Hydroxyapatite of Great Promise for Biomaterials.

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Abstract

Since 1971's success in fabrication of sintered hydroxyapatite, we have developed many biomaterials based on hydroxyapatite. In the present paper, the outline of fundamental studies and a few applications of hydroxyapatite for dental and medical use are described.

1. Introduction

In the past 20 years, there have been many new developments in biomaterials and techniques. There are several types of biomaterials made of metals, ceramics, polymers and composites. Among them, it has become recently well known that ceramics are successful materials for dental and medical implants because of good biocompatibility. It is so-called bioceramics. Hydroxyapatite, which is one of the bioceramics, was developed as an epoch-making new biomaterial by Aoki et al in Japan and by Jarcho in the USA during 1971-1973. In 1975, it was found in Japan that the sintered hydroxyapatite has the best osteocompatibility in comparison with previous implant materials.

The chemical formula of hydroxyapatite is represented as $Ca_{10}(PO_4)_6(OH)_2$ and is very similar to bone or tooth mineral composition. Up to date, we have developed dental and medical implant materials based on hydroxyapatite. In the dental field, dental cements, dentifrices, artificial tooth roots, and bone fillers have been used in practical applications. In the medical field, use for artificial bones, joints and percutaneous devices, as well as tracheal and blood vessels has been actively investigated.

2. Biomaterials

It is not so easy to define the word "Biomaterials". According to a definition of the Clemson Advisory Board for Biomaterials, 1974, a biomaterial is a systemically, pharmacologically inert substance designed for implantation within or incorporation with a living system. At the present time, however, this definition

is old and a little discrepant. For example, in this definition a biomaterial is limited to an inert material in the living body, but currently it is regarded that a biomaterial reacts to living tissue and functionally incorporates with a living body. Incidentally, biomaterials will become more important and rapidly develop in the medical and dental fields.

Biomaterials are basically three types of materials, including ceramics, metals and polymers. Table 1 shows several properties of each, though these properties are not always exact. Each material has an advantage and disadvantage. In the future, a composite material combining two or more types will be developed.

Table 1. The Chemical and Physical Properties of Materials

	Ceramics	Metals	Polymers
Biocompatibility	Excellent	Good	Good
Chemical resistance	Excellent	Good	Good
Thermal resistance	Excellent	Good	Poor
Thermal expansion	Little	Medium	Great
Heat conductivity	Good	Excellent	Poor
Hardness	Hard	Medium	Soft
Compressibility	Great	Medium	Little
Tensile strength	Medium	Strong	Weak
Brittleness	Great	Little	Little
Moldability	Difficult	Ordinary	Easy
Cost	Expensive	Cheap	Cheap

3. Bioceramics

Bioceramics is made of new ceramics. In the last 15 years, researchers in several countries, especially the USA, Germany and Japan, have successfully developed several new bioceramics for medical and dental prostheses. Table 2. shows the kinds and applications of bioceramics.

Bioceramics are divided into two types, bioinert and bioactive ceramics. Bioinert ceramics are alumina, zirconia, carbon, and so on. Bioactive ceramics are hydroxyapatite, TCP, bioglass and so on. Among them, hydroxyapatite is the most viable material and of great promise for biomaterials or bioceramics.

Table 2. Kinds and Applications of Bioceramics

Chemical formula of bioceramics.	Applications for medical and dental uses	
(1) Hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$	Artificial bone	(1)(2)(4)(6)
(2) Alumina Al_2O_3	Artificial joint	(1)(2)(3)(6)(7)
(3) Carbon C	Artificial tooth root	(1)(2)(3)(4)(5)(7)
(4) Tricalcium phosphate $Ca_3(PO_4)_2$	Bone filler	(1)(4)
(5) Bioglass $SiO_2 \cdot CaO \cdot Na_2O \cdot P_2O_5$	Bone replacer	(1)(4)
(6) Crystallized glass $SiO_2 \cdot CaO \cdot MgO \cdot P_2O_5 \cdot CaO \cdot P_2O_5$	Bone fixer	(1)(2)(5)
(7) Zirconica ZrO_2	Artificial valve	(3)
(8) Others	Artificial tendon	(3)
	Artificial blood vessel	(1)(2)(3)
	Artificial tracheal	(1)(3)
	Skin terminal	(1)(3)
	Others	

4. Hydroxyapatite

4-1 Chemical composition

"Apatite" is a general term for crystalline minerals with a composition of $M_{10}(ZO_4)_6X_2$. The name is from the Greek "apato". Many elements occupy the M, Z and X sites.

