Solid-liquid equilibrium in the system 2-keto-L-gulonic acid + sodium-2-keto-L-gulonate + hydrochloric acid + sodium chloride + water

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Abstract

The reactive solid-liquid equilibrium (SLE) in the quinary system 2-keto-L-gulonic acid (HKGA) + sodium-2-keto-L-gulonate (NaKGA) + hydrochloric acid (HCl) + sodium chloride (NaCl) + water was studied experimentally at 298 K and ambient pressure. The precipitation of three solid species was observed: HKGA monohydrate ($\text{HKGA} \cdot \text{H}_2\text{O}$), NaKGA monohydrate ($\text{NaKGA} \cdot \text{H}_2\text{O}$), and NaCl. A thermodynamic model based on the Pitzer model to calculate the activity coefficients in the liquid phase for the SLE was developed and unreported Pitzer parameters were fitted to the experimental data of this work. The equilibrium constant for the dissociation of HKGA and the solubility products of $\text{HKGA} \cdot \text{H}_2\text{O}$ and $\text{NaKGA} \cdot \text{H}_2\text{O}$ at 298 K were calculated from experimental data, whereas the equilibrium constant for the autoprotolysis of water and the solubility product of NaCl were adopted from literature data. The agreement between the experimental data and the results from the model is excellent, both regarding the liquid phase composition and the solid species in solid-liquid equilibrium.

Keywords: electrolytes, 2-keto-L-gulonic acid, Pitzer model, solid-liquid equilibrium

1. Introduction

2-Keto-L-gulonic acid (HKGA) is a key intermediate in the production process of L-ascorbic acid (vitamin C). Since vitamin C is an important product for many industries, such as food, animal nutrition, and health industry, HKGA is produced in large scale. HKGA is mainly produced by fermentation [1–3]. A crucial step thereby is the separation and purification of the products during downstream processing. Crystallization is an interesting option for the downstream processing of HKGA [4, 5], but requires information on the solid-liquid equilibrium (SLE) in the considered systems. The solids that are crystallizing from the fermentation broth in the HKGA process depend to a large extent on pH value and salt load, both parameters are strongly adjusted during the

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process. For instance, during the fermentation, the decrease of the pH value due to the formation of the acid HKGA has to be compensated by addition of basic components that often contain sodium, such as sodium carbonate (Na_2CO_3) [6, 7] or sodium hydroxide (NaOH) [5, 8, 9]. At the resulting neutral pH values, not the acid HKGA, but its sodium salt sodium-2-keto-L-gulonate (NaKGA) is obtained as solid during crystallization [4, 5, 10]. If one wants to crystallize the acid HKGA directly, the pH value has to be lowered prior to crystallization, e.g. by the addition of hydrochloric acid (HCl).

A model system that can be used for describing the process steps mentioned above is the system 2-keto-L-gulonic acid (HKGA) + sodium-2-keto-L-gulonate (NaKGA) + hydrochloric acid (HCl) + sodium chloride (NaCl) + water. It is the goal of the present work to provide experimental data and a thermodynamic model of the SLE in this system.

Several subsystems of this system have been studied in the literature. The SLE in the system HCl + NaCl + water has been extensively studied in experiments [11–16]. Furthermore, in a previous work of our group, the solid-liquid phase diagrams in the system HKGA + NaKGA + water were studied at temperatures in the range 275 - 313 K and ambient pressure [10]. It was found that both HKGA and NaKGA crystallize exclusively as monohydrates $\text{HKGA} \cdot \text{H}_2\text{O}$ and $\text{NaKGA} \cdot \text{H}_2\text{O}$, respectively, at the studied conditions, which is in line with other reports in the literature [4, 5, 17]. In that previous work, a thermodynamic model for describing the SLE in the system HKGA + NaKGA + water was developed, which is based on an extended version of the Debye-Hückel theory [10]. This simple model was shown to give an excellent description of the experimental data and was also successfully applied to describe the SLE in the related system HKGA + vitamin C + water [18]. However, this model was found to be not satisfactory for mixtures with high concentrations of HCl .

