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Solubility of Uric Acid in Lithium Chloride Solutions

Galina Sadovska[1], **Ivan Kron**[2], and **Erich Königsberger**[3,*]

[1] Department of Inorganic Technology, University of Pardubice, 532 10 Pardubice, Czech Republic
[2] Institute of Medical Chemistry and Biochemistry, Medical Faculty, P. J. Safarik University, 040 66 Kosice, Slovak Republic
[3] Department of Chemistry, Division of Science and Engineering, Murdoch University, Murdoch, WA 6150, Australia

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Summary. The solubility of anhydrous uric acid was measured in 0.30 mol dm^{-3} LiCl solutions as a function of hydrogen ion concentration at 25 and 37°C. No influence of the lithium ion on the solubility of uric acid was detected. The "litholytic" effect of lithium reported in literature can possibly be explained by the higher solubility of lithium hydrogenurate as compared to other alkali metal hydrogenurates.

Keywords. Uric acid; Solubility; Lithium; Urolithiasis; Computer simulations.

Introduction

Formation of uric acid stones in the human urinary tract belongs to a complex metabolic disorder [1]. As the solubility of uric acid increases with pH [2–4], solubilisation of uric acid calculi by alkalisation of urine constitutes an important conservative treatment of uric acid urolithiasis. Amongst the solubilisation studies performed *in vitro*, the work of *Javor et al.* [5] is of particular interest. The authors have found that uric acid calculi are better soluble in lithium carbonate solutions than in sodium and potassium (hydrogen-) carbonate solutions and attributed this result to a "litholytic effect" of the lithium ions.

Lithium is ingested by humans in trace amounts from dietary sources. It is considered to have an essential function in the physiological regulation of mood [6], although its occurrence in the average human body amounts to only 0.7 mg [7]. In much higher concentrations, lithium is effective as a medication for mania and

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* Corresponding author. E-mail: koenigsb@chem.murdoch.edu.au
Dedicated to Professor *Heinz Gamsjäger* on the occasion of his 70th birthday

mood swings including manic depressive disorders. As a frequent adverse effect of long-term medication, lithium treatment induces weight gain in a considerable number of patients [8].

The hypothesis that lithium is effective for the treatment of bladder stones (introduced in 1843) and gout (1853) has been declared to be ill-founded in 1941 [9]. Nevertheless, lithium therapy has still been investigated later [10, 11]. To probe the proposed "litholytic effect" of lithium [5], solubilities of uric acid were measured accurately in LiCl solutions of constant ionic strength as a function of hydrogen ion concentration.

Results and Discussion

Solubility data for anhydrous uric acid in 0.30 mol dm^{-3} LiCl solutions at 25 and 37°C are shown in Fig. 1 as a function of $pH = -\log([H^+]/\text{mol dm}^{-3})$. Also shown in Fig. 1 are uric acid solubilities in 0.30 mol dm^{-3} NaCl solutions (dotted lines), which have been found to agree well with solubilities measured in various other electrolyte solutions including artificial urine [3]. All these results were correlated [2–4] by considering equilibria (1) and (2).

$$H_2U(s) \rightleftharpoons H_2U(aq) \quad K_s \tag{1}$$

$$H_2U(aq) \rightleftharpoons H^+ + HU^- \quad K_1 \tag{2}$$

The concentration of the urate ion (U^{2-}) is negligible at $pH < 9$, which covers the physiologically important *pH* range. The solubility of uric acid is given by (3).

$$[H_2U(aq)]_{tot} = [H_2U(aq)] + [HU^-] = K_s(1 + K_1/[H^+]) \tag{3}$$

Regression analysis of the present data for 0.30 mol dm^{-3} LiCl solutions (Table 1) results in $pK_s = 3.80 \pm 0.02$ and $pK_1 = 5.25 \pm 0.03$ at 25°C and $pK_s = 3.53 \pm 0.01$ and $pK_1 = 5.16 \pm 0.01$ at 37°C. These values compare to

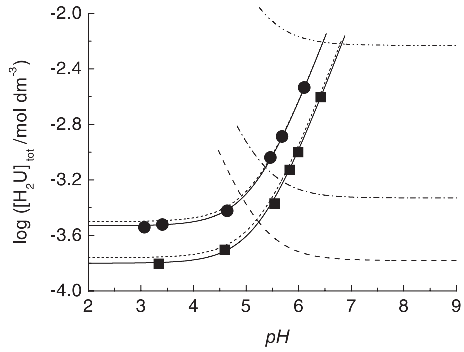

Fig. 1. Solubility of anhydrous uric acid in 0.30 mol dm^{-3} LiCl solutions at 25°C (squares) and 37°C (dots); solid lines: calculated values, using the equilibrium constants derived in this study; dotted lines: the corresponding uric acid solubilities in (0.15–0.30) mol dm^{-3} NaCl solutions [2, 3]; dashed line: solubility of sodium hydrogenurate in 0.30 mol dm^{-3} NaCl solutions at 37°C [2]; dash-dot line: solubility of potassium hydrogenurate in 0.30 mol dm^{-3} KCl solutions at 37°C [4]; dash-dot-dot line: solubility of lithium hydrogenurate in 0.30 mol dm^{-3} LiCl solutions at 37°C [4]

