Strontium–Copper–Calcium Hydroxyapatite Solid Solutions: Preparation, Infrared, and Lattice Constant Measurements

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Homogeneous solid solutions of strontium, copper, and calcium hydroxyapatite $(Ca_lSr_mCu_n)_{10}(PO_4)_6$ $(OH)_2$ with fixed $n = 1$ have been prepared over the entire compositional range by coprecipitation in aqueous media by the addition of ammonium dihydrogen phosphate to solutions of strontium, copper, and calcium nitrate made strongly basic with aqueous ammonia. The infrared spectra and lattice constants of the solid solutions have been measured and found to vary linearly with composition between those of the pure end members. © 1989 Academic Press, Inc.

Introduction

The mechanism of incorporation of strontium and copper into bone has been of great interest ever since the release of radioactive strontium (^{90}Sr) into the atmosphere from nuclear bomb tests and the tragedy of "knee-knock" disease caused by copper pollution during the excavation of copper mines. Calcium hydroxyapatite (CaHA), $Ca_{10}(PO_4)_6(OH)_2$, the principal inorganic constituent of human bones and teeth (*1*), belongs to an isomorphous series of compounds known as apatite.

Calcium hydroxyapatite, which exists in nature as the mineral hydroxyapatite and is similar if not identical to bone mineral, can be prepared from aqueous solution (*2, 3*).

Apatite undergoes a series of cationic and anionic replacement reactions (*5*). The $Ca^{2+} \rightarrow Sr^{2+}$ and/or Cu^{2+} replacement reactions in CaHA are of extreme biological significance and are interesting in view of their action on calcified tissue. They form the basis of incorporation of Sr^{2+} and Cu^{2+} into the human skeletal system according to the equation

$$Ca_{10}(PO_4)_6(OH)_2 + mSr^{2+} + nCu^{2+} \rightarrow$$
$$Ca_{10-(m+n)} Sr_mCu_n(PO_4)_6(OH)_2$$
$$+ (m + n) Ca^{2+},$$
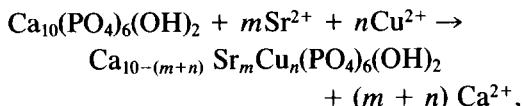
when $n = 1$. Solid solutions of strontium, copper, and calcium hydroxyapatite were prepared separately earlier (*6*) by firing mixtures containing various proportions of strontium, copper, and calcium hydroxyapatites at about 1300°C. These samples prepared by the solid state reaction, were, however, found to be nonhomogeneous. We now report the preparation of the homogeneous solid solutions of strontium–copper–calcium hydroxyapatite over the entire compositional range by the method of coprecipitation in aqueous media (*7, 8*).

Experimental

Materials. Chemicals used for the preparation of these samples were reagent grade.

Water used in the preparation and the washing was boiled to remove CO_2 and then used immediately.

Preparation. Stoichiometric quantities of 0.250 M ammonium dihydrogen phosphate (Solution A) and 0.250 M strontium, copper, or calcium nitrate (Solution B) were prepared separately in CO_2-free doubly distilled water. Both solutions were made more basic than pH 11 by addition of aqueous ammonia, and this high basicity was maintained during the precipitation reaction and subsequent digestion. Then a part of Solution B was put in a flask (2 liter) fitted with two separating funnels and a delivery tube. For the preparation of pure CaHA, an excess of calcium ion was necessary to prevent the uptake of excess phosphate; accordingly a considerable cation excess was used throughout. Solution A and Solution B were poured individually into the separating funnels and added dropwise to the flask simultaneously. Precipitation was carried out in a CO_2-free atmosphere and the precipitation medium was well stirred by bubbling CO_2-free air to prevent the formation of carbonato-apatites.

The precipitate and mother liquor were aged by boiling under reflux for 1.5 hr to improve the homogeneity and crystallinity of the precipitate and, since any alteration of pH of the medium during precipitation could lead to the formation of calcium-deficient apatite *(9)*, maintainance of the desired pH during precipitation was ensured by testing the filtrate after separation of the precipitate. The precipitate was allowed to settle overnight and then washed repeatedly with doubly distilled water until the wash water reached pH 7. The precipitate was then filtered, dried at 110°C for few hours, and analyzed complexometrically by EDTA *(10)*. Densities were determined using toluene *(11)* as a solvent and molar volumes were calculated.

Infrared absorption techniques. Samples used for IR studies were washed with acetone and air-dried. Spectra were recorded on a Grating Model 577 infrared spectrophotometer (Perkin–Elmer) in KBr medium. A few milligrams of the sample was ground with two drops of Nujol in an agate mortar. About 50 mg of a fine polyethylene powder (Vestolena 6016 Chem. Werke Huels, Germany) was added. The resulting paste was melted and lightly pressed between glass plates at about 150°C to form a slightly wedge-shaped film with an average thickness of 0.1 mm.

