We are IntechOpen, the world’s leading publisher of Open Access books
Built by scientists, for scientists

3,900
Open access books available

116,000
International authors and editors

120M
Downloads

154
Countries delivered to

TOP 1%
Our authors are among the most cited scientists

12.2%
Contributors from top 500 universities

WEB OF SCIENCE™
Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com
Chapter 2

Biomimetic Porous Bone-Like Apatite Coatings on Metals, Organic Polymers and Microparticles

Takeshi Yabutsuka

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.71390

Abstract

When pH and temperature of simulated body fluid (SBF) are raised, fine particles of calcium phosphate are precipitated. Recently, the authors’ research group found that these fine particles were highly active to induce formation of porous bone-like apatite in SBF, or body fluid, and named them ‘apatite nuclei.’ By using apatite nuclei, the author successfully imparted high bioactivity, that is, apatite-forming ability, to various kinds of bioinert biomaterials such as metals and organic polymers in a series of recent studies. These materials spontaneously formed porous bone-like apatite layer on their surfaces in SBF in a short time and showed high bioactivity in vitro. In addition, the author also successfully fabricated microcapsules consisted of porous bone-like apatite by using apatite nuclei.

Keywords: porous bone-like apatite, apatite nuclei, bioactive metals, bioactive organic polymers, apatite microcapsules

1. Introduction

1.1. Bioactive materials

When artificial materials such as metals, ceramics and organic polymers are implanted in the body, these materials are generally encapsulated with noncalcified fibrous tissue and separated from the surrounding living tissue. Such biological response is known as a normal immune reaction of the living body with respect to exogenous materials. In early 1970s, L.L. Hench found that Na$_2$O-CaO-SiO$_2$-P$_2$O$_5$-type glass (bioglass®) showed bone-bonding ability without the isolation from surrounding living tissue [1]. Since the discovery of bioglass®, ceramic materials such as glass-ceramic Ceravital® containing crystalline apatite [2], sintered
hydroxyapatite \((\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2)\) [3], glass-ceramics Cerabone® A-W containing crystalline apatite and wollastonite \((\text{CaO} \cdot \text{SiO}_2)\) [4, 5], and so on have been found to bond with living bone. Most of the ceramics mentioned above forms apatite layer on their surface and can bond with living bone through the apatite layer in living body [6, 7]. This apatite layer consists of minute crystallites containing carbonate ions in chemical composition [8] and is similar to apatite, which contains living bone [9, 10]. On the apatite layer, osteoblast actively proliferates and differentiates [6, 11]. Hence, bone tissue is formed on the apatite layer and the artificial materials can be also found to bond with the surrounding bone tissue through the apatite layer. Such material property is often defined as ‘bioactivity’ in the research field of ceramic biomaterials.

1.2. Simulated body fluid

In early 1990s, T. Kokubo proposed an acellular simulated body fluid (SBF) with ion concentrations similar to those of human blood plasma [12–14]. It is possible to reproduce the abovementioned apatite formation reaction on most of the bioactive materials by soaking the materials in SBF. Hence, we can predict bioactivity, that is, apatite-forming ability, of specimens by soaking them in SBF and evaluating apatite formation on their surface. Table 1 shows the ion concentrations of simulated body fluid and human blood plasma. The SBF can be prepared by dissolving \(\text{NaCl}, \text{NaHCO}_3, \text{KCl}, \text{K}_2\text{HPO}_4 \cdot 3\text{H}_2\text{O}, \text{MgCl}_2 \cdot 6\text{H}_2\text{O}, \text{CaCl}_2\) and \(\text{Na}_2\text{SO}_4\) in pure water and maintaining the pH value at 7.40 with \((\text{CH}_2\text{OH})_3\text{CNH}_2\) and 1 mol dm\(^{-3}\) HCl solution at 36.5°C. The details of preparation method of SBF and the bioactivity test are certified by ISO 23317 [14].

