How Pure a Calcium Deficient Hydroxyapatite can be produced ?

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Introduction

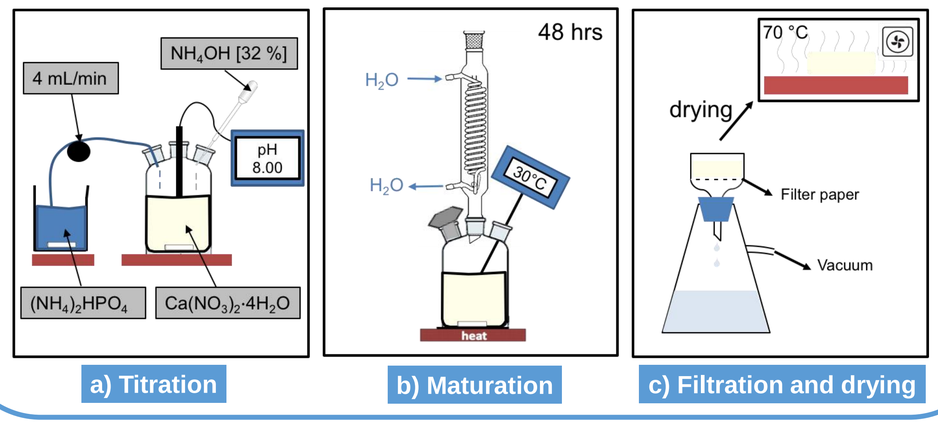
Dopants (*e.g.* Sr, Na, Mg…) have been introduced in calcium phosphate (CaP) ceramics to modify their biological, chemical and physical properties. However, there is generally no comprehensive details provided on the purity of the CaP used when assessing the effect of doping. Indeed, studies investigating biological effect of doped CaP rarely give information about the content of other impurities [1]. Or, CaP raw materials contain quite large amounts of impurities, which can lead sometimes to non-intentionally co-doped CaP. These impurities can affect the CaP intrinsic solubility and to some extent modify its physiological integrity/behaviour [2], leading to a high variability in the results and/or misleading conclusions. Therefore it is of primary importance to determine the overall content of impurities in the CaP and to produce very pure and reliable control samples. The aim of this study was to determine how pure a CaP can be synthetized using a series of commercial starting products.

Materials and Methods

1. Raw Materials

Synthesis n°	Raw Materials (brand, art. n°, lot. n°)
1	**$Ca(NO_3)_2\ 4H_2O$:** Sigma, C4955, MKBV3330V, (≥ 99.0%) **$(NH_4)_2HPO_4$:** Fluka,09840,BCBP9558V, (≥ 99.0%) **NH_4OH:** Roth, P093.1, 216238252
2	**$Ca(NO_3)_2\ 4H_2O$:** Sigma, C4955, MKCC5930, (≥ 99.0%) **$(NH_4)_2HPO_4$:** Fluka,09840,BCBR7916V, (≥ 99.0%) **NH_4OH:** Roth, P093.1, 067253691
3	**$Ca(NO_3)_2\ 4H_2O$:** GFS, Art n°A1506, C795037 (99.999%) **$(NH_4)_2HPO_4$**: Fluka, Art n°43391, BCBR9912V (99.998%) **NH_4OH**: Sigma, Art n°33881-8, SZBF3200V (≥99.99%)
4	**$Ca(NO_3)_2\ H_2O$:** Merck, Art n°13477-34-4, B1371623640 (99.95 **$(NH_4)_2HPO_4$:** Fluka, Art n°43391, BCBL5076V (99.998%) **NH_4OH**: Sigma, Art n°33881-8, SZBF3200V (≥99.99%)
5	**Ca(NO3)" 4H2O:** Alfa, Art n° 44515, 23388 (99.9995%) **$(NH_4)_2HPO_4$:** Fluka, Art n°43391, BCBR9912V (99.998%) **NH_4OH:** Sigma, Art n°33881-8, SZBF3200V (≥99.99%)
6	**$Ca(NO_3)_2\ H_2O$:** Sigma, Art n°202967, MKBM4437V (99.997 % **$(NH_4)_2HPO_4$**: Fluka, Art n°43391, BCBL5076V (99.998%) **NH_4OH:** SigmaArt n°33881-8, SZBF3200V (≥99.99%)

2. Synthesis



a) Titration | b) Maturation | c) Filtration and drying

3. Characterization

X-Ray diffraction (XRD): identification and quantification of CaP phases.

