

Calcium Phosphate Research - Ripe for Change

(磷酸钙的研究臻于变革)

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The chemistry of the principal mineral component of tooth tissue, hydroxyapatite, has been recognized for many years to be fundamental to the understanding of a number of issues in dentistry, in particular dental caries, calculus formation, and remineralization. In addition, aspects of odontogenesis, saliva physiology (including palliative treatments for xerostomia), etching and bonding for restorations, laboratory testing of materials for intra-oral use, and caries prevention are intimately dependent on such chemistry. The interest is also much broader since hydroxyapatite is also the principal mineral of bone, and calcium phosphates in general are significant in the context of pathological calcifications. Given this importance, and the volume of the literature on these topics, it is surprising that our understanding is demonstrably deficient in several respects, although one or two recent reports have made important observations. Reasons for this state of affairs may be identified in a small number of critical areas.

The first issue is the question of solubility. As a mass per volume statement, defined in terms of the equilibrium between a solid and its solution, it is essential for a measurement that the solid is known be unchanged. However, calcium phosphates, in general, dissolve incongruently, meaning that the surface at least is of altered composition^[1] or constitution, and the solution analysis does not correspond to that of the original solid. This has long be known, manifest in the peculiar property that the apparent solubility varies with the amount of solid present^[2]-a thermodynamic nonsense, but almost universally ignored even

if understood.

The calculation of a solubility product constant (K_{sp}) depends both on the validity of a measured mass solubility, but also on the assumed solution speciation. That is, the complete set of ionic and neutral forms that derive from the components of the solid in the process of dissolution. This includes ion pairs such as CaOH^+ , and the results of the successive protonation of PO_4^{3-} , for example. For this calculation of K_{sp} to be done the equilibrium constants have to be known, but these calculations are dependent on modelling the solution adequately: that is, all species, and all equilibria, need to be explicitly accounted for. (It is evident that the inventory of accommodated species is incomplete^[3], as several reasonable possibilities are nowhere mentioned. This has arisen because computation has its own problems.

Even a simple solution system may involve around a dozen equilibria, but because the system of equations for those equilibria, mass balance and charge balance is non-linear, until the advent of cheap and fast computing even simple systems were simplified to enable numerical solutions of the equations to be obtained at all-no explicit algebraic solution is possible and successive approximation is the only way^[4]. The chemistry textbooks tell this story eloquently. As a result, not only have the systems been simplified, but consideration of other equilibria has been inhibited. This has resulted in a vast body of literature on equilibrium constants that must be inaccurate, even if adequate for many ordinary purposes. The situation for calcium-phosphate studies is that much worse be-

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cause many more equations may be involved, even in the minimal $\text{CaO-H}_3\text{PO}_4\text{-H}_2\text{O}$ ternary system.

The argument therefore becomes rather involved: K_{sp} calculation depends on speciation, which depends on solution equilibrium constants, which depends on assumed species, which depends on computational capacity, which in turn affects the calculation of K_{sp} . We do not need to add that the accuracy of the analytical determination of solution composition is insufficient to resolve between possibilities, and that of the solid is likewise not better than about $\pm 0.1\%$.

We may also note in passing another aspect of the dissolution and reprecipitation phenomena of this system. There are many possible phases, including amorphous materials, each of which may be non-stoichiometric, with substitutional and deficiency deviations from ideal composition and constitution^[5]. The non-congruent dissolution mentioned earlier may result in an Ostwald Succession of phases of varying stability (indeed, there is evidence that this is precisely what occurs over the depth of a dental carious lesion - it is not simply a matter of reducing amount of mineral). Likewise, precipitation cannot be relied on to produce the expected phase immediately, if ever, especially if this is triggered far from the equilibrium position^[6]. Hence, there is a time aspect which is rarely given any consideration, but which clearly affects the interpretation of data.

As we move into a more physiological context the problems worsen. A major factor is carbon dioxide. Generally described as an important part (if not the most important part) of the buffering system of human saliva, it is well known to complicate analyses because it is so readily lost from samples, and especially through "barriers" such as paraffin oil and silicone. However, it is not just bicarbonate that matters. Evidence has emerged^[7] that it is strongly involved in complex formation with calcium and phosphate, as was reported many years ago for seawater^[8]. These equilibria clearly need to be accommodated in the solution description for the calculation of K_{sp} , which entails knowledge of the likely numerous possible species and their formation constants-all of which is presently lacking.

Further complications with saliva-like media include a host of similar possible complexes involving organic acids: lactate, acetate, tartrate, citrate and

so on. These conceivably are readily able to form dissimilar-ligand complexes: phosphate-Ca-tartrate, for example. Carbonate is also on the list of such ligands. Survey of the literature shows that none of these species has even been studied, yet if the hypothesis of their involvement is true, their impact on our understanding of saliva chemistry must be far-reaching. At the very least, they affect the solubility of hydroxyapatite.

It should be apparent from this set of interlinked problems that much research effort will be necessary to resolve the basic questions. In the Dental Materials Science laboratory at The University of Hong Kong, we have made a start, but perhaps a more concerted and widespread assault on the several topics needs to be made. Certainly, the old assumptions and simplifications have been shown to be untenable, and that novel approaches are essential. But the contention here is that unless the blinkers are removed, and a rational approach to a very complicated system is instituted, using the most powerful techniques available - both experimental and computational - calcium phosphate chemistry will remain mired in confusion for many years yet.

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