Anhydrous Uric Acid: Nature and Occurrence of a New Form in Urinary Calculi

Abstract. *A second form of anhydrous uric acid has been found in urinary calculi; it is probably derived as an artifact from uric acid dihydrate during storage. It has been prepared in the laboratory by desiccation of uric acid dihydrate. Mixtures of these two substances sometimes give x-ray powder patterns that resemble that of xanthine on weak photographs, but are distinguishable by their infrared spectra.*

Uric acid and uric acid dihydrate have been identified as constituents of urinary calculi (*1–3*). We have now found a second form of anhydrous uric acid (uric acid II) in four modern stones from Turkey and in an old stone from the Norfolk and Norwich Hospital collection of bladder calculi. Uric acid II is the major constituent of the surface of one of the Turkish stones, it occurs as a trace on the surface of the other three Turkish stones and in the interior of one, and it is present in all exposed regions of half a stone from the Norfolk and Norwich Hospital Museum (Table 1).

The two forms of anhydrous uric acid are very similar; the crystallographic data follow: uric acid I (monoclinic, pseudo-orthorhombic): $P2_1/n$, $a = 13.12$ Å, $b = 7.40$ Å, $c = 6.21$ Å, $\beta = 90.5°$; uric acid II (monoclinic): $P2_1/n$ (*4*), $a = 13.02$ Å, $b = 7.59$ Å, $c = 6.18$ Å, $\beta = 93.1°$.

The spacings and relative intensities of the lines on the x-ray powder diffraction photographs (Table 2) were obtained by use of a high-resolution Nonius Guinier–type camera. The main differences in the patterns are a shift to lower theta values of some of the strongest lines, a more rapid falling-off in intensity of the high-angle lines, and the appearance of a weak line at 5.46 Å in the powder pattern of form II. The two substances can be distinguished with a camera of 6-cm diameter only if the camera radius is carefully standardized to take into account such factors as film shrinkage.

The samples of stone containing uric acid II contained uric acid dihydrate also. Mixtures of these substances in certain proportions can give powder patterns strongly resembling that of xanthine if the photograph is not very intense. In such instances the infrared spectrum of the mixture resolves any ambiguity, since the xanthine and uric acid spectra differ considerably, especially in the space region 10 to 15 μ (Table 3).

Table 1. Occurrence of uric acid II in bladder and kidney stones. In the case of the Turkish stones, the ages of the patients were not available. Symbols: A1, uric acid I; A2, urio acid dihydrate; A3, uric acid II; B, ammonium acid urate; C1, whewellite; C2, weddellite. Traces are indicated by parentheses.

Source	Sex	Date	Stone: Portion	Stone: Composition
		From Turkey (6)		
Bladder	M	Modern	Interior	B, (A3)
			Surface	A3, A2, (C2)
Bladder	M	1966	Surface	A2, C1, (A3)
Kidney	M	1966	Surface	A2, C1, (A3), (A1)
Kidney	F	Modern	Surface	A1, (C1), (A2), (A3)
		From Norwich, England (7)		
Bladder	M (aged 55)	1790	Nucleus	A3, A2, A1
			Interior, surface	A1, (A3)

Table 2. Spacings and relative intensities of the lines in the x-ray powder photographs of the two forms of anhydrous uric acid. Abbreviations: w, weak; m, medium; s, strong; v, very.

Uric acid I (*3*)		Uric acid II	
d (Å)	*I*	*d* (Å)	*I*
6.56	38	6.50	m
5.63	20	5.70	m
4.91	48	5.46	w
4.76	6	4.94	ms
4.47	1	4.79	m
3.86, 3.84	55	4.55	vvw
		3.93	s
3.70	5	3.80, 3.78	m
3.59	2		
3.28	14	3.23	vs
3.18	70	3.16	vvs
3.09	100	2.99	m
3.00	2	2.93	s
2.87, 2.86	25	2.85, 2.87	w band
2.82	2	2.73	w
2.80, 2.79	10	2.66	vw
2.70	1	2.56	w
2.63, 2.62	3	2.48	vvw
2.57	18		

Table 3. Infrared bands for uric acid and xanthine in the region 10 to 15 μ. These values were obtained on a Perkin-Elmer Infracord, with the sample as a Nujol mull. Abbreviations as for Table 2. Nonionized uric acid includes both anhydrous forms and dihydrate.

Position (μ)	Strength	Width
	Nonionized uric acid	
10.03	s	narrow
11.35	m	broad
12.7	s	very broad
13.36	vs	narrow
14.12	s	medium
	Xanthine	
10.39	m	very narrow
11.09	m	broad
11.66	sh	broad
11.93	s?	shoulder
13.00	vs	narrow
13.29	w	medium
13.76	vs	narrow
14.34	vw	medium

Uric acid dihydrate can decompose to uric acid (*1*), apparently directly to form I in the presence of water vapor, but to form II when stored over phosphorus pentoxide or silica gel. Form II was also obtained from a sample of dihydrate left open in a refrigerator at 5° to 7°C and a relative humidity of about 25 percent (*5*). Synthetic uric acid II is metastable and will change spontaneously into form I at room temperature. The uric acid II found in urinary calculi is presumably more stable, possibly as a result of such things as dissolved coloring matter.

The occurrence of uric acid dihydrate and uric acid II together in calculi on exposed parts of the stones suggests that there is every likelihood of uric acid II being formed as an artifact, during storage, by the dehydration of the dihydrate.

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References and Notes

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2. R. Shirley, *Science* **152**, 1512 (1966); K. Lonsdale and P. Mason, *ibid.*, p. 1511.
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4. As in uric acid dihydrate (*1*), some forbidden *h0l* reflections, with $h + l$ odd, are faintly present.
5. The water vapor around the sample was in equilibrium with surfaces at —10°C and contained only about 2 mg of water per liter.
6. From Hacettepe Medical Center, Ankara, Turkey, by courtesy of Dogan Remzi.
7. From the Norfolk and Norwich Hospital Museum, England, by courtesy of Ridley Thomas.
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