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Calcium Oxalate Trihydrate in Urinary Calculi

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Summary. Visual examination, electron-microscopic observation and infrared-spectroscopic analysis demonstrate that the thermodynamically unstable calcium oxalate trihydrate, which supposedly plays an important role in the formation of certain urinary calculi, is a commonly occurring constituent of urinary stones.

Key words: Calcium oxalate trihydrate.

Introduction

Whewellite (calcium oxalate monohydrate; hereafter COM) and weddellite (calcium oxalate dihydrate; COD) are among the most common constituents of urinary calculi. There exists a third hydrate of calcium oxalate, the trihydrate (COT) which has a higher solubility than both COM and COD. Experiments involving spontaneous precipitation have shown that, although COM is the thermodynamically stable phase, all three hydrates can be crystallized from aqueous solutions in which the calcium and oxalate concentrations may vary over a wide range including the physiological domain [3, 5, 14, 16]. The precipitation of slightly soluble salts such as these is largely governed by kinetic factors and may be expected to proceed according to Ostwald's rule of stages which, when applied to such crystallization processes, may be stated as follows: When the formation of several phases is possible, the one with the highest solubility will form first and will then transform, sooner or later, to the thermodynamically most stable phase [9].

The nature of the calcium oxalate hydrate formed from solution and the rate of transformation of higher hydrates to the stable monohydrate, depend on factors such as temperature, pH, stirring rate, calcium/oxalate concentration ratio, degree of supersaturation, ionic strength, and the presence of impurities. The experimental demonstration of the initial formation of COT not only in pure aqueous solutions, but also in physiological urine samples [4] and artificial urines [12] has led to many speculations about the role of COT in the formation of urinary calculi as well as to considerable research efforts on various aspects of the COT problem [1, 4–6, 8, 12, 15, 16].

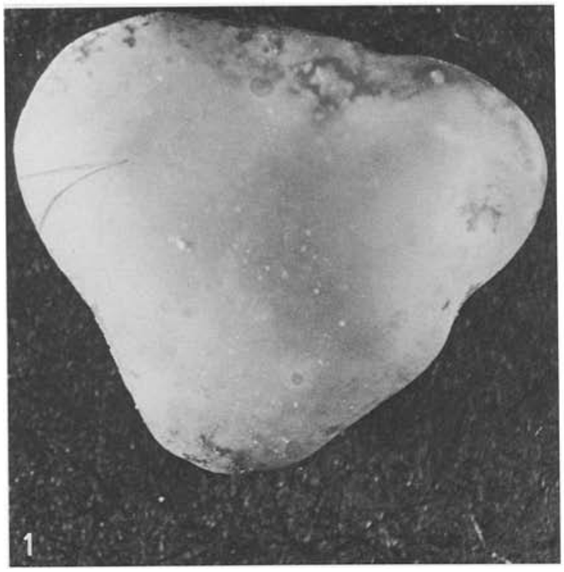
Despite its alleged importance in stone formation, only two observations of COT in urinary calculi have been reported in the literature, both authors describing an isolated occurrence discovered by accident [6, 11]. Schäfer and Dosch [14] were able to identidy COT in urinary sediments, but could not demonstrate its presence in urinary calculi.

Materials and Methods

The observations reported were made in the course of routine examinations of 220 urinary calculi from patients of the Urologic Clinic of the town of Worms, Federal Republic of Germany. The patients did not belong to a selected group. The analyses are made by infrared spectroscopy, with sample preparation by the KBr pellet technique. Normally pellets of 13 mm diameter are prepared, but when only small amounts of sample were available, paper masks were employed which permitted the recording of spectra with microgram quantities. The samples in question were further characterized by optical and scanning electron microscopy.

Results

Among the 220 calculi which were routinely examined there were 88 of which the outer part consisted essentially of whewellite. Of these calculi 27 were partly or wholly covered by a layer with a thickness of up to a few hundred microns. This layer, if sufficiently thick, looked like a white frosting on a cake, otherwise it gave the appearance of a bluish-gray varnish. In addition to the oxalate calculi just mentioned there was one uric acid calculus which also demonstrated such a coating. A photograph of a typical specimen is shown in Fig. 1. Investigations with a polarizing microscope revealed the presence of very small ($\leqslant 10\ \mu m$) crystals in this outermost layer. These crystals appeared to



