

Modulation of Tartrates with Various Counterions on the Phases of Calcium Oxalate in Gelatinous Systems

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Abstract: Effect of various counterions of tartrate on the crystallization of calcium oxalate in gel system was investigated using scanning electron microscopy and X-ray diffraction. Various tartrates with hydrogen (H_2tart), sodium (Na_2tart), potassium (K_2tart), ammonium ($(NH_4)_2tart$), and a mixture of sodium and potassium cations ($NaKtart$) were considered. For H_2tart , Na_2tart , and $(NH_4)_2tart$, calcium oxalate dihydrate (COD) was induced. However, for K_2tart and $NaKtart$, calcium oxalate trihydrate (COT) was obtained.

Keywords: Calcium oxalate, gel, tartrate.

As the main component of uroliths, calcium oxalate (CaOxa) has three different hydrated forms, calcium oxalate monohydrate (COM), dihydrate (COD) and trihydrate (COT)¹. The monoclinic COM is the thermodynamically most stable phase, followed by the triclinic COT and the tetragonal COD. COM and COD are the major components of most of the urinary calculi. COT has been rarely found in urines and in kidney stones², but it might be important as a possible precursor in their formation.

Urinary stones grow in a gelatinous medium which is probably one of the reasons for the oriented striated growth of the crystals specifically encountered in the urinary calculi^{3,4}. The viscous nature of gel provides simulation of biological fluids in which the biomolecules grow⁵. On the other hand, tartaric acid and its salts are shown to be potent substances to cure the urolithiasis. In clinic, potassium sodium citrate shows different therapeutic efficiency on uroliths from potassium citrate and ammonium citrate. There is no report about the effect of the counterions of tartrate on the crystallization of the mineral crystals in uroliths. With this in mind, in the present paper, a comprehensive study of the effect of counterions of tartrate on the crystallization of CaOxa in gelatinous medium is presented.

Various tartrates such as tartaric acid (H_2tart), sodium tartrate (Na_2tart), potassium tartrate (K_2tart), ammonium oxalate ($(NH_4)_2tart$), sodium potassium tartrate ($NaKtart$), and various oxalates such as H_2Oxa , Na_2Oxa , K_2Oxa , $(NH_4)_2Oxa$, $KNaOxa$, and chloroform *etc.* were of analytical purity. Double distilled water was used.

A double diffusion growth technique was used for the growth of CaOxa crystals.

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Silica hydrogels were prepared from a pure sodium metasilicate solution (0.246 mol/L) of density 1.03 g/mL by acidification with 5% (v/v) acetic acid. 5.0 mL 0.5 mol/L CaCl₂ solution was added to one limb of the U-tube and 5.0 mL 0.20 mol/L oxalates to the other limb. Various tartrates were also added to the limb with oxalates. For H₂tart, Na₂tart, K₂tart, (NH₄)₂tart, and NaKtart, H₂Oxa, Na₂Oxa, K₂Oxa, (NH₄)₂Oxa, and KNaOxa were used as reactants, respectively. After 10 days of crystallization, the CaOxa crystals were taken out, and were measured by powder X-ray diffraction (XRD) and scanning electron microscopy (SEM) according to the previous work⁴.

The phase composition of the CaOxa crystals was estimated from the intensity ratio of the major X-ray diffraction lines of COM (I_{COM}), COD (I_{COD}), and COT (I_{COT}), respectively, as shown in eq. (1)⁶ for COT.

$$\text{Estimated } COT\% = \frac{I_{COT}}{I_{COM} + I_{COD} + I_{COT}} \quad (1)$$

Figure 1 shows the SEM images of CaOxa crystals grown in the presence of various tartrates. For H₂tart (**Figure 1a**), Na₂tart (similar as H₂tart, not shown), and (NH₄)₂tart (**Figure 1b**), only COM and bipyramidal COD were obtained. However, for K₂tart (**Figure 1c**) and NaKtart (**Figure 1d**), the rod-like COT crystals were induced.