1.3. Apatite nuclei

When pH and temperature of SBF are raised, fine particles of calcium phosphate are precipitated. Generally, calcium phosphate formation in an aqueous solution can be described as shown in (Eq. (1)) by applying hydroxyapatite as a representative calcium phosphate.

\[
10\text{Ca}^{2+} + 6\text{PO}_4^{3-} + 2\text{OH}^- = \text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2
\]  

<table>
<thead>
<tr>
<th>Ion</th>
<th>Ion concentration/mM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SBF</td>
</tr>
<tr>
<td>(\text{Na}^+)</td>
<td>142.0</td>
</tr>
<tr>
<td>(\text{K}^+)</td>
<td>5.0</td>
</tr>
<tr>
<td>(\text{Mg}^{2+})</td>
<td>2.5</td>
</tr>
<tr>
<td>(\text{Ca}^{2+})</td>
<td>1.5</td>
</tr>
<tr>
<td>(\text{Cl}^-)</td>
<td>147.8</td>
</tr>
<tr>
<td>(\text{HCO}_3^-)</td>
<td>4.2</td>
</tr>
<tr>
<td>(\text{HPO}_4^{2-})</td>
<td>1.0</td>
</tr>
<tr>
<td>(\text{SO}_4^{2-})</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Table 1. Ion concentrations of simulated body fluid (SBF) and human blood plasma.
When pH value or concentration of the aqueous solution increases, apatite formation is promoted from a viewpoint of the abovementioned chemical equilibrium because of an increase of $OH^-$ or $Ca^{2+}$ and $PO_4^{3-}$. In addition, the reaction is accelerated under high-temperature environment because of an increase of chemical reaction rate of calcium phosphate formation. Yao et al. found that thus-precipitated fine particles of calcium phosphate showed high activity for induction of porous bone-like apatite formation in SBF and named the particles ‘apatite nuclei’ [15].

### 1.4. Bioactive materials’ design by utilizing the function of apatite nuclei

As described in Section 1.3, apatite nuclei, precipitated by raising pH or temperature of SBF, actively induce apatite formation in SBF or body environment. By using apatite nuclei, excellent implant materials possessing various mechanical properties as well as high bioactivity and bioaffinity can be developed by combining it with various kinds of bioinert materials such as metals and organic polymers. Recently, we found that high apatite-forming ability can be imparted by the following method [16].

- Micropores are formed on the surface of the substrate by acid treatment or sandblasting process.
- The abovementioned micropores-formed substrate or porous substrate is soaked in SBF, and pH and temperature of SBF is increased. By this treatment, apatite nuclei are precipitated in the pores of the substrate.

When this material is implanted into a bone defect, it is thought that apatite nuclei induce apatite formation and this material subsequently bonds with living bone through the formed bone-like apatite layer (Figure 1). As a result, it is expected that the materials can bond with living bone through the formed apatite layer.

