promoting osseointegration and thus has potential for dental and orthopedic applications [47].

2.1.3 Polymer nanocomposites

Polymer matrix nanocomposites (PMNC) consists of a polymer or copolymer and non-filter or non-particle in the polymer matrix [48]. This new class of nanocomposite materials has been received significant attention in biomedical applications owing to lightweight, ease of production, and some ductile nature [49,50]. In orthopedic applications, the modulus of the PMNC need be comparable to the bone for efficient load transfer [51]. In addition, they should be non-toxic, non-corrosive, and easy to remove when it is required [52]. As a result, a polymer based nanocomposite implant should fulfill certain design and functional criteria such as mechanical properties, biocompatibility, biodegradability, and possibly aesthetic demands [52]. Poly(vinyl alcohol) or PVA is one of the vinyl polymers with high hydrophilicity, flexibility and biocompatibility which has been widely employed in biomedical applications [53]. However, its application in the orthopedic surgery has been restricted owing to inadequate durability and mechanical strength [54]. In a study conducted by Mohanapriya et al. [54], PVA was reinforced with TiO₂ nanoparticles to improve thermo-mechanical stabilities, surface properties and osteoblastic

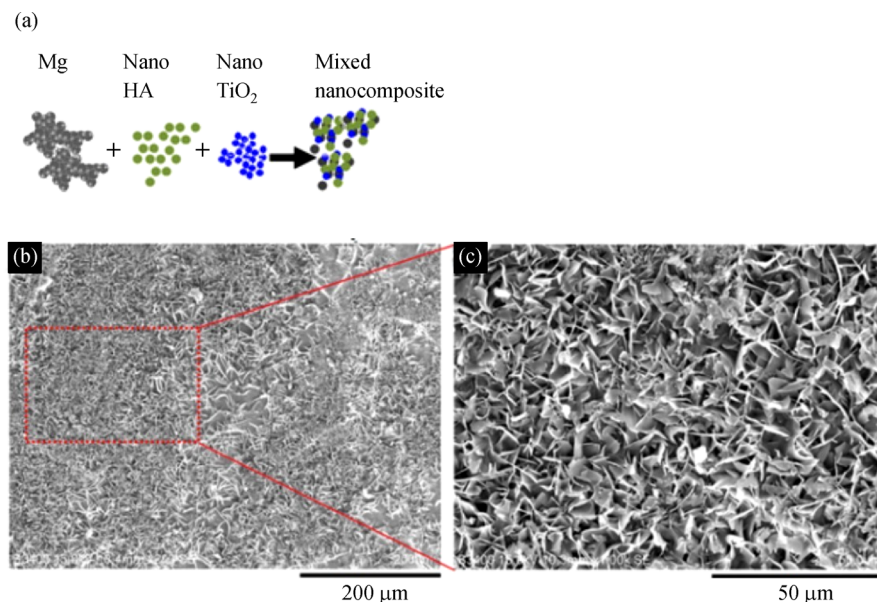


Fig. 2 (a) Schematic illustration of Mg/Ha/TiO₂ nanocomposite, and (b,c) FESEM micrographs of MgO coated Mg/Ha/TiO₂ nanocomposite (adapted and re-drawn from [45])

cell adhesion. Therefore, a PVA-TiO₂ nanocomposite film with adequate mechanical and biocompatible properties was developed. Findings revealed that the optimum composition of TiO₂ nanoparticles resulted in mechanically stable nanocomposite films with enhanced mechanical properties as well as corrosion resistance. In addition, results from cell adhesion and *in vitro* bioactivity tests indicated that TiO₂ promoted the interaction between cell and substrates and enhanced apatite. Figure 3 schematically illustrates a higher degree of interaction of osteoblast with PVA-TiO₂ nanocomposite surface compared to the pure PVA film. Moreover, cytotoxicity and cell adhesion of this developed nanocomposite film revealed that PVA-TiO₂ nanocomposite possibly is a promising candidate for bone implant applications.