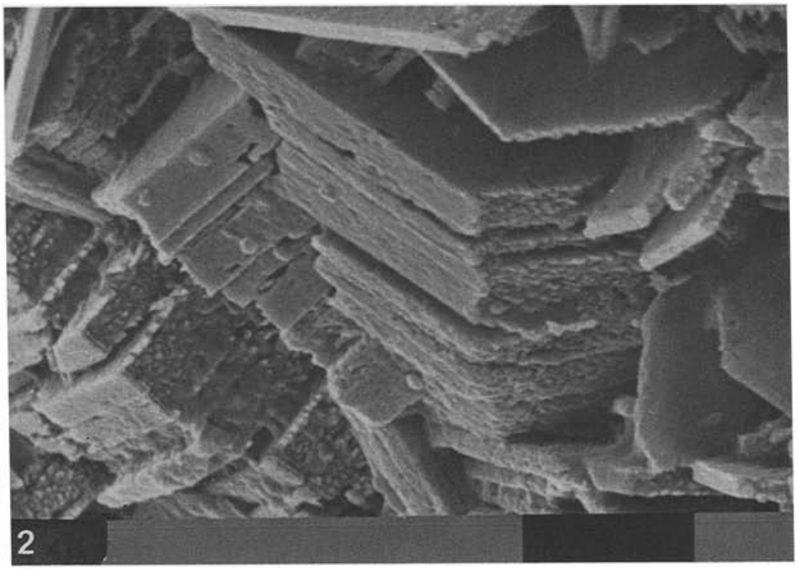


Fig. 1. Photograph of a typical COT-covered calcium oxalate calculus (diameter: approximately 3.5 mm)

Fig. 2. Scanning electron micrograph of COT in a urinary calculus (length of black scale bar – 4 μm)

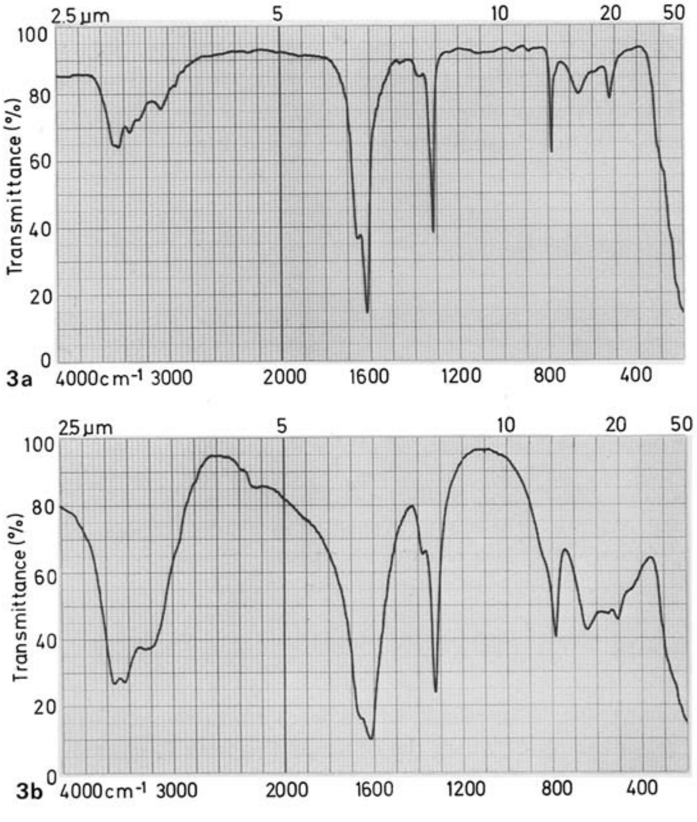


Fig. 3a, b. Infrared spectrum of natural COT (a). b Infrared spectrum of synthetic COT

have a lower relief and birefringence than the main constituent, COM. It was not possible to determine their optical properties precisely, but the estimated values indicate that the crystals might be COT, whereas COD was unlikely [10, 7].

Using scanning electron microscopy and infrared spectroscopy the outer layer has been identified as COT by comparison with synthetic material. The SEM picture in Fig. 2 closely resembles the one shown in [6] and shows the splitting up into layers, characteristic of COT, which is generally not observed in the case of COM or COD. The infrared spectra of the natural and synthetic COT are shown in Figs. 3a and 3b, respectively. They are similar to the spectra of COM and COD, but differ from them in that the main oxalate band near 1630 cm^{-1} (which is due to the asymmetric carboxyl stretching vibration) has an additional shoulder on the high-frequency side near 1660 cm^{-1}. There are also differences in the region of the OH stretching bands of the H_2O molecules. The shoulder near 1660 cm^{-1} is less pronounced in the synthetic than in the natural sample, probably indicating a partial decomposition to COM. Re-examination of the samples after several weeks showed that the synthetic COT had completely transformed into COM, whereas the natural product was found to be only partially decomposed. The greater stability of natural as compared to synthetic COT is possibly caused by the incorporation of impurities which retard the decomposition by blocking nucleation sites for COM [4].