### 2. Fabrication of bioactive metals by incorporation of apatite nuclei as precursors of apatite

#### 2.1. Bioactive metals

Metals have high mechanical strength and high fracture toughness. Among them, stainless steel (SUS), cobalt-chromium (Co-Cr) alloys, titanium (Ti) and its alloys have
been widely used as implant materials. However, most of them do not have bioactivity or have extremely poor bioactivity. Hence, these materials without any pretreatment cannot spontaneously form apatite coatings in living body in most cases. For this reason, effective methods for imparting high bioactivity to these metallic biomaterials are desired. As a representative surface modification of metals for bioactivity, hydroxyapatite coating by plasma spray method has been widely used in practical use as artificial hip joint [17]. However, this method required heating process at a temperature over 10,000°C and it is difficult to optimize the composition and crystallinity of hydroxyapatite for the bone conduction in living body. Kokubo et al. reported that NaOH and heat treatment are an effective way to impart bioactivity to the surface of Ti metal and its alloys [5, 18, 19]. In fact, the NaOH- and heat-treated Ti metal showed apatite formation within 1 day in SBF and attained high bioactivity. From these properties, the Kokubo’s method has been already used in clinical use as a surface modification for artificial hip joint. However, this method cannot be applied to SUS and Co-Cr alloys [19]. As one of the most effective method for solving this problem, incorporation of apatite nuclei described in Section 1.4 can become an effective candidate to impart bioactivity to various kinds of bioinert metallic biomaterials. Recently, the author successfully imparted bioactivity to pure Ti metal [20–22], Ti-6Al-4 V alloy [23], Ti-15Mo-5Zr-3Al alloy [22, 24, 25], Ti-12Ta-9Nb-3 V-6Zr-O alloy [22], pure zirconium (Zr) metal [23], Co-Cr alloy [26] and SUS [27, 28] by incorporation of apatite nuclei on their surfaces based on the materials’ design described in Section 1.4. Among them, the author introduces the details of bioactive SUS as a representative case of bioinert metallic biomaterials in this chapter.

2.2. SUS as an orthopedic material

SUS is a typical biomaterial with high mechanical strength and high-corrosion resistance and has been already used as orthopedic implants such as artificial hip joint. However, SUS has no bioactivity. If an effective bioactivity treatment for SUS is established, range of its application is largely extended. Bioactivity treatment utilizing apatite nuclei described in Section 1.4 is one of the effective methods used for surface modification of SUS to impart bioactivity. As a novel micropores formation process, the authors established a formation process of roughened surface with fine pores on metals and organic polymers by doubled sandblasting process [29] by using the grinding particles with 14 μm of average particle size as first process, and then using the particles with 3 μm of average particle size as second process. The authors clarified that thus-formed fine pores contributed to the improvement of adhesion property of porous bone-like apatite layer formed on the bioactive materials in SBF in the process shown in Figure 1 because of an improvement of mechanical interlocking effect. As described in this section, the authors formed micropores on the surface of SUS plates by the doubled sandblasting process. Then the authors precipitated apatite nuclei in the pores of SUS to impart bioactivity.

2.3. Fabrication process of bioactive SUS

2.3.1. Micropores formation by the doubled sandblasting process

First, in order to prepare micropores on the surface, the SUS plates (JIS SUS 316 L) were treated by a sandblasting process using alumina-grinding particles with 14 μm (JIS #800) of
average particle size. Then, the plates were treated by that with 3 μm (JIS #4000) of average particle size. Figure 2 shows the SEM micrograph of the surface of the SUS plate after the sandblasting process. It can be seen that the SUS plate possessed the roughened surface with fine pores formed by the sandblasting process.

2.3.2. Impartation of apatite-forming ability: incorporation of apatite nuclei as precursors of apatite

After the micropores formation, the following process was conducted for apatite nuclei precipitation in the pores to impart bioactivity to the surface of the SUS plate. First, the pH value of SBF was increased to 8.40 by dissolving tris(hydroxymethyl)aminomethane at 25°C. Subsequently, the SUS plates were soaked in the SBF and the solution was pressed by cold isostatic pressing machine to make the solution penetrate into the pores. In order to precipitate apatite nuclei in the pores of the specimens, the solution was heated by using electromagnetic induction at 2.5 kW for 2 hours while soaking the specimens in the solution. Hereafter, the authors denote these treatments as ‘alkaline SBF treatment’. Figure 3 shows the SEM micrograph and the EDX profile of the surface of the SUS plate after the alkaline SBF treatment. It can be seen that the surface morphologies were slightly rounded off in comparison with just after the sandblasting process shown in Figure 2 and some types of coatings were formed on the plates. In the EDX profile, peaks of P and Ca were detected. It is considered that the SUS plate has been effectively heated in SBF by electromagnetic induction because the iron, which is a main chemical component of SUS, has high magnetic susceptibility. As a result, nucleation and growth of calcium phosphate were further promoted and the apatite nuclei formed under alkaline condition grew to some types of calcium phosphate coating on the surface of the SUS plate in the alkaline SBF treatment. Hereafter, the SUS plate after the alkaline SBF treatment is denoted as ‘bioactive SUS’.