X-ray diffraction techniques. After drying at 110°C and then heating 4 hr at 950°C, samples were obtained that gave sharp X-ray diffraction patterns of the pure hydroxyapatite phases. The X-ray diffraction patterns of the samples were obtained with Siemens powder diffractometer with a NaCl (TL) counter employing CuK_α (nickel filtered) radiation with a 2θ scanning speed of 1° per minute.

Lattice constant measurements. SrHA, CuHA, and CaHA are hexagonal with lattice constant a_0 and c_0. These were determined for our samples by measuring the diffraction angle 2θ of the three planes (312), (213), and (321). Each sample was thoroughly mixed with 25% NaCl (recrystallized from HCl) as a standard. The lattice constant of NaCl at 26°C was taken to be 5.6403 Å *(12)*. A least-squares calculation on the corrected values of sin θ for the three reflections then gave the parameters a_0 and c_0 for each sample. The average probable error in unit cell parameters is less than ±0.003 Å.

Results and Discussion

The results of chemical analysis of the samples are given in Table I. A molecular formula for each of the samples was assigned on the basis of the results of chemical analysis (Table I), assuming that 1 mole of sample contained a total of 10 mole of strontium, copper, and calcium. Observed

TABLE I

CHEMICAL ANALYSIS OF STRONTIUM, COPPER, AND CALCIUM HYDROXYAPATITES
AND THEIR SOLID SOLUTIONS

	Wt%				g-at. ratio $\frac{Ca + Sr + Cu}{P}$	
Formulation	Ca	Sr	Cu	P		Molar volume
1. $Ca_{10}(PO_4)_6(OH)_2$	39.89	—	—	18.51	1.667	338.271
2. $Ca_{8.07}Sr_{0.98}Cu_{0.95}(PO_4)_6(OH)_2$	30.12	7.99	5.62	17.32	1.666	343.245
3. $Ca_{7.03}Sr_{1.99}Cu_{0.98}(PO_4)_6(OH)_2$	25.1	15.53	5.55	16.57	1.666	355.034
4. $Ca_{6.04}Sr_{2.95}Cu_{1.01}(PO_4)_6(OH)_2$	20.71	22.12	5.49	15.91	1.667	349.951
5. $Ca_{5.05}Sr_{3.99}Cu_{0.96}(PO_4)_6(OH)_2$	16.63	28.72	5.01	15.28	1.666	351.457
6. $Ca_{4.03}Sr_{5.01}Cu_{0.96}(PO_4)_6(OH)_2$	12.76	34.7	4.82	14.69	1.667	360.300
7. $Ca_{3.00}Sr_{6.06}Cu_{0.94}(PO_4)_6(OH)_2$	9.14	40.38	4.54	14.14	1.667	358.297
8. $Ca_{2.02}Sr_{7.01}Cu_{0.97}(PO_4)_6(OH)_2$	5.95	45.13	4.52	13.66	1.667	345.108
9. $Ca_{1.06}Sr_{7.99}Cu_{0.95}(PO_4)_6(OH)_2$	3.01	49.76	4.29	13.22	1.666	357.452
10. $Sr_{9.01}Cu_{0.95}(PO_4)_6(OH)_2$		54.20	4.31	12.77	1.666	354.217
11. $Sr_{10}(PO_4)_6(OH)_2$		59.19		12.56	1.667	364.612
12. $Cu_{10}(PO_4)_6(OH)_2$			51.27	15.00	1.668	347.718

values of atomic ratios of Ca/P, Sr/P, Cu/P for the end members and of (Ca + Sr + Cu)/P were found to be 1.666 (theoretical 1.67), consistent with the formation of homogeneous solid solutions (11). This was further supported by the closeness of the values of molar volumes of the end members and those of the intermediate samples which lie within the range of end members.

The formation of solid solutions can be confirmed further by X-ray diffraction analysis (13, 14). Lattice parameters showed unit cell dilation and contraction consequent upon the introduction of the larger Sr^{2+} ion (1.13 Å) and the smaller Cu^{2+} ion (0.72 Å) in place of two Ca^{2+} ions in the apatite lattice. This of course is the real evidence for solid solution in this series and clearly shows that these preparations are not mixtures of two components or one component with adsorbed material.

Infrared spectra of mixed hydroxyapatites were carried out in the range 4000–400 cm^{-1}. The results of the IR measurements are collected in Table II.

