1
Introduction

Owing to their abundance in nature (as phosphate ores) and presence in living organisms (as bones, teeth, deer antlers, and the majority of various pathological calcifications), calcium phosphates are inorganic compounds of special interest to human beings. They were discovered in 1769 and have been investigated since then [1, 2]. According to the databases in scientific literature (Web of knowledge, Scopus, Medline, etc.), the total amount of currently available publications on the subject exceeds 40 000 with an annual increase of, at least, 2000 papers. This is a clear confirmation of their importance.

By definition, all known calcium phosphates consist of three major chemical elements: calcium (oxidation state +2), phosphorus (oxidation state +5), and oxygen (reduction state −2), as a part of the phosphate anions. These three chemical elements are present in abundance on the surface of our planet: oxygen is the most widespread chemical element of the earth's surface (~47 mass%), calcium occupies the fifth place (~3.3 to 3.4 mass%), and phosphorus (~0.08 to 0.12 mass%) is among the first 20 of the chemical elements most widespread on our planet [3]. In addition, the chemical composition of many calcium phosphates includes hydrogen, as an acidic orthophosphate anion (for example, HPO_4^{2-} or $H_2PO_4^{-}$), hydroxide (for example, $Ca_{10}(PO_4)_6(OH)_2$), and/or incorporated water (for example, $CaHPO_4{\cdot}2H_2O$). Regarding their chemical composition, diverse combinations of CaO and P_2O_5 oxides (both in the presence of water and without it) provide a large variety of calcium phosphates, which are differentiated by the type of the phosphate anion. Namely, ortho-(PO_4^{3-}), meta-(PO_3^{-}), pyro-($P_2O_7^{4-}$), and poly-($(PO_3)_n^{n-}$) phosphates are known. Furthermore, in the case of multicharged anions (valid for orthophosphates and pyrophosphates), the calcium phosphates are also differentiated by the number of hydrogen ions attached to the anion. Examples include mono- ($Ca(H_2PO_4)_2$), di- ($CaHPO_4$), tri- ($Ca_3(PO_4)_2$), and tetra- ($Ca_2P_2O_7$) calcium phosphates. Here, one must stress that prefixes "mono," "di," "tri," and "tetra" are related to the amount of hydrogen ions replaced by calcium [4–6]. However, to narrow down the subject, only calcium *ortho*phosphates (abbreviated as $CaPO_4$) will be considered and discussed. Their names, standard abbreviations, chemical formulae, and solubility values are listed in Table 1.1 [7, 8]. Since all of them belong to $CaPO_4$, strictly speaking, all abbreviations in Table 1.1 are incorrect; however, they have been

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Table 1.1 Existing calcium orthophosphates and their major properties [7, 8].

Ca/P molar ratio	Compound	Formula	Solubility at 25 °C, −log(K_s)	Solubility at 25 °C (g l^{-1})	pH stability range in aqueous solutions at 25 °C
0.5	Monocalcium phosphate monohydrate (MCPM)	$Ca(H_2PO_4)_2 \cdot H_2O$	1.14	~18	0.0–2.0
0.5	Monocalcium phosphate anhydrous (MCPA or MCP)	$Ca(H_2PO_4)_2$	1.14	~17	a)
1.0	Dicalcium phosphate dihydrate (DCPD), mineral brushite	$CaHPO_4 \cdot 2H_2O$	6.59	~0.088	2.0–6.0
1.0	Dicalcium phosphate anhydrous (DCPA or DCP), mineral monetite	$CaHPO_4$	6.90	~0.048	a)
1.33	Octacalcium phosphate (OCP)	$Ca_8(HPO_4)_2(PO_4)_4 \cdot 5H_2O$	96.6	~0.0081	5.5–7.0
1.5	α-Tricalcium phosphate (α-TCP)	$\alpha\text{-}Ca_3(PO_4)_2$	25.5	~0.0025	b)
1.5	β-Tricalcium phosphate (β-TCP)	$\beta\text{-}Ca_3(PO_4)_2$	28.9	~0.0005	b)
1.2–2.2	Amorphous calcium phosphates (ACP)	$Ca_xH_y(PO_4)_z \cdot nH_2O$, $n = 3–4.5$; 15–20% H_2O	c)	c)	~5–12 d)
1.5–1.67	Calcium-deficient hydroxyapatite (CDHA or Ca-def HA) e)	$Ca_{10-x}(HPO_4)_x(PO_4)_{6-x}(OH)_{2-x}$ $(0 < x < 1)$	~85	~0.0094	6.5–9.5
1.67	Hydroxyapatite (HA, HAp, or OHAp)	$Ca_{10}(PO_4)_6(OH)_2$	116.8	~0.0003	9.5–12
1.67	Fluorapatite (FA or FAp)	$Ca_{10}(PO_4)_6F_2$	120.0	~0.0002	7–12
1.67	Oxyapatite (OA, OAp, or OXA) f), mineral voelckerite	$Ca_{10}(PO_4)_6O$	~69	~0.087	b)
2.0	Tetracalcium phosphate (TTCP or TetCP), mineral hilgenstockite	$Ca_4(PO_4)_2O$	38–44	~0.0007	b)

