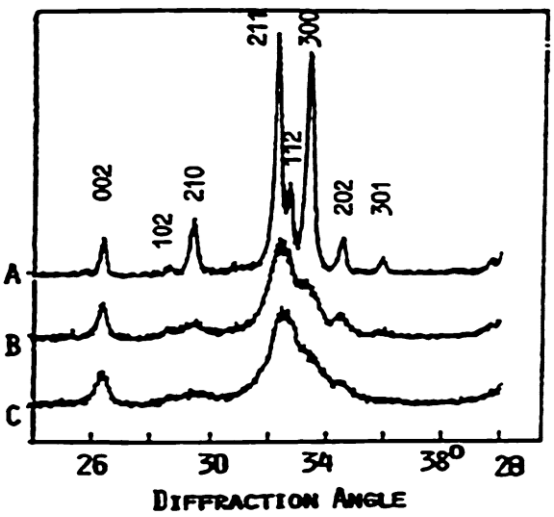
Biologic Apatite

The name "apatite" describes a family of compounds having similar structure (hexagonal system) in spite of a wide range of compositions. These minerals have the general formula $M_{10}(PO_4)_6X_2$, where M could be one of several metals (usually calcium, Ca), P is most commonly phosphorus (P), and X is commonly hydroxide (OH) or a halogen such as fluorine (F) or chlorine (Cl).

Biologic apatites are the inorganic phases of calcified tissues (teeth and bones). The similarity in composition of calcined bone to the apatite mineral, and in the X-ray diffraction patterns of bone and mineral apatites (HA and fluorapatite (FA) and similarity in composition (principally calcium and phosphate ions) led to the conclusion that the inorganic phases of bones and teeth are basically calcium hydroxyapatite. Enamel, dentin, and bone apatite differ in crystallinity, reflecting crystal size (Fig. 2) and concentrations of minor constituents mainly Mg and CO_3. Studies on the effect of Mg and CO_3 ions on the properties of synthetic apatites demonstrated that incorporation of these ions independently causes the growth of smaller and more soluble apatite crystals. The effects of CO_3 incorporation on apatite crystal size and morphology and on dissolution properties are much more pronounced than that of Mg. The crystal size (nanometers) of biological HA is much smaller than can be produced in synthetic HA. Current commercial synthetic calcium phosphate biomaterials classified on the basis of composition include HA, $Ca_{10}(PO_4)_6(OH)_2$; α - and β-tricalcium phosphates (α -TCP β-TCP), $Ca_3(PO_4)_2$; and biphasic calcium phosphate (BCP), an intimate mixture of HA and β -TCP with varying HA/ β-TCP ratios. Other commercial HA biomaterials are derived from biologic materials (e.g., processed human bone, bovine bone derived, hydrothermally converted coral or derived from marine algae) Biologic apatites are usually calcium-deficient (i.e., with Ca/P molar ratio less than the stoichiometric value of 1.67 obtained for pure HA, $Ca_{10}(PO_4)_6(OH)_2$, it have been idealized as calcium HA, and may occur as one of the mineral phases that include other calcium phosphates, e.g., amorphous calcium phosphate (ACP), $Ca_x(PO_4)_y$; dicalcium phosphate dehydrate (DCPD), $CaHPO_4 \cdot 2H_2O$; octacalcium phosphate (OCP), $Ca_8H_2(PO_4)_6 \cdot 5H_2O$; magnesium-substituted tricalcium phosphate (β-TCMP, $(Ca,Mg)_3(PO_4)_2$); and calcium pyrophosphate dihydrate (CPPD), $Ca_2P_2O_7 \cdot 2H_2O$.



Fig(2) X-ray diffraction profiles of biologic apatites from adult human enamel (a)(, dentin (b), and bone (c).