The concentration of tartrates affected the phase composition of CaOxa crystals. As the concentration of tartrates increased, the percentage of COM in CaOxa crystals decreased and that of COD or/and COT increased. For K₂tart and NaKtart, the percentage of COD was always about 5-10%, which is independent on their concentrations from 0.01 to 0.50 mol/L. But the percentage of COT increased as increasing their concentrations. For example, when the concentrations of NaKtart increased from 0.01, to 0.1 and 0.5 mol/L, respectively, the percentage of COT increased from 0 (**Figure 2a**) to 37.5 (**Figure 1d**) and 80% (**Figure 2b**), respectively.

However, for H₂tart, Na₂tart, and (NH₄)₂tart, in the concentration less than 0.1 mol/L, COM was dominant. The content of COD was about 5-12% and did not change apparently. As the concentrations were higher than 0.1 mol/L, the percentage of COD increased as the concentration increased. If the concentration of H₂tart, Na₂tart, and (NH₄)₂tart increased to 0.5 mol/L, the content of COD was increased to about 40, 65, and 60%, respectively. But COT was not induced in all the concentration range from 0.01 to 0.5 mol/L.

The CaOxa crystals were measured by XRD. The XRD patterns of the CaOxa crystals in the presence of H₂tart, Na₂tart, or (NH₄)₂tart showed similar features. But they were different from those in the presence of K₂tart or NaKtart. **Figure 3** shows the XRD patterns of CaOxa crystals grown in the presence of 0.1 mol/L of (NH₄)₂tart and NaKtart. For (NH₄)₂tart, the diffraction peaks assigned to the ($\bar{1}01$), (020), ($\bar{2}02$), and (130) faces of COM crystals are dominant (**Figure 3a**). For NaKtart, new peaks assigned to the (100), (001), (200), and ($2\bar{1}1$) peaks of COT appeared (**Figure 3b**). The characteristic diffraction peaks of COD, appearing at 0.618, 0.442, 0.278, and 0.224 nm, were very weak.

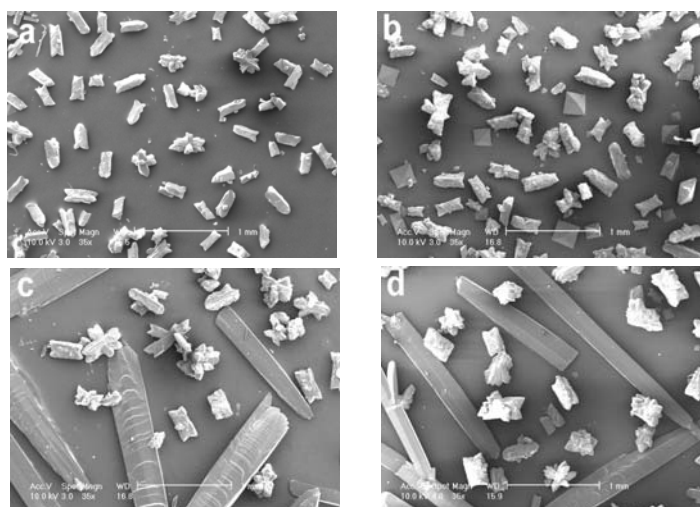
Cody *et al.*⁷ reported that when 1.6 nm × 1.6 nm areas of crystal surface models of COM, COD, and COT were analyzed, it became apparent that the divalent structurally-specific tartrate dianion (tart²⁻) would find eight possible adsorption sites on COM, five

on COT, and only three on COD. That is, COM is most able to adsorb the tartrate because it contains the most sites per unit area where adsorption is possible. Since COD and COT contain fewer adsorption sites, the probability of a binding of the tartrate dianion can only be increased, if the concentration of the tartrates is increased. It can be seen from **Figure 1** that $K_2\text{tart}$ and NaKtart have strong ability to induce COT formation, while H_2tart , Na_2tart , and $(\text{NH}_4)_2\text{tart}$ have strong ability to induce COD formation.