Studies indicate that ceramic-polymer nanocomposites are more effective for application in bone tissue regeneration due to the improvement in mechanical properties and bioactivity as compared to the ceramics and polymers [55]. Cui et al. [56] developed n-HA/collagen/PLA bone scaffold nanocomposite which can be applied in bone tissue engineering [56]. Findings revealed that the elastic modulus of the nanocomposite was 47.3 MPa with 10% PLA that is close to the compressive modulus of trabecular bone (50 MPa). *In vivo* evaluation indicates that n-HA/collagen/PLA bone scaffold nanocomposite is a potential candidate material for bone tissue engineering. In another study, a novel polymer nanocomposite with good mechan-

ical properties and biocompatibility was developed for replacing conventional polymer composites reinforced with large hydroxyapatite microparticles. Polypropylene (PP), hexagonal boron nitride (hBN) nanoplatelets and nanohydroxyapatite (nHA) were employed for preparation of PP-hBN-nHA nanocomposite. Mechanical and biological results revealed that this nanocomposite is a suitable candidate for orthopedic applications [57]. Figure 4 shows the scanning electron microscopy (SEM) images of fractured surface of PP-hBN-nHA nanocomposite.

2.2 Natural-based nanocomposites

Recently, nanostructured biomaterials such as nanocomposites have become increasingly popular with bone tissue engineering, due to their capability of promoting cell adhesion and proliferation which leads to new bone growth as compared to conventional materials in micro scales [58,59]. Specially, nanocomposites consisting biopolymeric matrices and bioactive nanosized fillers are extensively used in bone tissue engineering due to the hierarchical nature of the bone [60]. These materials should possess high mechanical strength, biodegradability and osteointegration [61]. For instance, calcium phosphates (CaP) has desirable osteoconductivity, resorbability, and biocompatibility [62] while biopolymers possess suitable biological performance, resemblance to extracellular matrices and desirable degradation rates [63]. Thus,

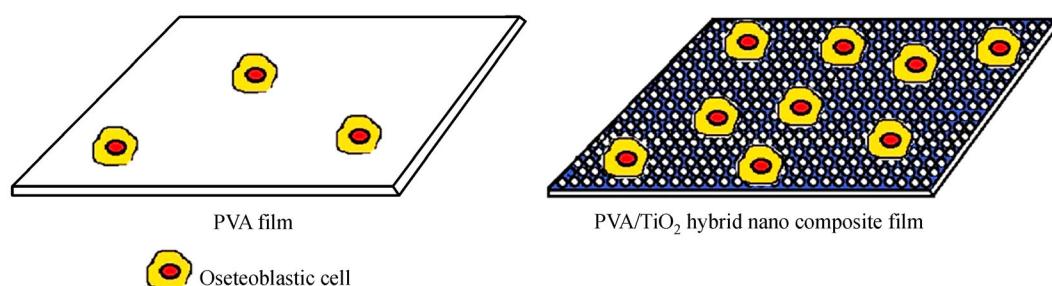


Fig. 3 Schematic illustration of higher degree of interaction of osteoblast with PVA/TiO₂ hybrid nanocomposite surface compared to the pure PVA film [54]

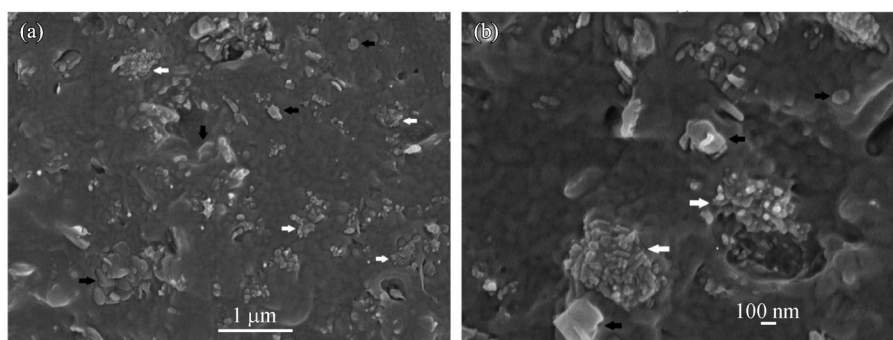


Fig. 4 SEM micrographs showing fractured surface of PP-hBN-nHA nanocomposite at (a) low and (b) high magnifications. Black arrow: hBN; white arrow: nHA [57]