To elucidate the SLE in the quinary system HKGA + NaKGA + HCl + NaCl + water, the ternary subsystems HKGA + HCl + water, NaKGA + NaCl + water, HKGA + NaCl + water, and NaKGA + HCl + water were studied experimentally in the present work at 298 K and ambient pressure. Three different solid species were observed: $\text{HKGA} \cdot \text{H}_2\text{O}$, $\text{NaKGA} \cdot \text{H}_2\text{O}$, and NaCl . A thermodynamic model for describing the SLE in the quinary system was developed. The Pitzer model was used to calculate the activity coefficients in the liquid phase.

2. Experiments

2.1. Chemicals

Anhydrous 2-keto-L-gulonic acid (HKGA) was obtained from Cargill. Sodium hydroxide (NaOH) pellets were purchased from Sigma-Aldrich. Hydrochloric acid (HCl , 0.32 g/g) and sodium chloride (NaCl) were obtained from Carl Roth. As solvent, ultra pure water was used, which was produced

with a Milli-Q purifier from Millipore (Elix Essential 5). Table 1 gives an overview of all chemicals used in this work, including the chemicals for the preparation of the eluents for the analysis by ion chromatography (IC) and high-performance liquid chromatography (HPLC).

Table 1: Suppliers and purities of chemicals used in this work.

Chemical name (abbreviation)	Formula	Supplier	Purity ^{a)}
Hydrochloric acid 0.32 g/g	HCl	Carl Roth	n.a.
2-Keto-L-gulonic acid (HKGA)	C ₆ H ₁₀ O ₇	Cargill	>0.98 g/g
Nitric acid 0.1 N	HNO ₃	Merck	n.a.
Sodium carbonate	Na ₂ CO ₃	Th. Geyer	>0.998 g/g
Sodium chloride	NaCl	Carl Roth	>0.995 g/g
Sodium hydrogen carbonate	NaHCO ₃	Sigma-Aldrich	>0.997 g/g
Sodium hydroxide	NaOH	Sigma-Aldrich	>0.99 g/g
Sulfuric acid 1 M	H ₂ SO ₄	Carl Roth	n.a.

^{a)}Supplier specification.

46

47 2.2. Experimental Procedure

48 2.2.1. Preparation of sodium-2-keto-L-gulonate monohydrate (NaKGA·H₂O)

Since pure sodium-2-keto-L-gulonate (NaKGA) or the monohydrate (NaKGA·H₂O) could not be purchased, it was produced from 2-keto-L-gulonic acid (HKGA) and sodium hydroxide (NaOH) as follows: a solution of HKGA in water ($w_{\text{HKGA}} \approx 0.35$ g/g) was prepared. The solution was neutralized to a pH value of approximately 7 by gradually adding an aqueous solution of 0.3 g/g NaOH, which was prepared from NaOH pellets and water, while mixing with a magnetic stirrer and measuring the pH value with a pH meter from Metrohm (type 780). The NaOH solution was added at ambient temperature. However, the mixture was cooled in an ice bath during the neutralization due to the exothermic acid-base reaction. After the neutralization, the stirring was continued while keeping the mixture in the ice bath until the precipitation of solid NaKGA · H₂O was observed. The solid was separated from the liquid by filtration and dried in a drying chamber from Heraeus (UT 6060) at 323 K and ambient pressure.

60 2.2.2. Sample preparation and equilibration

Samples, each consisting of water and two of the solutes HKGA, NaKGA · H₂O, HCl, and NaCl, were prepared gravimetrically using a laboratory scale from Mettler Toledo (AG204). For the samples consisting of water, NaCl, and HKGA or NaKGA · H₂O, about 5 g of water was poured into 30 ml glass vessels and NaCl and HKGA or NaKGA · H₂O were added as solids while stirring with a magnetic stirrer. The total mass of the solids was about 5 g for all samples, but the ratio of NaCl to HKGA or NaCl to NaKGA · H₂O was varied to obtain samples with large amounts of NaCl and low amounts of HKGA or NaKGA · H₂O as well as vice versa. Also samples containing only water and NaCl, samples containing only water and HKGA, and samples containing only water

69 and NaKGA · H₂O were prepared.