The general formula of the apatite considered here is $M_{10}(RO_4)_6X_2[M_5(RO_4)_3X]$, where M is a divalent cation like Ca, Sr, or Cu; RO_4 is the orthophosphate, PO_4; and X is the monovalent anion, OH. In this formula, when M or X is replaced by a related ion, the positions of the phosphate bands in the IR spectrum change. As a part of physicochemical investigations, it is of great interest to know the nature of the change and the general trends of bands.

In aqueous solution, the orthophosphate in the free or isolated state exhibits tetrahedral symmetry and is a member of the Td point group. The assignments of IR bands for simple aqueous phosphates are well established [$v_3(1017$ $cm^{-1})$ and $v_4(567$ $cm^{-1})$] (15, 16). The CaHA and its solid solutions with strontium and copper are interesting solid state examples of fairly simple molecules of tetrahedral symmetry (17, 18). This is the symmetry imposed by the static field of the surrounding ions. In addition to this field, there is dynamic interaction between the ions, which also has a strong influence on the internal vibration of PO_4^{3-}. According to the selection rules, there are nine internal vibrations of phosphate groups, six of which are due to the movements of at-

TABLE II

Unit Cell Dimensions and IR Spectra of Strontium, Copper, and Calcium Hydroxyapatites and Their Solid Solutions

Apatite	a-axis (Å)	c-axis (Å)	c/a	Unit cell volume $((\sqrt{3}/2)\,_a2_c)$	Frequency (cm^{-1})		
					PO_4^{3-} ν_3	PO_4^{3-} ν_4	OH^- ν_3
1. $Ca_{10}(PO_4)_6(OH)_2$	9.37	6.86	0.732	521.60	1075	570	3550
2. $Sr_{10}(PO_4)_6(OH)_2$	9.74	7.26	0.745	596.47	1077	572	3585
3. $Cu_{10}(PO_4)_6(OH)_2$	8.83	6.53	0.740	440.93	1065	555	3500
4. $Ca_{7.03}Sr_{1.99}Cu_{0.98}(PO_4)_6(OH)_2$	9.42	6.88	0.730	528.71	1075	565	3570
5. $Ca_{5.05}Sr_{3.99}Cu_{0.96}(PO_4)_6(OH)_2$	9.46	7.02	0.742	544.06	1074	568	3577
6. $Ca_{3.00}Sr_{6.06}Cu_{0.94}(PO_4)_6(OH)_2$	9.55	7.07	0.740	558.41	1075	570	3573
7. $Ca_{1.06}Sr_{7.99}Cu_{0.95}(PO_4)_6(OH)_2$	9.64	7.16	0.743	576.23	1072	567	3570

oms. The remaining three vibrations are due to the atoms which are antisymmetric with respect to the mirror plane. Under ideal symmetry conditions, only two infrared active modes are observable (19, 20): ν_3, the P–O stretch, in the region 1000–1100 cm and ν_4, the P–O bending, in the region 500–570 cm^{-1}.

From the spectra of the samples included in Table II it can be seen that the ν_3 and ν_4 frequencies corresponding to the PO_4^{3-} ion are ν_3(1075 cm^{-1}) and ν_4(570 cm^{-1}) for CaHA, ν_3(1077 cm^{-1}) and ν_4(575 cm^{-1}) for SrHA, and ν_3(1065 cm^{-1}) and ν_4(555 cm^{-1}) for CuHA and its solid solutions (both frequencies lie in the above-mentioned region). The shape of the peaks is also affected by the introduction of strontium and copper ions into the samples.

The hydroxyl ion has one normal mode. This corresponds to the stretching of the O–H bond. The frequency ν_3 corresponding to the OH$^-$ ion is observable at 3550 cm^{-1} (calcd 3578 cm^{-1}) for CaHA. In the case of SrHA, the free O–H stretching mode appears at 3585 cm^{-1} whereas in the case of CuHA, the absorption band of the OH$^-$ ion appears at 3500 cm^{-1}. The frequency of this absorption, 3578 cm^{-1} (21), is lower than those of bands assigned to ν_3(OH) in water vapor, 3755 cm^{-1} (22), in Ca(OH)$_2$, 3644

cm^{-1} (23), in Mg(OH)$_2$, 3698 cm^{-1} (24); and in Li OH, 3678 cm^{-1} (25). Nakamoto et al. have shown the relationship of the O–O distance to the stretching mode and have indicated that the wavenumber for the OH stretching mode should increase with increasing O–O distance. From Table II it is seen that lattice parameters and unit cells expand or contract with the substitution of larger or smaller ions, respectively. According to Nakamoto's curve, the OH stretching frequency should increase from Ca to Sr and decrease to Cu hydroxyapatite. But for solid solutions of Sr, Cu, and Ca hydroxyapatite, the OH stretching frequency lies in between the above region, as seen from Table II.

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