2.4. Apatite-forming ability of bioactive SUS: porous bone-like apatite coatings in biomimetic environment

Next, bioactivity of thus-obtained bioactive SUS was evaluated by soaking in SBF at pH 7.40, 36.5°C, which is corresponded to physiological environment. Figure 4 shows the thin-film...
X-ray diffraction (TF-XRD) profiles of the surface of the bioactive SUS after soaking in SBF for 0 day (i.e., before soaking in SBF), 1 day, 3 days and 7 days. Before soaking in SBF, diffraction peaks of apatite were not detected. This result suggested that the calcium phosphate coating formed in the alkaline SBF treatment was consisted of amorphous calcium phosphate (ACP). After soaking in SBF for 1 day, 3 days and 7 days, diffraction peaks of apatite were clearly detected. Figure 5 shows the SEM micrograph and the EDX profile of the surface of the bioactive SUS after soaking in SBF for 1 day. It was observed that the whole surface was covered with porous coating, which consisted of needle-like crystallites, which characterize bone-like apatite, in the SEM observation. In the EDX profile, the intensity of the peaks of P and Ca was relatively increased in comparison with those after the alkaline SBF treatment shown in Figure 3. From these results, it is indicated that apatite formation was induced within 1 day and high bioactivity was imparted to the SUS by the alkaline SBF treatment.

Figure 3. (a) SEM micrograph and (b) EDX profile of the surface of the SUS plate after the alkaline SBF treatment.

Figure 4. TF-XRD profile of the surface of the bioactive SUS after the soaking in SBF for 0 day, 1 day, 3 days and 7 days.
2.5. Adhesion property of porous bone-like apatite coating formed on the bioactive SUS

The adhesive strength between the bioactive SUS and the porous bone-like apatite coating formed by soaking in SBF for 14 days was measured by a modified ASTM C-633 method [30–33]. For the reference, the author prepared the specimens, which were applied same treatments without the doubled sandblasting treatment. The average adhesive strength between the formed apatite layer and the bioactive SUS with alkaline SBF treatment was 15.4 MPa, and for the SUS without the sandblasting treatment was 1.5 MPa. The SUS treated with doubled sandblasting treatment showed higher adhesive strength than untreated ones. This is because a mechanical interlocking effect between the SUS plate and the porous bone-like apatite coating was attained by the formation of micropores.

2.6. Case of the other types of metals

As described in Section 2.1, the author reported that this bioactivity treatment was applicable not only to SUS but also to other kinds of metallic biomaterials such as Ti metal and its alloys, Zr metal and Co-Cr alloy by optimizing the condition of micropores formation and apatite nuclei precipitation according to the kinds of materials. Also in the case of these metals, apatite formation was induced within 1 day in SBF [20–26]. In addition, it is reported that most of the bioactive ceramics show apatite formation within 1 week in SBF [34]. Hence, it is suggested that the alkaline SBF treatment was an effective method to impart high bioactivity to bioinert or poorly bioactive metals.