70 For the samples consisting of water, HCl, and HKGA or NaKGA · H₂O, about 5 g of water was

71 poured into 30 ml glass vessels to which about 5 g of HKGA or NaKGA · H₂O was added while

72 stirring with a magnetic stirrer. Different amounts of aqueous 0.32 g/g HCl were added to the

73 vessels. In both cases, the added amount of HCl was limited due to degradation processes at very

74 acidic conditions.

75 In all samples, a solid phase was observed after the preparation. The vessels were sealed and

76 equilibrated at a constant temperature of 298 K in an incubator from Memmert (ICP600) for 3 days.

77 The temperature in the vessels was measured with a calibrated PT100 thermometer connected to a

78 digital multimeter from Prema (type 5017) with an accuracy of ± 0.1 K. In preliminary experiments,

79 it was verified that an equilibration time of 3 days is sufficient to reach equilibrium. The solid phase

80 was kept suspended during equilibration by stirring with magnetic stirrers. After the equilibration

81 time, the stirring was stopped to allow the solid phase in each sample to settle. Liquid was

82 isothermally drawn from the clear supernatant of all vessels using syringes with syringe filters

83 from Rotilabo (5 μ m pore size). The drawn liquid was gravimetrically diluted with water for

84 the analysis by ion chromatography (IC) and high-performance liquid chromatography (HPLC).

85 The solid phase was separated from each vessel by filtration and dried in a drying chamber from

86 Heraeus (UT 6060) at 323 K and ambient pressure. The dried solid was gravimetrically dissolved

87 and diluted with water and analyzed by IC and HPLC.

88 2.2.3. Analysis

Ion chromatography (IC) was used to determine the mass fractions of sodium ions (Na⁺) and chloride ions (Cl⁻). For the IC analysis, a system from Metrohm (930 Compact IC Flex) with a conductivity detector was used. For the analysis of Na⁺, a cation exchange column from Metrohm (Metrosep C 6-250/4.0) in combination with 4.0 mM nitric acid (HNO₃), which was prepared from 0.1 M HNO₃ and water, as eluent was used. For the analysis of Cl⁻, an anion exchange column from Metrohm (Metrosep A Supp 5-250/4.0) in combination with an aqueous solution of 3.2 mM sodium carbonate (Na₂CO₃) and 1.0 mM sodium hydrogen carbonate (NaHCO₃) as eluent was used. The uncertainty of the mass fractions of Na⁺ and Cl⁻ determined by IC was below 2% as demonstrated by analyzing synthetic samples of known composition.

For determining the overall mass fraction of 2-keto-L-gulonate ions (KGA⁻) in the liquid and solid phase of the samples, high-performance liquid chromatography (HPLC) was used. In the systems considered in this work, KGA⁻ can be present in the ionic form KGA⁻ or in the undissociated form HKGA in the liquid phase and as HKGA · H₂O or NaKGA · H₂O in the solid phase in equilibrium. In the HPLC analysis, all forms are quantified together and cannot be distinguished. For the HPLC analysis, a system from Agilent (1200 series) with an anion exchange column (Hi-Plex H 7.7 x 300

mm) and a refractive index (RI) detector was used. As eluent, 10 mM sulfuric acid (H_2SO_4), which was prepared from 1 M H_2SO_4 and water, was used. The uncertainty of the overall mass fraction of KGA^- determined by HPLC was below 2% as demonstrated by analyzing synthetic samples of known composition.

The overall mass fraction of hydrogen ions (H^+), considering dissociated H^+ and H^+ bound in the acid group of undissociated HKGA in the liquid phase and bound in the acid group of $\text{HKGA} \cdot \text{H}_2\text{O}$ in the solid phase, was calculated from the electroneutrality condition:

$$w_{\text{H}^+} = M_{\text{H}^+} \left(\frac{w_{\text{Cl}^-}}{M_{\text{Cl}^-}} + \frac{w_{\text{KGA}^-}}{M_{\text{KGA}^-}} - \frac{w_{\text{Na}^+}}{M_{\text{Na}^+}} \right) \quad (1)$$

with the mass fractions w_i and the molar masses M_i of the species i . The concentration of hydroxide ions (OH^-) was thereby neglected since only neutral to acidic mixtures were considered in this work. The mass fraction of water was calculated from mass balances.

