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Atomic Force Microscopy Study of the Effect of Poly(aspartic acid) on Calcium Oxalate

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Kidney stone disease is a urological disorder that affects 10% of the human population, resulting in considerable pain and potential renal failure. It is known that certain macromolecules, such as osteopontin (OPN), can limit the formation of calcium oxalate monohydrate (COM) crystals, the major constituent of kidney stones. An explanation for this effect is provided by the Cabrera-Vermilyea (C-V) model, which proposes that trace amounts of adsorbed impurities can pin growth steps, forcing them to curve, thereby reducing the effective supersaturation. This "kinetic inhibition"is distinct from the well-known freezing-point depression, in which the thermodynamic phase diagram is altered by the presence of impurities. However, microscopic evidence for the C-V model is limited.

We have been using the atomic force microscope (AFM) to investigate COM crystallization in situ in the presence of OPN, peptides derived from OPN, and synthetic macromolecules such as poly(aspartic acid) (poly-ASP). The presence of poly-ASP causes a rapid change in growth-step morphology and drastically slows the growth. At low poly-ASP concentrations, we see a dependence on crystallographic direction, with one direction displaying strong pinning while others continue to grow. This results in "finger-like"features at a threshold concentration that depends strongly on the polymer length. In this talk, we model these growth features using inhibitor diffusion, adsorption to growth steps, and incorporation into the growing crystal.

An understanding of the microscopic details of calcium oxalate crystallization is not only important for the development of potential therapies for kidney stone disease, but will also provide insights into the inhibition mechanism that will be transferable to other natural and commercial crystallization systems.

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