Table 1. Solubility of anhydrous uric acid, $[H_2U(aq)]_{tot}$, as a function of $pH = -\log([H^+]/\text{mol dm}^{-3})$ in 0.30 mol dm^{-3} LiCl solutions at 25 and 37°C

T/°C			
25		37	
pH	$[H_2U(aq)]_{tot}$/mmol dm^{-3}	pH	$[H_2U(aq)]_{tot}$/mmol dm^{-3}
3.340	0.157	3.068	0.287
4.595	0.198	3.410	0.300
5.542	0.426	4.641	0.378
5.829	0.745	5.464	0.915
5.991	1.00	5.687	1.30
6.419	2.50	6.106	2.92

$pK_s = 3.76 \pm 0.03$ and $pK_1 = 5.26 \pm 0.04$ at 25°C and $pK_s = 3.49 \pm 0.03$ and $pK_1 = 5.19 \pm 0.04$ at 37°C for 0.15 mol dm^{-3} NaCl [2]. The solubility of uric acid in other electrolyte solutions of ionic strength $0.15 < I/\text{mol dm}^{-3} < 0.30$, including artificial urine, is also correlated by the latter constants [2–4].

At low *pH* the solubility of uric acid in LiCl solutions is slightly lower than in the other electrolyte solutions but overall there is no significant difference (see also Fig. 1). Thus, a "litholytic effect" of Li^+ was not detected in this work. Earlier studies using lithium and sodium acetate solutions also have arrived at the conclusion that lithium has no influence on the solubility of uric acid *in vitro* [12, 13].

A likely explanation for the findings of *Javor et al.* [5] can be based on the solubilities of the alkali metal hydrogenurates. Amongst those, the lithium salt has the highest solubility [4], whereas the solubilities of the corresponding sodium and potassium salts are considerably lower [2, 4] (Fig. 1). Therefore, uric acid calculi may dissolve in lithium carbonate solutions without precipitation of lithium hydrogenurate. On the other hand, when sodium or potassium (hydrogen-) carbonate solutions are used, the corresponding hydrogenurates may precipitate on the surface of the uric acid calculus and prevent further dissolution even if the *pH* is being increased.

Experimental

Analytical reagent grade chemicals, A-grade glassware and bidistilled water were employed throughout. High-purity uric acid, $C_5H_4N_4O_3$ (99%+, ALDRICH-Chemical Co.) was used directly. X-Ray diffraction analysis and scanning electron microscopy confirmed that this commercial sample was pure anhydrous uric acid.

All solubility measurements were performed in a similar manner to that reported previously [2, 3]. Briefly, the initial solution was placed in the solubility cell [14] and percolated through the solid phase of uric acid by a prehumidified N_2-gas stream at (25.00 ± 0.02) and (37.00 ± 0.02)°C. In the *pH* variation method [15] employed here, the ionic strength was kept constant at 0.30 mol dm^{-3} (LiCl) and the initial HCl or LiOH concentration was varied systematically from one experiment to another. An ORION 940 *pH* meter was used to record the *pH* of the solutions. In each experiment, a constant *pH* value was obtained after *ca.* 6 hours indicating that solubility equilibrium had been attained.

Generally, the galvanic cells employed for *pH* measurements can be represented as

$$\mathrm{Ag}|\mathrm{AgCl}|\,5.0\,\mathrm{mol\,dm^{-3}\,NaCl}|\,5.0\,\mathrm{mol\,dm^{-3}\,NaCl}|\mathrm{S_A}\ \text{or}\ \mathrm{S}|\ \text{glass electrode} \qquad \text{(A)}$$

where S_A is the calibrating solution and S is the test solution. SCHOTT H2680 glass electrodes and home-made silver–silver chloride reference electrodes with *Wilhelm*-type salt bridges [16] were used to measure $-\log[\mathrm{H}^+]$ of the solution during the reaction with the solid phase. Cell (A) was calibrated before and after each experiment with solutions S_A which contained $0.290\,\mathrm{mol\,dm^{-3}}$ LiCl and $0.010\,\mathrm{mol\,dm^{-3}}$ HCl. A salt bridge solution of $5.0\,\mathrm{mol\,dm^{-3}}$ NaCl was used as it had been found [3] that no liquid junction potential corrections were necessary for this salt bridge because it obviously keeps variations of the liquid junction potential at a minimum.

At the end of a solubility measurement, the saturated uric acid solution was diluted with $0.100\,\mathrm{mol\,dm^{-3}}$ NaOH solution and the total concentration of urate was determined at 293.6 nm using a Perkin Elmer LAMBDA 15 UV/VIS Spectrometer with $0.100\,\mathrm{mol\,dm^{-3}}$ NaOH as the reference solution. It was found that at this wavelength, *pH* of the solutions does not have strong influence on the peak position and absorption of urate. *Beer–Lambert*'s law is well obeyed in the concentration range from 0.025 to $0.15\,\mathrm{mmol\,dm^{-3}}$ with a molar absorption coefficient of $13375\,\mathrm{dm^3\,mol^{-1}\,cm^{-1}}$ [3]. As urate solutions are not very stable with time, the spectrophotometric measurements were carried out immediately after the preparation of urate solutions.

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