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Examination of the Reaction Products in the Aqueous-Phase Preparation of Hydrated Calcium Diphosphates

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The formation of by-products during the preparation of hydrated calcium diphosphates ($Ca_2P_2O_7 \cdot nH_2O$, $n=2$ or 4) was examined in samples which were obtained through the literature methods. When $CaH_2P_2O_7$ was used as the reactant ($2CaH_2P_2O_7 + nH_2O \rightarrow Ca_2P_2O_7 \cdot nH_2O + H_4P_2O_7$), the product contained not only hydrated calcium diphosphate but also calcium ammonium diphosphate and/or acidic calcium diphosphate, depending on the reaction medium (0.05 M NH_4OH, 2.2 M $Ca(CH_3COO)_2$, or water). When $K_4P_2O_7$ and $CaCl_2$ were reacted in an aqueous solution of KCl, a significant amount of diphosphate ion (*ca.* 57%) was hydrolyzed to orthophosphate ion. The product was amorphous when the molar ratio of the reactant Ca^{2+} to diphosphate ion was higher than 1.0. Several kinds of crystalline calcium potassium diphosphate were found in the product when the ratio was lower than 1.0. Therefore, it was concluded that hydrated calcium diphosphates prepared in the aqueous phase by the literature methods are generally contaminated with several kinds of by-product.

Keywords——calcium diphosphate; diphosphate hydrolysis; amorphous calcium phosphate; calcium diphosphate preparation; calcium phosphate

Calcium diphosphate (calcium pyrophosphate; Ca_2PPi) is used as a feed supplement and/or food additive, and in dentifrice.[1] On the other hand, it is known that deposition of Ca_2PPi in arthrosis and yellow ligament causes pyrophosphate arthropathy[2] and cervical radiculomyelopathy.[3]Thus, Ca_2PPi is physiologically important.

In the previous paper,[4] it was shown that diphosphate ion (PPi; pyrophosphate ion) is hydrolyzed to phosphate ion (Pi; orthophosphate ion) in the presence of Ca^{2+}, forming amorphous calcium phosphate (ACP) and/or hydroxyapatite (HAP). Therefore, it seems necessary to examine the formation of by-products during the aqueous-phase preparation of Ca_2PPi. In the present paper, the literature methods[5] for preparation of Ca_2PPi were examined from this point of view.

Experimental

Materials——All chemicals used were of reagent grade from Nakarai Chemicals Ltd. or Wako Pure Chemical Industries Ltd. These were used without further purification. $CaH_2P_2O_7$ was prepared according to the literature.[5] Its formation was confirmed by means of chemical analysis ($Ca^{2+}/PPi = 1.0$) and by the X-ray powder diffraction patterns.[5]

Methods——Hydrated calcium diphosphates were prepared by the following four methods (A—D) according to the literature[5]: (A) $CaH_2P_2O_7$ (1 g) was added to 0.05 M NH_4OH (20 ml), and the mixture was allowed to stand for 24 h at room temperature. The product is expected to be $Ca_2P_2O_7 \cdot 4H_2O$ (orthorhombic). (B) A mixture of 2.2 M Ca $(CH_3COO)_2$ (35 ml) and $CaH_2P_2O_7$ (17 g) in water (425 ml) was allowed to stand at room temperature for a few hours. $Ca_2P_2O_7 \cdot 4H_2O$ (monoclinic) should be formed. (C) $CaH_2P_2O_7$ (1.1 g) in water (100 ml) was allowed to stand at room temperature for a week. $Ca_2P_2O_7 \cdot 2H_2O$ (triclinic) is expected to appear. (D) A saturated $CaCl_2$ solution was added to a solution of $K_4P_2O_7$ (1 g) and KCl (10 g) in water (60 ml). As the mixing ratio was not defined,[5] various precipitates were formed by changing the molar ratio of mixing of $CaCl_2$ to $K_4P_2O_7$, $(Ca^{2+}/PPi)_i^l$, from 0.67 to 6.0. The gelatinous suspension formed was then diluted to 100 ml with water allowed to stand undisturbed for 2 weeks at 45 °C to form crystals of $Ca_2P_2O_7 \cdot 2H_2O$ (monoclinic). These precipitates were collected on a 0.22 μm Millipore filter, washed with water, and then dried at room temperature *in vacuo*.

The content of PPi in the product was determined by ethylenediaminetetraacetate (EDTA) chelatometry after transformation of the PPi in the product to $Zn_2P_2O_7$ according to the method of Kato *et al.*[6] Total content of phosphorus (Pi+2PPi) was determined by colorimetry at 720 nm for the orthophosphate ammonium molybdate complex after hydrolysis of PPi to Pi according to the method of Gee *et al.*[7] The content of Pi was obtained from the difference between the content of total phosphorus and that of diphosphate. Potassium and calcium contents were determined by flame photometry (Hitachi model 209) and EDTA chelatometry, respectively. X-Ray powder diffraction patterns were obtained with Cu $K\alpha$ radiation on a Norelco Geiger counter diffractometer (Philips Electronics and Pharmaceutical Industry). The analytical methods have been described in detail elsewhere.[4]