3. Fabrication of bioactive organic polymers by incorporation of apatite nuclei as precursors of apatite

3.1. Bioactive organic polymers

Organic polymers have various mechanical properties and are easily processed in various shapes such as sticks, plates, films, sponges and fibers. Because of these properties, organic polymers have been widely used as various implant materials such as artificial hip joint,
artificial knee joint, artificial knuckle joint and artificial ligament. Generally, however, organic polymers are not bioactive and cannot bond with living bone in living body. If organic polymers acquire bioactivity, implant materials with various mechanical properties as well as high bioactivity can be developed. As a conventional method to impart bioactivity to organic polymers, the method that bioactive ceramics particles such as sintered hydroxyapatite are dispersed in polymeric matrix have been mainly applied. Among them, HAPEX™, which contains 40 vol% of hydroxyapatite in high density polyethylene matrix [35], has been already in practical use as an orbital implant and a middle ear implant. However, such method is difficult to control bioactivity of the materials because most of ceramics particles are buried inside the polymeric matrix and bioactivity was performed by only the particles exposed to the surface of the materials [36]. As one of the most effective method for solving this problem, the alkaline SBF treatment described in Section 1.4 can act as an attractive candidate to impart bioactivity also to polymeric biomaterials, similar to the case of metals. Recently, the author successfully established the surface modification technique to impart bioactivity to ultrahigh-molecular weight polyethylene (UHMWPE) [37], polyethylene terephthalate (PET) [24], poly-l-lactic acid (PLLA) [38], polyetheretherketone (PEEK) [39–41], carbon fiber-reinforced PEEK (CFR-PEEK) [42], glass fiber-reinforced PEEK (GFR-PEEK) [42] and glass fiber-reinforced poly(m-Xylyleneadipamide)-6 (GFR-MXD6) [43]. Among them, the author introduces the details of bioactive PEEK as representative cases of polymeric biomaterials in this chapter.

3.2. PEEK as orthopedic materials

PEEK is well known as one of the next-generation polymeric materials with high mechanical toughness. In addition, PEEK is in the spotlight of orthopedic or dental fields because of its more similar elastic modulus with cortical bone than metallic biomaterials such as Ti alloys, SUS and Co-Cr alloys and ceramic biomaterials such as alumina, zirconia and sintered hydroxyapatite. From these mechanical properties, it is expected that PEEK becomes a candidate for replacing conventional metallic or ceramic bone substitutes in clinical use [44]. Although PEEK has biocompatibility, bioactivity of PEEK is extremely poor. If high bioactivity is imparted to PEEK, the range of its clinical or dental use such as minimally invasive orthopedic treatment will be largely extended. As described in this section, micropores were formed on PEEK by sulfuric acid treatment. Then apatite nuclei were precipitated in the pores and bioactivity was imparted to PEEK by incorporation of apatite nuclei.

3.3. Fabrication process of bioactive PEEK

3.3.1. Micropores formation by sulfuric acid treatment

First, in order to form micropores on the surface of the PEEK, PEEK plates were treated with 98% sulfuric acid at room temperature. Figure 6 shows the SEM micrograph of the surface of the PEEK after the sulfuric acid treatment. It can be seen that cancellous micropores around 500 nm in diameter were formed on the whole surface of the plate.
3.3.2. Impartation of apatite-forming ability: incorporation of apatite nuclei as precursors of apatite

Next, the author conducted surface modification to impart bioactivity to PEEK by incorporation of apatite nuclei. As a pretreatment for the apatite nuclei incorporation, the surfaces of the micropores-formed PEEK were treated with glow-discharge in O₂ gas atmosphere. By this treatment, reactive functional groups, which have hydrophilic property, were supplied on the surfaces of organic polymers [45]. The pH value of SBF was increased to 8.4 by dissolving tris(hydroxymethyl)aminomethane at 25°C. In order to precipitate apatite nuclei in the micropores, the micropores-formed PEEK was soaked in this SBF and kept at 70°C for 24 hours. Hereafter, this treatment is denoted as ‘alkaline SBF treatment’. Figure 7 shows the SEM micrograph and the EDX profile of the surface of the micropores-formed PEEK after the alkaline SBF treatment. It can be seen that the surface morphology was different from Figure 6, after the sulfuric acid treatment. In the EDX profile, peaks of P and Ca were detected. In the SEM micrograph, spherical particles of apatite nuclei were observed on the whole surface. It is considered that apatite nuclei were precipitated on the surface or inside the pores by the alkaline SBF treatment. Hereafter, this material is denoted as ‘bioactive PEEK’.