In order to verify whether potassium ion (K^+) plays an important role in the formation of COT, KCl was used as a substitute of K_2tart or NaKtart . The results showed that KCl can not induce COT formation. When the concentration of KCl increased from 0.01 to 0.5 mol/L, most of the crystals are COM and there is about 3-5% of COD. It suggests that K^+ ion could not induce the formation of COT in the absence of tart^{2-} . The formation of COT was attributed to the cooperation of K^+ and tart^{2-} ions. Actually, the other counterions, such as H^+ , Na^+ , and $(\text{NH}_4)^+$ ions, could induce COD formation only when they co-existed with tart^{2-} ions.

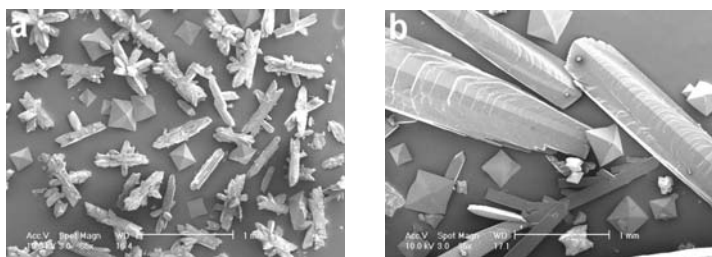
It was reported that only linear molecules with carboxylic group spacing of approximately three C-C bond lengths, *i.e.*, the propane spacing are able to inhibit COM

Figure 1 SEM images of CaOxa crystals grown in the presence of 0.1 mol/L

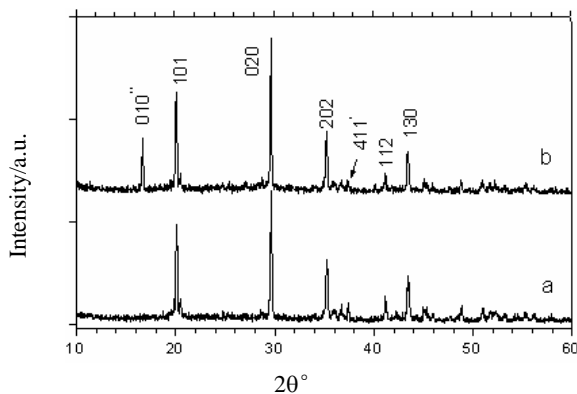


(a) H_2tart , (b) $(\text{NH}_4)_2\text{tart}$, (c) K_2tart , and (d) NaKtart , respectively. (the bar: 100 μm)

Figure 2 SEM images of CaOxa crystals grown in the presence of 0.01 mol/L



(a) and 0.5 mol/L (b) NaKtart , respectively. (Time: 10 d, T: 27°C, the bar: 100 μm)

Figure 3 XRD patterns of CaOxa crystals grown in the presence of 0.1 mol/L

(a) $(\text{NH}_4)_2\text{tart}$ and (b) NaKtart (The diffractive peaks with two asterisk show COT, one show COD and without show COM)

formation, and to favor COT or COD⁷. In fact, tartrate dianion has a linear structure with a carboxylic group spacing of three C-C bond lengths, and so they are able to inhibit the formation of COM and favor COT or COD. Furthermore, our work suggests that the inhibition of COM and the induction of COT or COD depends on the concentration and the nature of the cations in the tartrate salts.

Since COM was found to adsorb three times more than COT and ten to fifteen times more than COD⁸, *i.e.*, COM crystals might adhere most strongly to the tubule cell surface in kidney sections. In the animal models of urinary stones, COM was the principal crystalline constituent adhered to the tubule cell surfaces in kidney sections. There is much evidence that the nucleation and growth of COM in urine and subsequent trapping of the crystal within the kidney lead to stone formation, while forming COD or COT crystals may be protective. That is, if any additive can induce more percentages of COD or COT in crystallization of CaOxa, this reagent should be developed as a urolith inhibitor.

Acknowledgments

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