Results and Discussion

The molar ratio of Ca^{2+} to PPi, $(Ca^{2+}/PPi)_f^s$, and that of Pi to total phosphorus, $(Pi/(Pi+2PPi))_f^s$, in the products (samples (A)—(D)) are given in Table I. The values of $(Ca^{2+}/PPi)_f^s$ deviate from 2.0 by only a small amount (samples (A)—(C)), or significantly, depending on the initial mixing ratio of Ca^{2+} to PPi, $(Ca^{2+}/PPi)_i^l$ (sample (D)). The value of $(Pi/(Pi+2PPi))_f^s$ is zero or small for samples (A)—(C), but that for sample (D) is 0.57 ± 0.02 irrespective of the initial mixing ratio, $(Ca^{2+}/PPi)_i^l$. This means that *ca.* 57% of total phosphorus in the sample is present as Pi, which was formed through the hydrolysis of PPi during the preparation procedure. The hydrolysis mechanism has been discussed elsewhere.[4]

The fourth column in Table I shows the species of crystalline diphosphate detected through X-ray powder diffractometry. Sample (A) contains calcium ammonium salt because the reaction medium was 0.05 M NH_4OH. $Ca_2P_2O_7 \cdot 4H_2O$ (monoclinic) was not found in sample (B) although the literature says this species should appear.[5] Sample (C) contains acidic salts because the pH of the medium was low owing to protons released from the reactant $CaH_2P_2O_7$ in the absence of a buffering agent such as NH_4OH used in method (A) or $Ca(CH_3COO)_2$ used in method (B). Calcium potassium salts were found in sample (D) when $(Ca^{2+}/PPi)_i^l = 0.67$, because Ca^{2+} was insufficient in relation to PPi and K^+ was supplied as $K_4P_2O_7$ and KCl. The ratio of $(Ca^{2+}/PPi)_f^s$ became smaller than 2.0 (Samples (A), (C), and (D) in the case of $(Ca^{2+}/PPi)_i^l = 0.67$) owing mainly to the presence of ammonium, acidic, or

TABLE I. Composition of the Products and Species Detected by X-Ray Powder Diffractometry

Method	$\left(\frac{Ca^{2+}}{PPi}\right)_f^s$	$\left(\frac{Pi}{Pi+2PPi}\right)_f^s$	Species detected by X-ray powder diffractometry[5),a)]
(A)	1.99	0	$Ca_2P_2O_7 \cdot 4H_2O$ orthorhombic (s), $Ca_2P_2O_7 \cdot 4H_2O$ monoclinic (w), $Ca_3(NH_4)_2(P_2O_7)_2 \cdot 6H_2O$ (w), $CaH_2P_2O_7$ (w)
(B)	2.08	0.024	$Ca_2P_2O_7 \cdot 4H_2O$ orthorhombic (s), $CaH_2P_2O_7$(w)
(C)	1.92	0	$Ca_2P_2O_7 \cdot 2H_2O$ triclinic (s), $Ca_2P_2O_7 \cdot 4H_2O$ orthorhombic (s), $Ca_3H_2(P_2O_7)_2 \cdot 4H_2O$ (s), $Ca_3H_2(P_2O_7)_2 \cdot H_2O$ (w), $CaH_2P_2O_7$ (w)
(D)[b)]	1.90—2.85[c)]	0.57 ± 0.02[d)]	$CaK_2P_2O_7$ (s), $CaK_2P_2O_7 \cdot 4H_2O$ (s), and $Ca_5K_2(P_2O_7)_3 \cdot 6H_2O$ (s) (when $(Ca^{2+}/PPi)_i^l = 0.67$); and amorphous (when $(Ca^{2+}/PPi)_i^l = 1$—6)[e)]

a) Intensities estimated visually (s)=strong, (w)=weak. *b*) $(Ca^{2+}/PPi)_i^l = 0.67$—6.0. *c*) Increases with $(Ca^{2+}/PPi)_i^l$. *d*) Almost constant irrespective of the value of $(Ca^{2+}/PPi)_i^l$. *e*) The ratio of K^+ to Ca^{2+} in the product, $(K^+/Ca^{2+})_f^s$, decreased from 0.24 to 0 with increasing value of $(Ca^{2+}/PPi)_i^l$ from 0.67 to 6.0.

potassium salts. On the other hand, it became larger than 2.0 (samples (B) and (D) in the case of $(Ca^{2+}/PPi)_i^1 = 1$—6) owing mainly to the hydrolysis of PPi to Pi (see the third column in Table I) in the presence of the free Ca^{2+} arising from $Ca(CH_3COO)_2$ or $CaCl_2$.[4)]

Therefore, it seems difficult to obtain hydrated calcium diphosphates, which are not contaminated with by-products, through the literature methods mentioned above. On the other hand, anhydrous calcium diphosphate can be easily obtained by heating $CaHPO_4$ or $CaHPO_4 \cdot 2H_2O$ at 450 °C for 6 h without any by-products.[4,8)]

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