Thermodynamic basis for evolution of apatite in calcified tissues

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ABSTRACT

Bone remodeling and tooth enamel maturation are biological processes that alter the physico-chemical features of biominerals with time. However, although the ubiquity of bone remodeling is clear, why is well-crystallized bone mineral systematically replaced by immature nanocrystalline inorganic material? In enamel, a clear evolution is also seen from the first mineral formed during the secretory stage and its mature well-crystalline form, which then changes little in the adult tooth. This contribution provides the thermodynamic basis underlying these biological phenomena. We determined, for the first time, the energetics of biomimetic apatites corresponding to an increasing degree of maturation. Our data point out the progressive evolution of the enthalpy (ΔHf) and free energy (ΔGf) of formation toward more negative values upon maturation. Entropy contributions to ΔGf values remained small compared to enthalpy contributions. ΔHf varied from –12,058.9 ± 12.2 to –12,771.0 ± 21.4 kJ/mol for maturation times increasing from 20 min to 3 weeks, approaching the value for stoichiometric hydroxyapatite, –13,431.0 ± 22.7 kJ/mol. Apatite thermodynamic stability increased as its composition moved toward stoichiometry. These findings imply diminishing aqueous solubility of calcium and phosphate ions as well as decreased surface reactivity. Such thermodynamically driven maturation is favorable for enamel maturation since this biomineral is intended to resist external aggressions such as contact with acids. In contrast, maintaining a metastable highly reactive and soluble form of apatite is essential to the effective participation of bone as a source of calcium and phosphate for homeostasis. Therefore our data strongly suggest that, far from being trivial, the intrinsic thermodynamic properties of apatite mineral represent a critical driving force for continuous bone remodeling, in contrast to current views favoring a purely biologically driven cycle. These thermodynamic data may prove helpful in other domains relating, for example, to apatite-based biomaterials development or in the field of (geo)microbiology.

Keywords: Nanocrystalline apatite, hydroxyapatite, bone remodeling, enamel maturation, calorimetry, thermodynamics, metastability, biomimetic

INTRODUCTION

Calcified tissues are complex adaptive biomaterials optimized through evolution to provide a union of inorganic and organic constituents to serve both mechanical and biological functions. In particular, one can underline the sophisticated multi-scale architectures found in tooth enamel and bone, which control their mechanical and chemical properties (Weiner and Wagner 1998; Gómez-Morales et al. 2013). Along with morphological aspects, the chemical composition, crystal structure, and microstructure of such apatitic biominerals are adapted to their physiological functions. Enamel, for instance, is intended to protect erupted teeth against external aggressions (thermal, mechanical, chemical), and thus requires in its mature state a high degree of chemical and mechanical stability and low-aqueous solubility. These conditions are met thanks to a chemical composition and other physico-chemical features for mature enamel close to stoichiometric hydroxyapatite (HA, hexagonal, P6/m space group) (Bonar et al. 1991). In contrast, far from being inert, bone acts as an ion reservoir allowing for the continual regulation of mineral ion concentrations in body fluids (homeostasis) (Driessens et al. 1986). Therefore, bone mineral should be relatively soluble and should remain highly reactive. Such an increase in solubility and reactivity relative to well-crystallized stoichiometric hydroxyapatite can be attained through nonstoichiometry (ion vacancies) as well as by nanometric crystal dimensions and a low degree of crystallinity (Grynlas 1976).

Without taking into account the presence of secondary elements, the overall composition of biomimetic apatite can generally be satisfactorily described by formulas such as: Ca_{10-x}(PO_4)_{6-x}(HPO_4)_{x}(OH)_{2-x}, (proposed by Winand 1961) or Ca_{10-x-z}(PO_4)_{6-x}(HPO_4)_{z}(OH)_{2-z}, (proposed by Kühl and Nebergall 1963), where x and Z depend on factors such as conditions of formation and/or state of aging. The presence of carbonate ions is also observed, especially in mature biominerals (Gómez-Morales et al. 2013), whereas significantly lower carbonate amounts are found in immature ones (Rey et al. 1995). The reactivity of such nanocrystalline apatites is directly connected to specific substructural features: detailed works on such nanocrystalline

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