nanocomposite material combining nanosized CaP and biopolymers gained much interest in orthopedics owing to the capability of mimicking the structure and mechanical properties of bone tissues [60]. Calcium phosphates provides the required biocompatibility and osteoconductivity features while natural polymers offer different degradation rates [62,63]. So far, several natural polymer/CaP nanocomposite scaffolds have been developed for tissue engineering. For instance, a collagen/nano-HA nanocomposite scaffold possesses sufficient mechanical properties and high biological activity similar to the collagen control scaffold has been reported by Cuniffe's group [64]. In addition, Yan et al. [65] developed a nanocomposite scaffold consisting silk fibroin and nanosized CaP with a self-mineralization capability and no cytotoxicity. Barbani et al. [66] introduced gelatin/HA nanocomposite scaffolds with chemical composition, structural organization, and elastic modulus comparable to the natural bone. The findings from this study showed high interactions between the organic and inorganic elements of the matrix which are confirmed by the appropriate adhesion and proliferation on the scaffold of hMSCs.

3 Bone nanocomposite

Bone is natural nanocomposite with an amazing balance of toughness, stiffness and vibrational damping properties which serving physiological, protective, and mechanical functions [67,68]. It is a complex system of connected tissue which forms the skeleton of the body [69]. Bone plays as a store for minerals, such as CaP, which provides mechanical support. Bone is a dynamic tissue due to the ability of self-modeling and self-regenerating during the lifetime [70]. There are two main nanoscale phases in the bone matrix including organic and inorganic which is an interesting example of a natural nanocomposite material [69]. Each phase consists of multiple components including minerals, collagen, water, non-collagenous proteins, lipids, vascular elements, and cells. Some trace elements such as magnesium, potassium, citrate, carbonate, sodium, chloride, and fluoride enrich the bone minerals for different metabolic functions [69]. Bone is an extremely hard and tough nature product composed of soft (collagen) and

brittle (HA) components. The major role of collagen is to provide tensile strength and flexibility, whereas the bone minerals supply rigidity and toughness. The total composition of the natural bone is summarized in Table 1 [6].

The design of ideal nanocomposite for bone grafting requires fundamentals understanding of bone structure, composition, and architecture. The bone-building strategy involves a biological mechanism which has not been discovered yet [71]. The hierarchical structural organization of bone at the different scales such as nano, micro and macro are important for its mechanical properties [72]. Figure 5 illustrates the hierarchical structural organization of the natural bone. To determine the mechanical features of the bone, the mechanical properties of each component phase, and the structural relationship between them at the various levels of the hierarchical structural organization need to be investigated [72]. There are five levels and structures in a bone including macrostructure such as cancellous and cortical bone; microstructure (from 10 to 500 μm) such as Haversian systems, osteons, and single trabeculae; sub-microstructure (1–10 μm) such as lamellae; nanostructure (from a few hundred nanometers to 1 μm) such as fibrillar collagen and embedded mineral; and sub-nanostructure (> few hundred nanometers) molecular structure of constituent elements such as mineral, collagen, and non-collagenous organic proteins [73]. Table 2 represents the biomechanical properties of the bone. The mechanical properties of the bone are varied at different structural levels. For instance, Young's modulus of the bone is in the range of 14–20 GPa range while tensile strength is in the range of 50–150 MPa. There is an amount of water in the bone. The mechanical properties of the bone also depend on the amount of water exist in the bone [6].

4 Nanocomposite for bone grafting

A surgical procedure that replaces missing bone in order to repair bone fractures is called bone grafting [74]. First-generation bone graft did not fulfill the requirements as a stand-alone graft substitute. Therefore, designing an ideal bone graft which mimics the function and structure of the natural bone remains a great challenge [11]. Table 3 summarizes the different groups of bone substitutes: natural and synthetic biodegradable polymers, ceramics,

Table 1 The composition of bone [6]

Organic phase	wt-%	Inorganic phase	wt-%
Collagen	20	Hydroxyapatite	60
Water	9	Carbonate	4
Non-collagenous proteins	3	Citrate	0.9
Other traces: polysaccharides, lipids, cytokines		Sodium	0.7
Primary bone cells: osteoblasts, osteocytes, osteoclasts		Magnesium	0.5
		Other traces: Cl^- , F^- , K^+ , Sr^{2+} , Pb^{2+} , Zn^{2+} , Cu^{2+} , Fe^{2+}	