3.4. Apatite-forming ability of bioactive PEEK: formation of porous bone-like apatite coatings in biomimetic environment

Next, bioactivity of the bioactive PEEK was evaluated by SBF test similar to the case of SUS as described in Section 2.4. Figure 8 shows the TF-XRD profiles of the surface of the bioactive PEEK after the soaking in SBF for 0 day, 1 day, 3 days, 7 days and 14 days. After soaking in SBF for 1 day, diffraction peaks of apatite were detected. As elapse of soaking time, the intensity of the diffraction peaks increased and those of PEEK decreased. Figure 9 shows the SEM micrograph and the EDX profile of the surface of the bioactive PEEK after soaking in SBF for 1 day. It can be seen that the whole surface of the plate was covered with porous coatings consisted of needle-like crystallites, which characterize bone-like apatite, in the SEM observation.
and peaks of P and Ca were strongly detected in the EDX analysis. By considering the results of TF-XRD, SEM and EDX, it is revealed that porous bone-like apatite, which was induced by apatite nuclei, covered the whole surface of the bioactive PEEK within 1 day and the apatite layer grew thick as elapse of the soaking time.

3.5. Adhesion property of porous bone-like apatite coating formed on the bioactive PEEK

Similar to the case of metals, adhesive strength between the bioactive PEEK and the porous bone-like apatite coating formed by soaking in SBF for 14 days was measured by a modified ASTM C-633 method [30-33]. For the reference, the author prepared the specimens, which

---

**Figure 7.** (a) SEM micrograph and (b) EDX profile of the surface of the PEEK plate after the alkaline SBF treatment.

**Figure 8.** TF-XRD profiles of the surface of the untreated PEEK and the bioactive PEEK after the soaking in SBF for 0 day, 1 day, 3 days, 7 days and 14 days.
were applied same treatments without sulfuric acid treatment. The average value of adhesion strength of the porous bone-like apatite coating for the bioactive PEEK with the pores formed by the sulfuric acid treatment was 6.7 MPa. In contrast, PEEK without pores formation was 2.1 MPa. The PEEK with pores formed by the sulfuric acid treatment presented higher adhesion strength. This difference was caused by a mechanical interlocking effect between the PEEK and porous bone-like apatite layer by existence of the micropores, similar to the case of the SUS.

3.6. Case of the other types of polymers

As described in Section 2.1, the author reported that this bioactivity method was applicable not only to PEEK but also to other kinds of polymeric biomaterials such as UHMWPE, PET, PLLA, CFR-PEEK, GFR-PEEK and GFR-MXD6 by optimizing the condition of micropores formation and apatite nuclei precipitation according to the kinds of materials, similar to the case of the metals [24, 37, 38, 42, 43]. Also in the case of these polymers, apatite formation was induced within 1 day in SBF in most cases. Hence, it is suggested that the alkaline SBF treatment was an effective method to impart high bioactivity not only to metals but also to polymeric implant materials.

4. Fabrication of apatite microcapsules consisted of biomimetic porous bone-like apatite coatings by using apatite nuclei as precursors of apatite

4.1. Fabrication of microcapsule consisted of porous bone-like apatite

Drug delivery system (DDS) is one of the most attractive techniques in the medical and pharmaceutical fields. DDS can contributes to chemotherapy that can achieve low side effects because it can achieve an efficient local or controlled release of pharmaceutical drugs. The microcapsules can be filled with pharmaceutical drugs. Hence, the DDS carriers consisted of microcapsules have a possibility to be applied in many kinds of pharmaceutical fields. Apatite has high bioaffinity because it forms bone-like apatite coatings consisted of needle-like fine crystallites on its surface in living body and can avoid immune reaction. From the above idea, it is thought that microcapsules possessing high biocompatibility can be obtained by applying apatite. The porous bone-like apatite microcapsules can be fabricated by the following process [46, 47]:

Figure 9. (a) SEM micrograph and (b) EDX profile of the surface of the bioactive PEEK after the soaking in SBF for 1 day. The generation of cracks observed in Figure 9 (a) was caused when the specimen was air-dried after the SBF test.
• Apatite nuclei are attached to the surfaces of core particles.
• The microspheres are soaked in SBF.