The stoichiometry of the solid phases in equilibrium was elucidated from the IC and HPLC analysis under the assumption that, at the studied conditions, HKGA and NaKGA are only present as monohydrates $\text{HKGA} \cdot \text{H}_2\text{O}$ and $\text{NaKGA} \cdot \text{H}_2\text{O}$, respectively, in the solid phase, which is in line with report in the literature [4, 5, 10, 17], and that NaCl only precipitates in pure form as reported in the literature [19]. Different cases were distinguished based on the IC and HPLC analysis: if only KGA^- is found in a significant amount, the solid is only $\text{HKGA} \cdot \text{H}_2\text{O}$. If only Na^+ and Cl^- are found in a significant amount, the solid is only NaCl. If only Na^+ and KGA^- are found in a significant amount and the calculated overall mass fraction w_{H^+} is zero, the solid is only $\text{NaKGA} \cdot \text{H}_2\text{O}$. If only Na^+ and KGA^- are found in a significant amount and $w_{\text{H}^+} > 0$, the solid contains $\text{HKGA} \cdot \text{H}_2\text{O}$ and $\text{NaKGA} \cdot \text{H}_2\text{O}$. If Na^+ , Cl^- , and KGA^- are found in a significant amount and $w_{\text{H}^+} = 0$, the solid contains $\text{NaKGA} \cdot \text{H}_2\text{O}$ and NaCl. If Na^+ , Cl^- , and KGA^- are found in a significant amount and the overall mole fraction of H^+ equals the overall mole fraction of KGA^- , the solid contains $\text{HKGA} \cdot \text{H}_2\text{O}$ and NaCl, otherwise the solid contains all possible crystal species $\text{HKGA} \cdot \text{H}_2\text{O}$, $\text{NaKGA} \cdot \text{H}_2\text{O}$, and NaCl. In all cases, the mass fraction of hydrate water in the solid phase was calculated from mass balances confirming the assumed solid species. Furthermore, the solid phase determined with the above described procedure was verified by material balances considering the initial overall composition of the samples and the associated liquid phase composition in equilibrium.

3. Model

A scheme of the model of the reactive solid-liquid equilibrium is shown in Figure 1. The model considers the dissociation of HKGA, NaKGA, HCl, and NaCl as well as the autoprotolysis of water in the liquid phase. NaKGA, HCl, and NaCl are strong electrolytes and are therefore considered

113 to be fully dissociated in the liquid phase. By contrast, HKGA is a weak electrolyte and, hence,
 114 present in the dissociated (H^+ and KGA^-) and undissociated (HKGA) form in the liquid phase.
 115 The equilibrium constant for the dissociation of HKGA is $K_{\text{HKGA}}^{\text{diss}}$, the one for the autoprotolysis
 116 of water is $K_{\text{W}}^{\text{diss}}$. The possible solid phases in this system are $\text{HKGA} \cdot \text{H}_2\text{O}$, $\text{NaKGA} \cdot \text{H}_2\text{O}$, and
 117 NaCl , which are assumed to be completely immiscible.

Figure 1: Scheme of the model of the reactive solid-liquid equilibrium in the system $\text{HKGA} + \text{NaKGA} + \text{HCl} + \text{NaCl} + \text{water}$.

The solid-liquid equilibrium is characterized by the solubility products $K_{\text{HKGA} \cdot \text{H}_2\text{O}}^{\text{SP}}$, $K_{\text{NaKGA} \cdot \text{H}_2\text{O}}^{\text{SP}}$, and $K_{\text{NaCl}}^{\text{SP}}$. The thermodynamic equilibrium constants are defined by Eqs. (2) to (6).