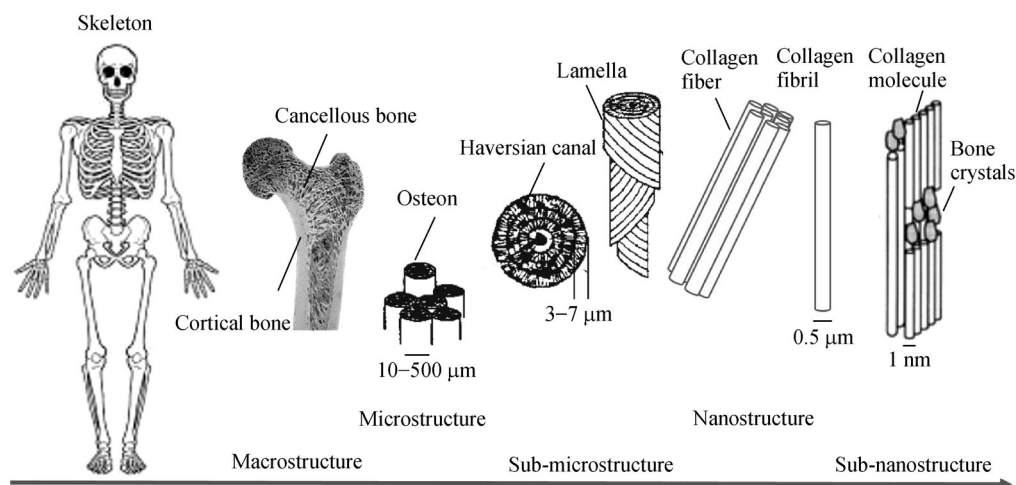


Fig. 5 Hierarchical structural organization of the natural bone (adapted and re-drawn from [73])

Table 2 Biomechanical properties of bone [6]

Properties	Measurement	
	Cortical bone	Cancellous bone
Compressive strength /MPa	170–193	7–10
Young's modulus /GPa	14–20	0.05–0.5
Tensile strength /MPa	50–150	10–20
Fracture toughness /(MPa·m ^{1/2})	2–12	0.1
Strain to failure	1–3	5–7
Surface/bone volume /(mm ² ·mm ⁻³)	2.5	20
Density /(g·cm ⁻³)	18–22	0.1–1.0
Apparent density /(g·cm ⁻³)	1.8–2.0	0.1–1.0
Total bone volume /mm ³	1.4×10^6	0.35×10^6
Total internal surface	3.5×10^6	7.0×10^6

metals, composites and nanocomposites [6,75]. Recently, researchers enhance the performance of the bone graft substitutes using the biomimetic process to create desirable nano-structure materials [76]. It is realized that nanocomposite materials possess the potential capacity for developing ideal bone grafting due to their nanoscale features that promote bone cell growth and consequently tissue formation [77,78]. Regarding to this fact that bone itself is a natural nanocomposite material with a complex hierarchical structure, thus nanocomposites as a new generation of materials are considered as a promising substitute in bone grafting [69]. These materials use a combination of different nanoscale bone graft in conjunction with osteogenic cellular components and osteoinductive growth factors. For instance, nanocomposite bone graft consists of nano-HA and collagen or nano-HA chitosan promotes superior osteoconduction and related functions as compared to the microscale bone grafts [79–81]. This type of nanocomposite bone graft shows similar structure and composition to the natural bone [82]. The possibility of

developing new bone grafts with enhanced performance is increased by innovations in the processing of nanocomposite materials [6].