Among the 27 + 1 calculi which showed layers of the type described above there were seven with layers of sufficient thickness to allow direct verification of their composition by infrared spectroscopy. A comparison with the layers of the remaining 21 calculi left little doubt that these, also, consisted of COT.

Discussion

Schäfer and Dosch [14] put forward a hypothesis relating the internal structure of calcium oxalate urinary calculi to

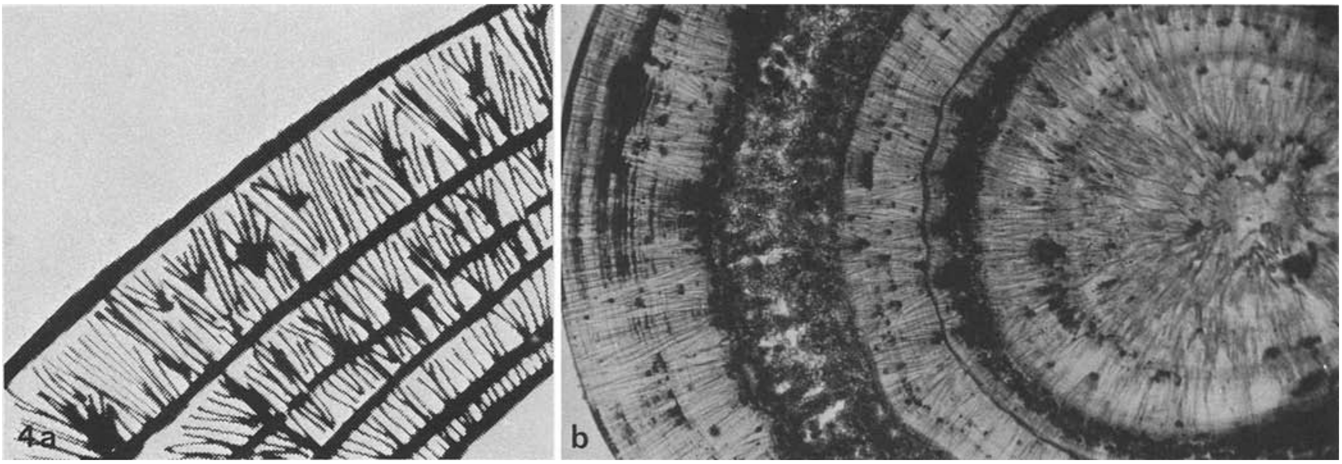


Fig. 4a, b. Drawing of a thin section of a type II whewellite calculus (**a**) (from [1], with kind permission of the authors). **b** Photograph of a thin section of a COM/COT calculus (distance from center to surface: 3 mm)

the conditions of formation, therein attributing an important role to COT. On the basis of morphological studies of thin sections of oxalate kidney stones they arrived at a classification into four types, a classification which is presented more explicitly by Schäfer and Bausch [13]: Types I and III are COM and COD calculi, respectively, in which these hydrates are the first-formed phases. Calculi of type II consist of COM which is assumed to be the result of a transformation from initially formed COT. These calculi are characterized by a dense layer-like structure. Type IV are COM calculi which are the result of a transformation either from COT with COD as the intermediate phase or from COD. They are generally less dense than type II calculi.

The drawing of a thin section of a type II calculus in Fig. 4a (reproduced from Schäfer and Dosch [14]) and the photograph of a thin section of one of the stones examined here, in Fig. 4b, show sufficient resemblance to warrant assignment of the stone to type II. The findings presented here therefore seem to confirm Schäfer and Dosch's hypothesis on the role of COT in the formation of an important type of calcium oxalate calculi.

Calcium oxalate trihydrate was found in more than 10% of all calculi examined (28 out of 220) and in about 30% of those calculi of which whewellite is the principal constituent of the outer part (27 out of 88). These findings demonstrate that calcium oxalate trihydrate is not a rare, but a common constituent of urinary calculi.

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