$$K_{\text{HKGA}}^{\text{diss}} = \frac{m_{\text{H}^+} \cdot m_{\text{KGA}^-}}{m_{\text{HKGA}} \cdot m_0} \cdot \frac{\gamma_{\text{H}^+} \cdot \gamma_{\text{KGA}^-}}{\gamma_{\text{HKGA}}} \quad (2)$$

$$K_{\text{W}}^{\text{diss}} = \frac{m_{\text{H}^+} \cdot m_{\text{OH}^-}}{m_0^2} \cdot \frac{\gamma_{\text{H}^+} \cdot \gamma_{\text{OH}^-}}{a_{\text{W}}} \quad (3)$$

$$K_{\text{HKGA} \cdot \text{H}_2\text{O}}^{\text{SP}} = \frac{m_{\text{HKGA}}}{m_0} \cdot a_{\text{W}} \cdot \gamma_{\text{HKGA}} \quad (4)$$

$$K_{\text{NaKGA} \cdot \text{H}_2\text{O}}^{\text{SP}} = \frac{m_{\text{Na}^+} \cdot m_{\text{KGA}^-}}{m_0^2} \cdot a_{\text{W}} \cdot \gamma_{\text{Na}^+} \cdot \gamma_{\text{KGA}^-} \quad (5)$$

$$K_{\text{NaCl}}^{\text{SP}} = \frac{m_{\text{Na}^+} \cdot m_{\text{Cl}^-}}{m_0^2} \cdot \gamma_{\text{Na}^+} \cdot \gamma_{\text{Cl}^-} \quad (6)$$

118 where m_i and γ_i are the molality and the activity coefficient of solute i in the liquid phase,
 119 respectively. m_0 is defined as 1 mol/kg. a_{W} denotes the activity of water in the liquid phase,
 120 which is normalized according to Raoult's law, whereas the activities of all other components (the
 121 solutes) are normalized as it is common for describing electrolyte systems: the solute's activity
 122 coefficient becomes unity at infinite dilution in the solvent and the molality scale is used for
 123 measuring the solute's concentration. The activity coefficients γ_i of the solutes i in the liquid
 124 phase were calculated with the Pitzer model [20]. The interaction parameters for the inorganic
 125 ions were taken from the literature [21]. Using only the Pitzer parameters from Ref. [21], the
 126 model is not able to correctly describe the SLE in mixtures with high concentrations of HCl. At
 127 high concentrations of HCl and the resulting low pH values, most of the KGA^- is expected to

128 be present in the undissociated form HKGA in the liquid phase according to Eq. (2). Hence, at
 129 high concentrations of HCl, high concentrations of H^+ , Cl^- , and HKGA are expected in the liquid
 130 phase. Therefore, the Pitzer parameters λ_{HKGA,H^+} and λ_{HKGA,Cl^-} that describe the interaction of
 131 undissociated HKGA with hydrogen ions (H^+) and of undissociated HKGA with chloride ions (Cl^-),
 132 respectively, were fitted to experimental data of this work. Both parameters were simultaneously
 133 fitted to minimize the deviation of the experimental and modeled liquid phase composition in SLE
 134 in the systems HKGA + HCl + water and NaKGA + HCl + water. The activity of water in the
 135 liquid phase was calculated from the osmotic coefficient.
 136 The equilibrium constant K_W^{diss} for the autoprotolysis of water was taken from the literature [22].
 137 The solubility product K_{NaCl}^{SP} was calculated from data on the solubility of pure NaCl in water at
 138 298 K from the literature [23]. The equilibrium constant K_{HKGA}^{diss} for the dissociation of HKGA
 139 at 298 K was determined from experimental data on the pH value of an aqueous solution with
 140 a known concentration of pure HKGA, cf. Ref. [10]. The solubility products $K_{HKGA \cdot H_2O}^{SP}$ and
 141 $K_{NaKGA \cdot H_2O}^{SP}$ were determined from experimental data on the solubility of pure HKGA in water
 142 and pure NaKGA in water at 298 K from this work, respectively.

143 4. Results and Discussion

In Table 2, the experimental results of this work for the composition of the liquid phase in
 mass fractions w and the coexisting solid phases in SLE are summarized. Table 2 also contains
 the corresponding Jänecke indices $J(Na^+)$ and $J(Cl^-)$ that are calculated from the experimental
 liquid phase composition in SLE as follows

$$J(Na^+) = 100 \frac{w_{Na^+}/M_{Na^+}}{w_{Na^+}/M_{Na^+} + w_{H^+}/M_{H^+}} \quad (7)$$

$$J(Cl^-) = 100 \frac{w_{Cl^-}/M_{Cl^-}}{w_{Cl^-}/M_{Cl^-} + w_{KGA^-}/M_{KGA^-}} \quad (8)$$