M= Ca, Sr, Ba, Cd, Pb etc.
Z= P, V, As, S, Si, Ge etc.
X= F, Cl, OH, O, Br, Vacancy etc.

Various apatitic compounds different in composition can be prepared by replacement of elements for each site. "Hydroxyapatite" is a member of the apatite group, and its composition is represented as the formula, $Ca_{10}(PO_4)_6(OH)_2$. Hydroxyapatite is a main component of bone and tooth minerals. An adult possesses two kilograms of hydroxyapatite.

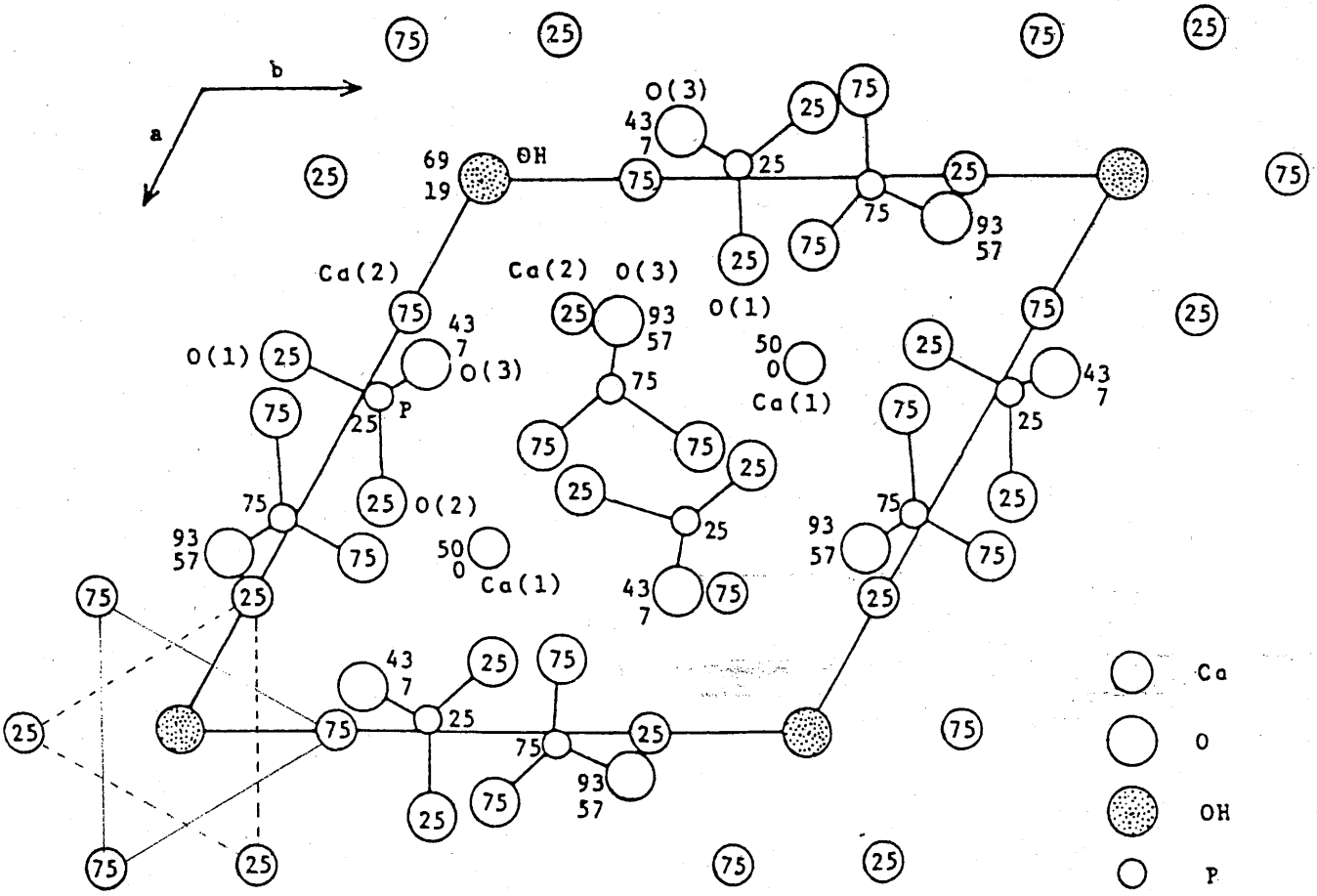
4-2 Crystal structure

The crystal structure of natural apatite was determined by Naray-Szabo (1930) and Mehmel (1930). Natural apatite is near $Ca_{10}(PO_4)_6F_2$ in composition. Hydroxyapatite is almost isostructural with fluor-apatite. In the structure of hydroxyapatite, the F atom is replaced by the OH group.

Hydroxyapatite is hexagonal, space group $P6_3/m$, with cell dimensions of a=9.423 and c=6.875 A. Fig.1 shows the crystal structure of hydroxyapatite projected along a c-axis. There are two crystallographically independent Ca atoms in the unit cell. The Ca(2) atom is surrounded by six O atoms belonging to PO_4 groups and an OH group, whereas the Ca(1) atom is nearly octahedrally surround-

ed by six O atoms. The Ca(2) atoms form a triangle normal to a c-axis. The Ca(2) triangles stack along the c-axis, rotating mutually 60° from each other. In the fluor-apatite structure, the F atom is located at the center of the Ca(2) triangle. In the hydroxyapatite structure, the OH group is not located at the center, but shifted above or below the center of the triangle. The P atom is surrounded by four O atoms and forms a tetrahedron. The PO_4 tetrahedron is almost regular with only slight distortion.

Fig. 1 The Crystal Structure of Hydroxyapatite



4-3 Preparation of sintered hydroxyapatite