5 Development of nanocomposite for bone grafting

Conventional materials employed in bone grafting were not close to the ideal bone substitutes due to their low level of bioactivity and difference mechanical properties as compared to the bone [99]. For instance, using conventional materials possibly mechanically destroy and cause allergy and inflammation in the normal bone owing to the abrasive and toxic particles such as nickel, cobalt, chromium, aluminum and vanadium in the metallic implant such as titanium alloys, stainless steel, cobalt chromium [100]. In addition, implantation of metal oxides such as alumina (Al₂O₃) and zirconia (ZrO₂) cause the same clinical and mechanical problems [99]. HA and β -TCP are bioactive ceramics and make a direct connection to the bone, however, brittleness of these two materials may cause crash in the bone [99]. The most important criteria for developing an ideal artificial bone is to select materials with the most similarity in composition, nanostructure, and biological response to the bone [99]. It seems that nanocomposite materials are the best selection to fulfill these requirements [99]. Nanocomposite materials are attracted in bone grafting implants due to the unique functional properties as mentioned in the previous sections. There are three processing methodologies including conventional, tissue engineering, and biomimetic for developing nanocomposite materials.

5.1 Convectional method

Conventional methods for producing nanocomposite

Table 3 Bone grafting materials used for bone repair and regeneration

Materials	Examples	Refs.
Polymers	Protein: Collagen, fibrin, gelatin, silk fibroin	[83–87]
Natural	Polysaccharides: Hyaluronic acid, chondroitin sulphate, cellulose, starch, alginate, agarose, chitosan, pullulan, dextran	
Synthetic	Poly-glycolic acid (PGA) Poly-lactic acid (PLA) Poly-(ϵ -caprolactone) (PCL) Poly-(lactide-co-glycolide) (PLGA) Poly-hydroxyethylmethacrylate (poly-HEMA)	[83,84,86–89]
Ceramics	Coralline or synthetic HA	[83,86,90–94]
Calcium phosphate	Silicate-substituted HA β -TCP Dicalcium phosphate dehydrate	
Bioglass and glass ceramics	Silicate bioactive glasses (45S5, 13-93) Borate/borosilicate bioactive glasses (13-93B2, 13-93B3, Pyrex®)	
Metals	Titanium and its alloys Tantalum Stainless steel Magnesium and its alloys	[83,95,96]
Composites	Calcium-phosphate coatings on metals HA/poly-(D,L-lactide) HA/chitosan-gelatin	[83,97,98]
Nanocomposites	Nano-HA/collagen, Nano-HA/gelatin, Nano-HA/chitosan, Nano-HA/PLLA	[6]

include mixing or blending a heterogeneous combination of at least two materials with different combinations or morphologies [101]. This method is not a new concept and it has widely employed for many years. Although blending techniques produce nanocomposite with tailor-made properties, however, control of homogeneity and uniformity is quite difficult [6]. The blending procedure begins with the incorporation of nanoscale components into the macroscopic material to form the nanocomposite. In this technique controlling the size and structure of the developed nanocomposite is complicated. Very few study have reported the blending of TiO₂ with HA to develop HA-based nanocomposite [37]. This nanocomposite is applicable as a coating layer for orthopedic metallic biomaterials such as cobalt chromium and titanium implants. First, titanium nanotubes as a reinforcement agent were synthesized and then mixed with the specific ratio to the sol-gel of HA [102]. Finally, the metallic implant was coated through dip coating process by HA-TiO₂ nanocomposite. The schematic illustration of dip coating process was shown in Fig. 6. The nanocomposite coating layer with this technique possibly is not uniform and possess different crystalline size. Titanium nanotubes heterogeneously distributed to the HA matrix due to the often agglomeration. In addition, no chemical interaction occurs between nanotubes and HA, possibly owing to the

lack of appropriate interfacial-bonding [103]. Therefore, the structure uniformity of this nanocomposite coating layer with the conventional method is not close to the natural bone.

5.2 Tissue engineered method

Tissue engineering is known as a common method for developing nanocomposites through the application of both bioengineering and biosciences [104]. A novel biological substitute developed by this method is able to improve, maintain and restore tissue function [104]. In bone tissue engineering, before scaffold implant into the body, a specific cell from patient is isolated in order to be cultured on the scaffold [105]. There are three vital factors including cells, scaffold and cell-matrix interaction which determine the success rate of bone tissue engineering [106]. The scaffold has a critical role in cells accommodation. In the formation process of the particular tissue, the cells undergo proliferation, migration and differentiation [107]. Bone tissue engineering includes the use of osteogenic cells with osteoconductive scaffold and osteoinductive growth factors that possibly form a bone graft [6]. A design strategy for a tissue-engineered nanocomposite graft is illustrated in Fig. 7. Owing to the osteoconductivity of HA, it is used as a scaffold matrix for bone tissue engineering.