144 from the mass fractions w_i and the molar masses M_i of the species i .
 145 Table 2 also contains numerical results for w_W as calculated with the model. They were obtained
 146 as described in the following: for each experimental data point, an unsaturated mixture with the
 147 same ratios of the solutes, i.e the same values of $J(Na^+)$ and $J(Cl^-)$, as found experimentally was
 148 considered. For each of these mixtures with fixed values of $J(Na^+)$ and $J(Cl^-)$, the water mass
 149 fraction at which the first precipitation of a solid occurs was calculated. Hence, the experimental
 150 data points were projected along the axis of the water mass fraction on the modeled SLE surface.
 151 The deviations between the modeled and the experimental results for the water mass fraction are
 152 always below 5% and below 2% for 75% of the data points.

Table 2: Experimental SLE data for the system HKGA + NaKGA + HCl + NaCl + water at 298 K and 1 bar. The composition of the liquid phase in equilibrium is specified using mass fractions w of the ions Na^+ , H^+ , Cl^- , KGA^- , and the solvent water (W). Also the mass fraction of water as calculated with the model for the respective concentration of the ions is given. w_{H^+} and w_{KGA^-} are overall mass fractions considering the ionic species as well as H^+ and KGA^- bound in undissociated HKGA in the liquid phase, respectively. The mass fraction of OH^- in the liquid phase is negligible. The solid phase is indicated by A: HKGA $\cdot$ H₂O, B: NaKGA $\cdot$ H₂O, C: NaCl.^{a)}

Liquid phase composition / g/g						Jänecke indices		Solid phase
Experiments					Model	$J(\text{Na}^+)$	$J(\text{Cl}^-)$	
w_{Na^+}	w_{H^+}	w_{Cl^-}	w_{KGA^-}	w_{W}	w_{W}			
0.000	0.0018	0.000	0.345	0.653	0.652	0.0	0.0	A
0.000	0.0018	0.000	0.346	0.652	0.652	0.0	0.0	A
0.000	0.0020	0.012	0.316	0.671	0.670	0.0	16.7	A
0.000	0.0022	0.025	0.287	0.685	0.685	0.0	32.5	A
0.000	0.0026	0.043	0.260	0.694	0.699	0.0	47.7	A
0.000	0.0031	0.070	0.229	0.699	0.711	0.0	62.4	A
0.009	0.0017	0.014	0.337	0.638	0.637	18.3	18.1	A
0.019	0.0017	0.029	0.327	0.624	0.621	32.6	32.3	A
0.029	0.0016	0.045	0.312	0.613	0.603	43.8	43.8	A
0.046	0.0021	0.094	0.269	0.589	0.603	49.2	65.7	A
0.041	0.0016	0.063	0.304	0.591	0.582	53.2	52.9	A
0.042	0.0014	0.052	0.344	0.561	0.579	55.8	45.3	B
0.036	0.0011	0.039	0.296	0.629	0.638	59.1	41.7	B
0.049	0.0014	0.067	0.318	0.564	0.558	60.4	53.4	A
0.056	0.0016	0.087	0.304	0.551	0.557	60.9	60.6	A
0.031	0.0007	0.026	0.253	0.691	0.696	65.4	35.6	B
0.072	0.0016	0.115	0.295	0.517	0.535	66.0	67.9	A+C
0.067	0.0015	0.104	0.291	0.536	0.533	66.0	66.0	A
0.074	0.0015	0.114	0.294	0.516	0.531	67.8	68.0	A+C
0.073	0.0014	0.110	0.295	0.520	0.525	69.0	67.0	A+C
0.079	0.0013	0.123	0.246	0.551	0.565	72.7	73.1	C
0.026	0.0003	0.013	0.216	0.745	0.749	77.6	24.1	B
0.088	0.0009	0.137	0.163	0.611	0.622	81.7	82.0	C
0.023	0.0000	0.000	0.188	0.789	0.789	100.0	0.0	B
0.029	0.0000	0.016	0.133	0.823	0.802	100.0	39.5	B
0.038	0.0000	0.035	0.109	0.818	0.805	100.0	63.8	B
0.049	0.0000	0.056	0.082	0.812	0.796	100.0	78.7	B
0.063	0.0000	0.080	0.062	0.795	0.776	100.0	87.5	B
0.079	0.0000	0.107	0.039	0.776	0.736	100.0	93.8	B
0.097	0.0000	0.136	0.039	0.728	0.721	100.0	95.0	B
0.105	0.0000	0.148	0.036	0.711	0.710	100.0	95.7	B+C
0.105	0.0000	0.149	0.036	0.710	0.710	100.0	95.7	B+C
0.105	0.0000	0.150	0.036	0.709	0.709	100.0	95.7	B+C
0.105	0.0000	0.149	0.035	0.711	0.709	100.0	95.7	B+C
0.105	0.0000	0.160	0.000	0.735	0.736	100.0	100.0	C
0.106	0.0000	0.157	0.000	0.737	0.736	100.0	100.0	C