Synthetic Apatite

Studies on synthetic apatites in the last 30 years were motivated by development of calcium phosphate-based biomaterials (principally HA, TCP, or biphasic) for bone repair, substitution, and augmentation and as scaffolds for tissue engineering in bone and teeth regeneration. The rationale for developing HA biomaterials was their similarity in composition to the biologic apatite and bone mineral. Synthetic HA can be made by solid-state reactions or by precipitation or hydrolysis methods and subsequent sintering at high temperatures, usually 1,000 °C and above. Synthetic apatites can also be prepared using hydrothermal, and sol-gel methods. Apatite nanocrystals are obtained when prepared by precipitation or hydrolysis at lower temperatures (25–60)°C. Synthetic apatite crystals approximating the size of human enamel apatite may be obtained by precipitation or hydrolysis methods with reaction temperature (80-90) °C. Apatites may also be prepared in sol-gel systems, by electrodeposition precipitation on metallic or polymeric substrates. Sintering of HA at temperatures above 1,200 °C results in thermal decomposition of apatite forming other calcium phosphates such as β-TCP and α-TCP. The combination of calcium phosphates (e.g., ACP, DCPA, DCPD, CDA, α-TCP, β-TCP) with other calcium compounds (CaO, $Ca(OH)_2$, $CaCO_3$), mixed with phosphate solutions or organic acids, results in the formation of apatitic calcium phosphate cements . Studies on synthetic apatites showed that substitutions for Ca, PO_4, or OH ions in the apatite structure result in changes in lattice parameters and crystallinity (reflecting crystal size) and dissolution properties. These calcium phosphate bioceramics include HA, β-TCP, BCP, bovine bone-derived apatites (unsintered and sintered), and coral-transformed apatite. Commercial HA biomaterials are usually prepared by precipitation at high pH and subsequent sintering at about 1,000–1,100 °C. The different preparations and origin (synthetic vs. biologic) are reflected in the difference in their initial crystallinity reflecting crystal size and their dissolution rates, increasing in the order HA << coralline HA < bovine bone apatite (sintered) << bovine bone apatite (unsintered) HA << BCP << β-TCP.

Synthetic HA in Implant Surfaces, Coatings and Composites

Porous HA and related calcium phosphates, in spite of their many desirable properties, are not strong enough to be used in load-bearing areas. The rationale for the development of "HA"-coated orthopedic and dental implants is to combine the strength of the metal (usually titanium or titanium alloy) and the bioactive properties of HA and other calcium phosphates. Dense HA particles are used as the source material for depositing implant coating by the plasma-spray technique. The high temperatures and other variable parameters involved in the plasma-spray process (e.g., velocity of feeding the HA powder, distance of the gun from the metal substrate) result in the partial transformation of the original HA into ACP and minor amounts of α-TCP, β-TCP, and

tetracalcium phosphate (TTCP, $Ca_4P_2O_9$). Plasma-sprayed "HA" coatings have nonhomogenous composition principally ACP/HA ratio), varying from the layer closest to the metal substrate to the outermost layer and varying from one manufacturer to another. Alternatives to the plasma-spray method are nanocoating, electrochemical deposition, and precipitation or chemical deposition, the latter method being also applicable to nonmetallic substrates. These other methods provide homogenous implant coating of the desired composition, e.g., HA, FA, CHA, and allow coating deposition at much lower temperatures.

During the last decade, HA or BCP has been used as an abrasive material for grit blasting to roughen the surface and provide a more bioactive surface (compared to alumina or silica abrasive), thus enhancing osseointegration of the implant

HA and related calcium phosphates are used as the inorganic component in composites with natural (e.g., collagen, chitosan) or synthetic (polylactic acid or polylacticglycolic acid, PLA or PLGA, high-molecular-weight polyethylene) polymers. The rationale for developing composite biomaterials is the fact that bone is a composite of a biologic polymer (collagen) and inorganic phase (carbonate apatite).

Critical Properties of Synthetic HA and Related Calcium Phosphates

Hydroxyapatite is considered bioactive, indicating that the ceramic may undergo ionization

in vivo and that the rate of dissolution may depend on many factors − including degree of crystallinity, crystallite size, processing condition (temperature, pressure, and partial water pressure), and porosity. Hydroxyapatite is soluble in an acidic solution while insoluble in an alkaline one and slightly soluble in distilled water.

Solubility in distilled water increases with addition of electrolytes. Moreover, the solubility of HA changes in the presence of amino acids, proteins, enzymes, and other organic compounds. These solubility properties are closely related to the biocompatibility of HA with tissues and its chemical reactions with other compounds. However, the solubility *rate* depends on differences in shape, porosity, crystal size, crystallinity, and crystallite size. The solubility of sintered HA is very low

Porosity (interconnecting macroporosity) is an important property of biomaterials to allow bony ingrowth and regeneration by facilitating migration, proliferation and differentiation of cells, as well as vascularisation. Many studies have proved that high porosity is expected to enhance osteogenesis. On the other hand, a porous surface reduces the probability of movement by enhancing the mechanical interlocking between the implant and host tissue. Bioactivity is defined as the property of the material to develop a direct, adherent, and strong bonding and interface with the bone tissue it is demonstrated in vitro and in vivo by the ability of the material to form carbonate apatite on the surface from the simulated body fluid in vitro or biologic fluid

in vivo. Material surface composition and surface roughness or topography influence cell response (proliferation, attachment, phenotypic expression) to the material.

Osteoconductivity is the property of the material that allows attachment, proliferation, migration, and phenotypic expression of bone cells leading to the formation of new bone in direct opposition to the biomaterial. HA and related calcium phosphates are generally considered to have all the above properties.