A suspension of 0.5M $Ca(OH)_2$ in 1000 ml distilled water was vigorously stirred and a solution of 0.3 M H_3PO_4 in 1000 ml distilled water was slowly added as drops over 1 to 2h under a condition of pH 7 to produce a gelatinous precipitate. The reaction mixture was stirred for a few hours and aged at room temperature for a week. The resulting slurry was filtrated. The filter cake was dried at 80°C and calcined at 800°C for 3h. The product has a Ca/P ratio of 1.67 estimated by standard EDTA titration for Ca and phosphomolybdate techniques for PO_4. The finely ground powder, mixed with 1 wt% cornstarch and a few drops of water, was pressed by a mold at a pressure of 60-80 MPa. The compact was heated in air at 1150, 1200, 1250 and 1300°C for 3h. In the X-ray powder diffraction paterns, α - and β -$Ca_3(PO_4)_2$ phases were not detected; the

maximum sensitivity for detection was 2% in these systems. The porosity values were calculated by assuming the theoretical density of 3.16 $g\,cm^{-3}$. The average grain sizes (See Table 3) were estimated by the linear intercept method from scanning electron micrographs of the specimens after etching in 0.1 M acetic acid solution for 5 min.

Table 3. Porosity and grain size results for sintered hydroxyapatite

Temperature(°C)	Time(h)	Porosity(%)	Grain size(m)
1150	3	19.4	1.04 ± 0.46
1200	3	9.1	1.32 ± 0.61
1250	3	3.9	2.03 ± 0.91
1300	3	2.8	3.40 ± 1.01

4-4 Mechanical Properties

The mechanical properties of hydroxyapatite ceramics are summarized in Table 4. The mechanical properties of the materials sintered at 1150°C with about 20% porosity were very low. The maximum compressive, flexural and static torsional strength of brittle polycrystalline materials depends on porosity and grain size. Rao and Boehm have reported that the compressive strength of apatite has an exponential dependence on porosity. The flexural strengths of the materials measured in this work tended to depend on porosity rather than grain size.