Inductively-Coupled Plasma Mass Spectroscopy (ICP-MS): quantification of the impurities content.

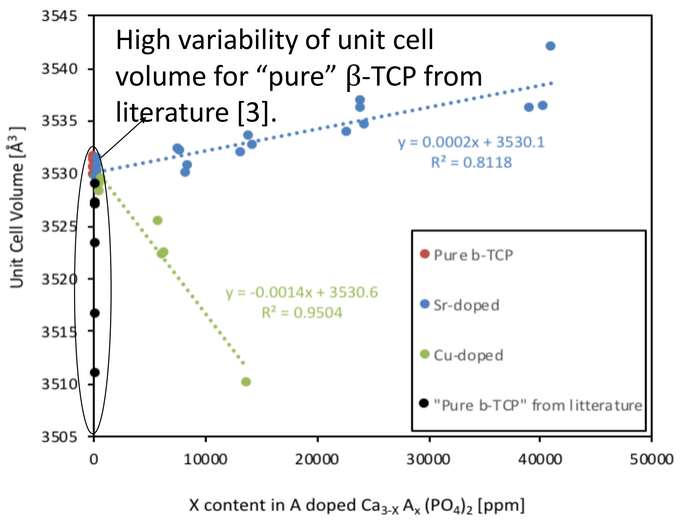
Results and Discussion

Synthesis n°	ICP-MS				XRD	Cost
	Cu Content [ppm]	Mg Content [ppm]	Na Content [ppm]	Sr Content [ppm]	Ca/P ratio [-]	Price [EUR/g]
1	<LOD	<62.05**	<LOD	295.22 ± 26.70*	1.50 ± 0.01*	0.57
2	< LOD	9.46 ± 2.37*	<LOD	207.54 ± 22.24*	1.50 ± 0.01*	0.57
3	<LOD	6.37 ± 2.79*	<LOD	8.34 ± 2.10*	1.50 ± 0.01*	14.71
4	<LOD	<5.95**	<LOD	18.48 ± 3.61*	1.50 ± 0.01*	17.56
5	<LOD	7.28 ± 2.37*	<LOD	38.45 ± 6.32*	1.51 ± 0.01*	11.86
6	13.17 ± 2.58*	<5.81**	<LOD	10.80 ± 3.35*	1.51 ± 0.01*	17.44

*: $U_{k=2}$
**: LOQ

The content of impurities varied between <1 (detection limit) and 330 ppm depending on the raw materials. The impurity content varied also significantly when using the same products but different lot numbers (e.g. syntheses 1 and 2). The use of ultrapure products (≥99.95%) decreased the impurity content (synthesis 3-6), but considerably increased the synthesis costs and up to 50 ppm impurities were still detected. Among the 45 tested elements (Zr, Si, Ti, Ge, Mo, W not included), only B, Fe, Al, and K were sometimes detected below 10 ppm. Ca/P molar ratios were determined by XRD and were equal to 1.50 ± 0.01 (number of samples, n=15).

β -TCP unit cell volume dilatation/shrinkage depends on the impurities content and type. For instance presence of Sr tended to increase the unit cell volume, whereas Cu decreased it. The high variability in the unit cell volume for “pure” β-TCP from literature reveals actually how impure they are...



Summary

This study suggests that quite often “pure” CaP encountered in literature are not that pure as claimed. Herein, the synthesised CDHA powders were found to contain impurities, in amounts and types that are highly dependent on the raw materials. Both the article and the batch/lot numbers of the raw material can modify the impurity content. Herein, the purest CDHA still contained at least 30 ppm of impurities, which is quite a lot considering that for ceramics, an impurity with a concentration of 100 ppm is already a dopant.

References

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[2] H. A. Bhatt et *al.*, J. Mater. Sci. Mater. Med. 2007; 18:883-893
[3] International Centre for Diffraction Data (2013)

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