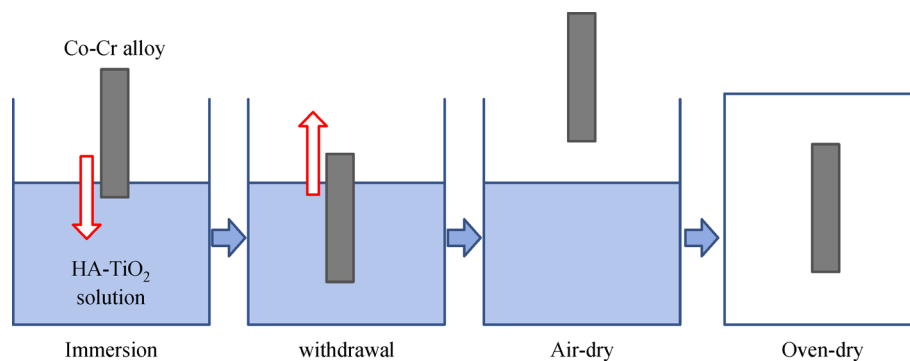


Fig. 6 Schematic illustration of dip coating process of Co-Cr alloy with HA-TiO₂ nanocomposite

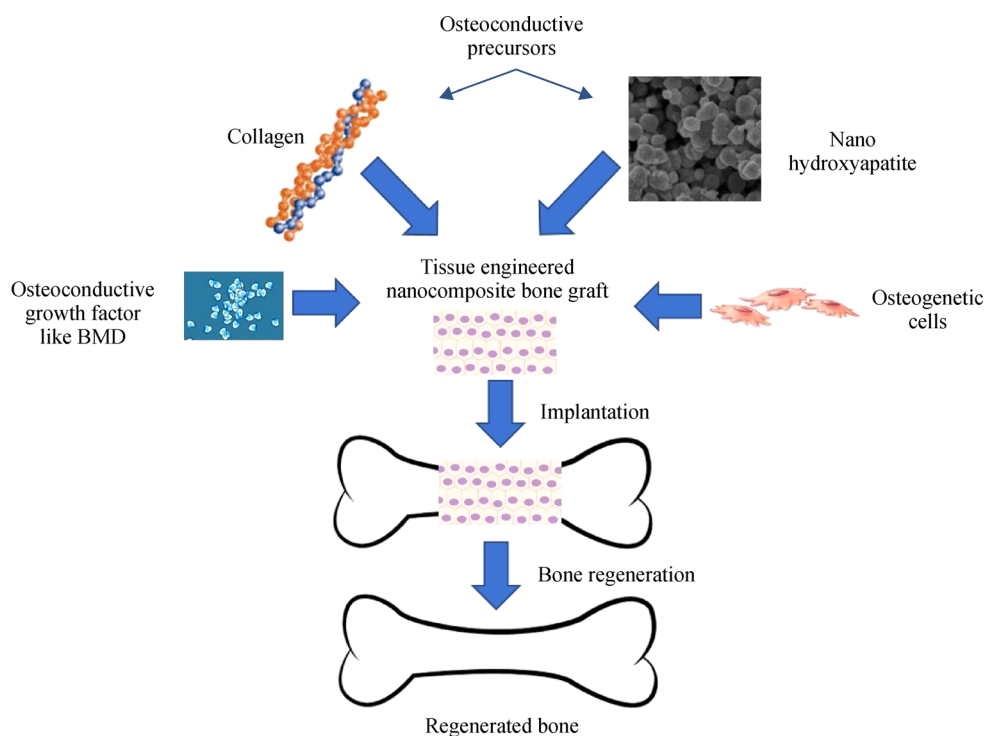


Fig. 7 Design strategy of tissue-engineered nanocomposite bone graft (adapted and re-drawn from [6])