Table 4. Compressive, flexural, torsional and dynamic torsional strengths, and moduli of elasticity in compression and bending, for sintered hydroxyapatite

Temperature (°C)	Compressive strength σ_C(MPa)	Flexural strength σ_F(MPa)	Torsional strength γ_{ST}(MPa)	Dynamic torsional γ_{DY}(MPa)	Modulus of elasticity in E_C(GPa)	Modulus of elasticity in E_B(GPa)
1150	308±46	61± 8	50± 7	57± 6	42.2±3.8	44.3±3.5
1200	415±46	104±11	62± 5	92± 6	74.6±4.1	80.0±6.4
1250	465±58	106±10	75± 4	76± 5	79.0±4.8	85.1±6.1
1300	509±57	113±12	76± 5	68± 5	81.4±4.6	87.8±6.0

The mechanical properties of cortical bone, dentine and enamel are listed in Table 5. Note that the strength of cortical bone depends both on the degree

Table 5. Mechanical properties of various hard tissues and references

Material	Compressive strength(MPa)	Tesnile strength(MPa)	Modulus of elasticity(GAp)
Cortical bone	88.3-163.8[7]	88.9-113.8[8]	3.88-11.7 [7]
Dentine	295 [10]	51.7[9]	18.2[10]
Enamel	384 [10]	10.3[9]	82.4[10]

of calcification and on fibre orientation. Static and dynamic torsional strengths of ox femoral cortex, measured by the method given in Section 2.2 were 52 ± 5 and 59 ± 7 MPa, respectively.

The compressive strength of the sintered hydroxyapatite is approximately 3 to 6 times as strong as that of cortical bone, and is very roughly 1.5 times as strong as that of dentine and enamel. The flexural strength of sintered hydroxyapatite is very similar to the tensile strength of cortical bone, and is 2 and 10 times as strong as the tensile strengths of dentine and enamel, respectively. The static and dynamic torsional strengths of hydroxyapatite are about 1.5 times as strong as those of cortical bone. The value of the modulus of elasticity is between 5 and 20 times as great as that of cortical bone and is about 5 times as great as that of dentine. The modulus of elasticity for the present hydroxyapatite is in close agreement with that of enamel which is composed of 98wt% hydroxyapatite.

4-5 Osteocompatibility of Hydroxyapatite

Sintered hydroxyapatite was formed into a column shape, diameter 5 mm, height 8-10 mm. These columns were implanted in the socket where the first molars of the mandible had been extracted and spread out by a dental bar.

After 8 weeks of implantation, the newly formed trabeculae were in close contact with the hydroxyapatite column. Infection and other rejection phenomena were not observed. According to a transmission electron micrograph, the newly formed bone directly bonded to the hydroxyapatite column, and the bone tissue was grown into micro pores on the column, independent of the pore size. It seems that the other surface of the hydroxyapatite was changed into new bone tissue.

It was concluded that hydroxyapatite has the best osteocompatibility in comparison with previous implant materials.

4-6 Applications of Hydroxyapatite

Many biomaterials based on hydroxyapatite have been applied to dental, orthopaedic and other medical uses. Table 6 summarizes these applications. In dental uses, an artificial tooth root made of hydroxyapatite seems the most significant.

Table 6. Hydroxyapatite for Medical and Dental Use

Medical Use	Dental Use
Artificial bone	Dentifries
Artificial joint	Cement
Bone filler	Canal
Artificial blood vassel	Bone filler
Artificial tracheal	Tooth root
Percutaneous device	Porous bone
	Porcelain tooth

In medical uses, a percutaneous device based on hydroxyapatite, will be great promise of biomaterials.