By this treatment, apatite formation is induced by the apatite nuclei and grows over the whole surface area of the core particles. As a result, porous bone-like apatite coats the whole surface of the particles and apatite microcapsules can be obtained (Figure 10). By this method, it is expected to encapsulate various kinds of functional particles or pharmaceutical drugs with apatite.

The development of sustained-release of drug is expected to contribute to have effects of the drug without side effects and reduce the burdens of patients. Porous bone-like apatite formed in SBF has flake-like crystalline structure and porous body [46, 47]. Focusing on these features of porous bone-like apatite, the author has intended to fabricate porous bone-like apatite microcapsules encapsulating various kinds of substances such as PLLA [48], silver [48], silica gel [48, 49], magnetite [50], maghemite [51, 52], agarose gel [53, 54] and corn oil [55]. Among them, the author introduces the details of encapsulation of corn oil in the porous bone-like apatite microcapsules as representative cases in this chapter.

4.2. Porous bone-like apatite microcapsules encapsulating corn oil

By utilizing surfactant such as albumin, oil droplets in micrometer level can be stabilized in water phase or water droplets in micrometer level can be stabilized in oil phase. The microencapsulation techniques by forming oil or water droplets can achieve an intravenous injection of the droplets containing pharmaceutical drug. As described in this section, the author fabricated porous bone-like apatite microcapsules encapsulating corn oil droplets containing ibuprofen, hydrophobic drug and nonsteroidal anti-inflammatory drug and evaluated the temporal change in release of the ibuprofen in vitro.

4.3. Preparation process of porous bone-like apatite microcapsules encapsulating corn oil

4.3.1. Fabrication of porous bone-like apatite microcapsules

Corn oil and ibuprofen were mixed. In order to dissolve ibuprofen in corn oil sufficiently, ethyl acetate was added in the mixture. After albumin aqueous solution was poured, the mixture was treated by ultrasonic vibration, so emulsion was formed. The emulsion was mixed

Figure 10. Fabrication process of apatite microcapsules by using apatite nuclei.
with 1.5 SBF, whose ion concentrations are 1.5 times in comparison with those of SBF, and apatite nuclei, thereafter, the mixture was treated by ultrasonic vibration to attach apatite nuclei on the surface of the oil droplets. After ethyl acetate was evaporated and removed from the mixture, the solution was kept at 36.5°C for 4 days. Figure 11 shows SEM micrograph and EDX profile of thus-obtained microcapsules. Spherical particles consisted of needle-like crystals, which characterize bone-like apatite, were observed. In the EDX measurement, phosphorus and calcium, main consistent of apatite, were detected. It is suggested that the apatite nuclei attached on the oil droplets induced formation of bone-like apatite and then the crystal growth of apatite was caused on the surface of the oil droplets. Figure 12 shows the powder X-ray diffraction (XRD) profile of the obtained apatite microcapsules. It can be seen that the peak positions of the apatite microcapsules corresponded to those of apatite, but shape of the pattern was broad. From this result, it was indicated that bone-like apatite covered the corn oil droplets during soaking in SBF.

4.4. Function of porous bone-like apatite microcapsules: drug release behavior

The author evaluated the release behavior of ibuprofen contained in corn oil droplets. Figure 13 shows the temporal change in the concentration of ibuprofen released from porous bone-like apatite microcapsules in phosphate buffer (pH 7.40 at 36.5°C) measured by high-performance liquid chromatography (HPLC). It can be seen that the concentration of

![Figure 11.](image1.png)  
(a) SEM micrograph and (b) EDX profile of the porous bone-like apatite microcapsules encapsulating corn oil.

