European Cells and Materials Vol. 7. Suppl. 1, 2004 (page 49) ISSN 1473-2262

Interactions between Cell and Calcium Phosphates Depend On Chemistry: Theoretical Considerations

M. Bohner

[1] *Dr Robert Mathys Foundation, Bischmattstr 12, 2544 Bettlach, Switzerland*

INTRODUCTION: In the last 3 decades, the number of publications devoted to calcium phosphate (CaP) materials has exploded. This is partly due to the discovery of CaP cements which allows the synthesis of granules and blocks with chemical and physical properties similar to the CaP crystals present in bone. These CaP crystals are octocalcium phosphate (OCP), dicalcium phosphate dihydrate (DCPD), and nanocrystalline apatites, such as calcium-deficient hydroxyapatite (CDHA), hydroxyapatite (HA) or carbonated apatite (CA).

So far, there is still a poor understanding of the mechanisms of dissolution-degradation-resorption occurring when these materials are implanted *in vivo*. The goal of the present communication is to elucidate these mechanisms. For that purpose, the solubility of calcium phosphate phases in serum is calculated. Results are then discussed and compared to *in vivo* results.

METHODS: To perform the solubility calculations, the following conditions were chosen (see also [1]): (i) The equilibrium of 42 inorganic species that are present in serum were considered [2]. (ii) The ionic strength and the pH of serum were assumed to be 0.15M and pH 7.4 respectively. (iii) The activity of Na^+, K^+, Ca^{2+}, Mg^{2+}, Cl^-, HPO_4^{2-} and HCO_3^- was varied until the total concentration of sodium, potassium, calcium, magnesium, chlore, phosphate and carbonate corresponded to the concentrations present in serum [3] (iv) Based on the concentrations of the different ions and the phase equilibria, the saturation of each calcium phosphate phase was determined. As a concentration range is given for calcium and phosphorus in serum [3], calculations were made with the minimum and maximum concentrations of calcium and phosphorus.

RESULTS: Solubility calculations show that serum was saturated toward DCP, OCP, β-tricalcium phosphate (β-TCP), CDHA, CA and HA (Table 1), indicating that these compounds do not spontaneously dissolve *in vivo*. The opposite is true for α-tricalcium phosphate (α-TCP). Finally, DCPD is a special case, since it is soluble in a serum containing a low concentration of calcium and phosphorus and insoluble in a serum containing a high concentration of Ca and P.

Saturation	DCP	DCPD	OCP	β-TCP
Low Ca & P	0.05	-0.11	0.21	0.52
Av. Ca & P	0.13	-0.02	0.29	0.59
High Ca & P	0.20	0.04	0.35	0.66
Saturation	α-TCP	CDHA	HA	CA*
Low Ca & P	-0.14	0.31	1.31	0.58
Av. Ca & P	-0.07	0.38	1.38	0.64
High Ca & P	0.00	0.45	1.44	0.70

*$Ca_{10}(PO_4)_6(CO_3)_{0.04}(OH)_{1.92}$

Table 1: saturation of serum towards various CaP phases. A positive value indicate that serum is saturated, hence preventing spontaneous dissolution.

DISCUSSION & CONCLUSIONS: Based on these observations, we can conclude that due to their solubility in serum, DCPD and α-TCP are expected to be dissolved *in vivo*, whereas the other calcium phosphates are expected to be removed by cells such as osteoclasts and macrophages. Interestingly, CDHA, CA and β-TCP have similar saturations in serum, suggesting that these three compounds should be resorbed at the same rate.

These conclusions are coherent with experimental *in vivo* data except for DCPD [4] and α-TCP. These two phases tend to be converted into nanocrystalline apatite, hence reducing the apparent resorption rate. However, in the presence of inhibitors of apatite growth, conversion can be postponed [5].

The conversion into an apatite is expected to occur at constant pH for α-TCP and at decreasing pH for DCPD. As DCPD solubility increases at lower pH values, DCPD conversion is autocatalytic. However, as apatites do not precipitate below pH 7.0, conversion proceeds at a controlled rate.

In conclusion, solubility calculations can be used to predict and understand the *in vivo* behavior of calcium phosphates.

REFERENCES: [1] G. Vereecke, J. Lemaître (1990) *J Cryst Growth* **104**:820-832. [2] WL Lindsay (1979) *Chemical Equilibria in Soils*, Wiley, New York. [3] V. Turitto, SM Slack (1998) Blood and related fluids in *Handbook of Biomaterial Properties* (eds J. Black, G. Hastings) Chapman & Hall, pp114-124. [4] G. Penel, N. Leroy N et al. (1999) *Bone* **25[2]S**:81S-84S. [5] M. Bohner, F. Theiss et al. (2003) *Biomaterials* **24[20]**:3463-3474.