^{a)}The standard uncertainties are: temperature $u(T) = 0.1$ K, mass fraction $u(w) = 0.006$ g/g.

In Table 3, the Pitzer parameters used in the model of this work are summarized. Table 3 includes the parameters $\lambda_{\text{HKGA},\text{H}^+}$ and $\lambda_{\text{HKGA},\text{Cl}^-}$ that were fitted to the experimental data of this work. The values of the activity-based equilibrium constants at 298 K for modeling the SLE in the considered system are summarized in Table 4.

Table 3: Pitzer interaction parameters used in the model of this work. All parameters that are not listed were set to zero.

Parameter	Value	Source
$\beta_{\text{Na}^+, \text{OH}^-}^{(0)}$	0.0864	[21]
$\beta_{\text{Na}^+, \text{Cl}^-}^{(0)}$	0.0765	
$\beta_{\text{H}^+, \text{Cl}^-}^{(0)}$	0.1775	
$\beta_{\text{Na}^+, \text{OH}^-}^{(1)}$	0.253	
$\beta_{\text{Na}^+, \text{Cl}^-}^{(1)}$	0.2664	
$\beta_{\text{H}^+, \text{Cl}^-}^{(1)}$	0.2945	
$C_{\text{Na}^+, \text{OH}^-}^\phi$	0.0044	
$C_{\text{Na}^+, \text{Cl}^-}^\phi$	0.00127	
$C_{\text{H}^+, \text{Cl}^-}^\phi$	0.0008	
$\theta_{\text{H}^+, \text{H}^+}$	0.036	
$\theta_{\text{Cl}^-, \text{Cl}^-}$	-0.05	
$\Psi_{\text{Na}^+, \text{H}^+, \text{Cl}^-}$	-0.004	
$\Psi_{\text{Na}^+, \text{OH}^-, \text{Cl}^-}$	-0.006	
$\lambda_{\text{HKGA}, \text{H}^+}$	0.2	this work
$\lambda_{\text{HKGA}, \text{Cl}^-}$	0.05	

Table 4: Values of the equilibrium constants for the dissociation and solubility at 298 K used in this work.

Equilibrium constant	Value
$K_{\text{HKGA}}^{\text{diss}}$	$2.35 \cdot 10^{-3}$
$K_{\text{H}_2\text{O}}^{\text{diss}}$	$4.57 \cdot 10^{-15}$
$K_{\text{HKGA} \cdot \text{H}_2\text{O}}^{\text{SP}}$	2.58
$K_{\text{NaKGA} \cdot \text{H}_2\text{O}}^{\text{SP}}$	0.33
$K_{\text{NaCl}}^{\text{SP}}$	38.57

The experimental data and the results of the model are represented graphically in Figure 2 in a Jänecke plot, which is a projection of the three-dimensional solid-liquid equilibrium surface along the axis of the water mass fraction. The composition of the liquid phase in equilibrium regarding the solutes (HKGA, NaKGA, HCl, NaCl) in the system is given by the Jänecke indices $J(\text{Na}^+)$ and $J(\text{Cl}^-)$. The water mass fraction in the liquid phase in equilibrium is indicated by the color code in Figure 2. The colored areas indicate the modeled composition of the liquid phase in equilibrium with a single solid phase as labeled within the areas. The solid lines indicate the presence of the two solid phases of the adjacent areas in equilibrium. The modeled SLE surface was obtained from flash-type calculations in which supersaturated mixtures with different values of $J(\text{Na}^+)$ and $J(\text{Cl}^-)$ were considered and the compositions of the resulting liquid phases and the coexisting solid

167 phases in SLE were calculated. The colored circles indicate the composition of the liquid phase of
 168 the experimental samples in SLE. The color code is the same as for the areas. Furthermore, the
 169 results of this work are depicted in four ternary phase diagrams in Figure 3, each panel representing
 170 one of the studied ternary subsystems. The circles and solid lines represent the composition of the
 171 liquid phase in SLE as found experimentally and calculated with the model, respectively.