![Figure 12.](image2.png)  
XRD profile of the porous bone-like apatite microcapsules encapsulating corn oil.
ibuprofen in the buffer did not increase rapidly in a short time but increased gradually. This profile suggested that the porous structure of bone-like apatite microcapsules can gradually release ibuprofen contained in corn oil through the micropores of the apatite coatings.

4.5. Other types of porous bone-like apatite microcapsules

As described in Section 4.1, this fabrication method for porous bone-like apatite microcapsules was applicable to other kinds of core materials such as encapsulating various kinds of substance such as PLLA [48], silver [48], silica gel [48, 49], magnetite [50], maghemite [51, 52] and agarose gel [53, 54] by optimizing the fabrication condition. In the case of silver, sustained release of silver was attained by existence of porous coatings of bone-like apatite. In the case of silica gel, sustained release of insulin was attained by conducting absorption of insulin solution into the silica-gel matrix [56]. In the case of magnetite, release of magnetite was inhibited in water by existence of the porous apatite coatings. In the case of agarose gel, sustained release of vitamin B$_{12}$ was attained by conducting insertion of vitamin B$_{12}$ solution in the apatite microcapsules [53]. In the case of maghemite, in addition, the author successfully achieved enzyme immobilization and collection by combination of bioaffinity of apatite with ferrimagnetism of maghemite.

5. Conclusion

In this chapter, the author introduced novel biomaterials utilizing porous bone-like apatite formation from apatite nuclei from a viewpoint of bioactive metals, bioactive organic polymers and apatite microcapsules. This methodology has high materials selectivity, and function of apatite nuclei enables us to impart bioactivity to various kinds of materials or to coat microparticles with porous bone-like apatite coating. It is expected that the porous bone-like apatite coating technique are promising methodology to be useful to fabricate novel medical, pharmaceutical and environmental materials by combination of bone-like apatite with various kinds of functional materials in micron scale.
Author details

Takeshi Yabutsuka

Address all correspondence to: yabutsuka@energy.kyoto-u.ac.jp

Department of Fundamental Energy Science, Graduate School of Energy Science, Kyoto University, Japan

References


[23] Kidokoro Y, Yabutsuka T, Takai S, Yao T. Bioactivity treatments for zirconium and 
Ti-6Al-4V alloy by the function of apatite nuclei. Key Engineering Materials. 2017;720:175-
179. DOI: 10.4028/www.scientific.net/KEM.720.175

493-494.545

precipitated Ti-15Mo-5Zr-3Al alloy by using doubled sandblasting process. Key 
631.231

[26] Yabutsuka T, Mizutani H, Takai S, Yao T. Fabrication of bioactive cobalt-chromium 
DOI: 10.4028/www.scientific.net/KEM.720.180

[27] Yabutsuka T, Karashima R, Takai S, Yao T. Fabrication of bioactive stainless steel by 
the function of apatite nuclei. Key Engineering Materials. 2016;696:151-156. DOI: 
10.4028/www.scientific.net/KEM.696.151

[28] Yabutsuka T, Karashima R, Takai S, Yao T. Effects of sandblasting conditions in prepara-
tion of bioactive stainless steels by the function of apatite nuclei. Phosphorus Research 
Bulletin. 2016;31:15-19. DOI: 10.3363/prb.31.15

[29] Yao T, Yabutsuka T. Material having pores on surface, and method for manufacturing 

908977168_0021

10.1002/(SICI)1097-4636(199722)38:2<121::AID-JBM6>3.0.CO;2-S

bonding strength by graded structure at interface between apatite layer and bioactive 
DOI: 10.1023/A:1015729507800

Bonding strength of the apatite layer formed on glass-ceramic apatite wollastonite-poly-
ethylene composites. Journal of Biomedical Materials Research. 2003;67A(3):952-
959. DOI: 10.1002/jbm.a.10131

and CRC Press; 2008

polyethylene—A mechanically compatible implant material for bone replacement. 
Biomaterials. 1981;2(3):185-186. DOI: 10.1016/0142-9612(81)90050-8