However, a biodegradable polymer such as collagen needs to be utilized to make a composite with HA to overcome its low biodegradability and lack of osteoconduction. Studies show that HA/collagen nanocomposite matrix is a promising material for successful bone tissue engineering. The scaffold supported the cellular growth and related function leading to form new bone. Investigations show that an ideal bone graft involves osteoconductive matrix in association with osteogenic cells and growth factor with similar composition, structure, physiochemical and a mechanical and biological feature to the natural bone [6]. Recently, surface functionalization of nanocomposite in bone tissue healing has attracted considerable attention. In a study conducted by Gentile et al. a functionalized porous membrane was developed that stimulates early events in

bone healing for initiating a regenerative cascade. Layer-by-layer assembly was applied to modify the surface of osteoconductive electrospun meshes, based on poly(lactic-co-glycolic acid) and nanohydroxyapatite, by using poly(allylamine hydrochloride) and poly(sodium 4-styrenesulfonate) as polyelectrolytes. Characterizations including scanning electron microscopy, infrared spectroscopy, and X-ray photoelectron spectroscopy confirmed the successful surface functionalization. In addition, the peptide incorporation enhanced cellular processes, with good viability and significant increase of alkaline phosphatase activity, osteopontin, and osteocalcin. The functionalized membrane induced a favorable *in vivo* response after implantation for four weeks in nonhealing rat calvarial defect model [108].

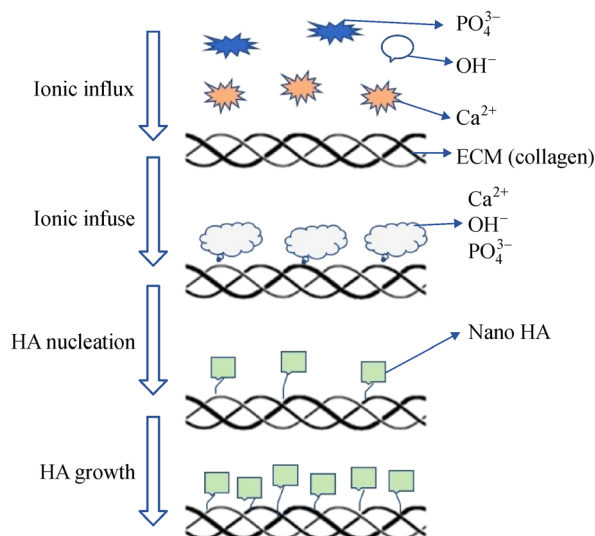


Fig. 8 Schematic illustration for a self-assembly of HA/collagen nanocomposite graft. Adapted and re-drawn from [6]

5.3 Biomimetic method

A microstructural processing which in part or whole, mimics or inspires the biological mechanism is called biomimetic method [109]. Biomimetic method for fabrication of nanocomposite bone graft based on nature strategies has received considerable attention to be beneficial over the conventional method. This method is a bottom-up approach starts with design and synthesis of molecules which can naturally self-assemble or self-organize into a higher order of microscale or macroscale structure [110,111]. Developing nanocomposite grafts with certain features of natural bone in terms of structure and composition through biomimetic self-assembly possibly imitate the natural process. In this method, a nanocomposite which simulates biomineralization after implantation is considered as a potential candidate for bone applications [112,113]. Figure 8 schematically illustrates the nucleation and growth of crystalline HA onto collagen in a controlled manner. By mimicking the biological phenomenon, this process provides a proper system for bone regeneration with higher osteoconductivity as compared to the pure HA and pure collagen [114].

6 Summary

Application of nanocomposites in orthopedics has had an attention for researchers in recent years. Novel properties and enhanced performance of nanocomposites make them suitable candidates to meet the emerging demands arising from advanced orthopedic products. Owing to the natural nanocomposite structure of the bone, nanocomposite materials are possibly the best candidates for orthopedics application by mimicking the structure and property of the

bone tissues. Different classification of nanocomposite materials including ceramic, metal, polymer, and natural-based nanocomposites provide a great opportunity to overcome the problems associated with conventional materials and thus propose enhanced performance as compared to the monolithic and microcomposite materials. Although a wide range of applications already exists for nanocomposites, however, many research needs to be conducted for a better understanding of nanocomposite materials in terms of structures and properties.

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