a) Stable at temperatures above 100 °C.
b) These compounds cannot be precipitated from aqueous solutions.
c) Cannot be measured precisely. However, the following values were found: 25.7 ± 0.1 (pH = 7.40), 29.9 ± 0.1 (pH = 6.00), and 32.7 ± 0.1 (pH = 5.28) [9]. The comparative extent of dissolution in acidic buffer is ACP ≫ α-TCP ≫ β-TCP ≫ CDHA ≫ HA > FA [10].
d) Always metastable.
e) Occasionally, it is called "precipitated hydroxyapatite (PHA)."
f) Existence of OA remains questionable.

extensively used in literature for decades and, to avoid confusion, there is no need to modify them.

In general, the atomic arrangement of all $CaPO_4$ is built around a network of orthophosphate (PO_4) groups, which stabilize the entire structure. Therefore, the majority of $CaPO_4$ are sparingly soluble in water (Table 1.1); however, all of them are easily soluble in acids but insoluble in alkaline solutions. In addition, all chemically pure $CaPO_4$ are colorless transparent crystals of moderate hardness but, as powders, they are of white color. Nevertheless, natural minerals of $CaPO_4$ are always colored because of the presence of impurities and dopants, such as ions of Fe, Mn, and rare earth elements [11, 12]. Biologically formed $CaPO_4$ are the major component of all mammalian calcified tissues [13], while the geologically formed ones are the major raw material to produce phosphorus-containing agricultural fertilizers, chemicals, and detergents [14–16].

References

1. Dorozhkin, S.V. (2012) Calcium orthophosphates and human beings. A historical perspective from the 1770s until 1940. *Biomatter*, **2**, 53–70.
2. Dorozhkin, S.V. (2013) A detailed history of calcium orthophosphates from 1770s till 1950. *Mater. Sci. Eng., C*, **33**, 3085–3110.
3. Lide, D.R. (2005) *The CRC Handbook of Chemistry and Physics*, 86th edn, CRC Press, Boca Raton, FL, 2544 pp.
4. LeGeros, R.Z. (1991) *Calcium Phosphates in Oral Biology and Medicine*, Monographs in Oral Science, vol. 15, Karger, Basel, 201 pp.
5. Elliott, J.C. (1994) *Structure and Chemistry of the Apatites and Other Calcium Orthophosphates*, Studies in Inorganic Chemistry, vol. 18, Elsevier, Amsterdam, 389 pp.
6. Amjad, Z. (ed.) (1997) *Calcium Phosphates in Biological and Industrial Systems*, Kluwer Academic Publishers, Boston, MA, 529 pp.
7. Dorozhkin, S.V. (2011) Calcium orthophosphates: occurrence, properties, biomineralization, pathological calcification and biomimetic applications. *Biomatter*, **1**, 121–164.
8. Dorozhkin, S.V. (2012) *Calcium Orthophosphates: Applications in Nature, Biology, and Medicine*, Pan Stanford, Singapore, 854 pp.
9. Ohura, K., Bohner, M., Hardouin, P., Lemaître, J., Pasquier, G., and Flautre, B. (1996) Resorption of, and bone formation from, new β-tricalcium phosphate-monocalcium phosphate cements: an in vivo study. *J. Biomed. Mater. Res.*, **30**, 193–200.
10. Daculsi, G., Bouler, J.M., and LeGeros, R.Z. (1997) Adaptive crystal formation in normal and pathological calcifications in synthetic calcium phosphate and related biomaterials. *Int. Rev. Cytol.*, **172**, 129–191.
11. Cantelar, E., Lifante, G., Calderón, T., Meléndrez, R., Millán, A., Alvarez, M.A., and Barboza-Flores, M. (2001) Optical characterisation of rare earths in natural fluorapatite. *J. Alloys Compd.*, **323–324**, 851–854.
12. Ribeiro, H.B., Guedes, K.J., Pinheiro, M.V.B., Greulich-Weber, S., and Krambrock, K. (2005) About the blue and green colours in natural fluorapatite. *Phys. Status Solidi C*, **2**, 720–723.
13. Lowenstam, H.A. and Weiner, S. (1989) *On Biomineralization*, Oxford University Press, 324 pp.
14. McConnell, D. (1973) *Apatite: Its Crystal Chemistry, Mineralogy, Utilization, and Geologic and Biologic Occurrences*, Applied Mineralogy, vol. 5, Springer-Verlag, Vienna and New York, 111 pp.

15. Becker, P. (1989) *Phosphates and Phosphoric Acid: Raw Materials Technology and Economics of the Wet Process*, Fertilizer Science and Technology Series, 2nd edn, Marcel Dekker, New York, 760 pp.

16. Rakovan, J.F. and Pasteris, J.D. (2015) A technological gem: materials, medical, and environmental mineralogy of apatite. *Elements*, **11**, 195–200.