172

Figure 2: Jänecke plot of the solid-liquid equilibrium in the system HKGA + NaKGA + HCl + NaCl + water. Colored circles: experimentally determined liquid phase composition. Colored areas and black lines: liquid phase composition calculated with the model. Areas indicate the presence of one solid phase in equilibrium as labeled within the areas. Lines indicate the presence of the two solid phases of the adjacent areas in equilibrium. The water mass fraction in the liquid phase found experimentally and calculated with the model is indicated by the color of the symbols and areas, respectively. The dashed lines indicate the composition of all mixtures consisting of HKGA + NaCl + water or NaKGA + HCl + water.

173 In the system HKGA + HCl + water, for which the results are depicted on the lower edge of
 174 Figure 2 and in Figure 3 a), only HKGA · H₂O was observed as solid phase, which is in line with
 175 the expectations. The concentration of HCl used in the experiments was limited due to the degra-
 176 dation of HKGA in very acidic solutions. This is indicated by the light gray area in Figure 3 a),
 177 which was therefore not studied in this work. Also the dark gray area, in which no liquid phase is
 178 expected, was not studied in this work.

Figure 3: Solid-liquid phase diagrams of the ternary subsystems a) HKGA + HCl + water, b) NaKGA + NaCl + water, c) HKGA + NaCl + water, and d) NaKGA + HCl + water at 298 K and ambient pressure. Symbols: experimental liquid phase composition. Solid lines: modeled liquid phase composition. L: unsaturated solution. L+A: SLE, the solid phase is $\text{HKGA} \cdot \text{H}_2\text{O}$. L+B: SLE, the solid phase is $\text{NaKGA} \cdot \text{H}_2\text{O}$. L+C: SLE, the solid phase is NaCl. L+A+B: SLE with two solid phases ($\text{HKGA} \cdot \text{H}_2\text{O}$ and $\text{NaKGA} \cdot \text{H}_2\text{O}$). L+A+C: SLE with two solid phases ($\text{HKGA} \cdot \text{H}_2\text{O}$ and NaCl). L+B+C: SLE with two solid phases ($\text{NaKGA} \cdot \text{H}_2\text{O}$ and NaCl). The shaded areas were not studied in this work.

179 The results for the system NaKGA + NaCl + water are depicted on the upper edge of Figure 2
180 and in Figure 3 b) where a solubility line with one eutonic point was found. The resulting phase
181 diagram consists of four regions: a region in which a homogeneous liquid phase is obtained (L), a
182 region in which saturated solution is in equilibrium with solid $\text{NaKGA} \cdot \text{H}_2\text{O}$ (L+B), a region in
183 which saturated solution is in equilibrium with solid NaCl (L+C), and a region in which saturated
184 solution is in equilibrium with solid $\text{NaKGA} \cdot \text{H}_2\text{O}$ and solid NaCl (L+B+C). The dark gray area,
185 in which only solid phases coexist, was not studied in this work.

186 For the system HKGA + NaCl + water, a phase diagram with one eutonic point was found, which
187 is depicted in Figure 3 c). Besides the region in which a homogeneous liquid phase is obtained (L),
188 three regions with solid phases were found: a region in which saturated solution is in equilibrium
189 with solid $\text{HKGA} \cdot \text{H}_2\text{O}$ (L+A), a region in which saturated solution is in equilibrium with solid
190 NaCl (L+C), and a region in which saturated solution is in equilibrium with solid $\text{HKGA} \cdot \text{H}_2\text{O}$
191 and solid NaCl (L+A+C). Again, the dark gray area, in which only solid phases coexist, was not
192 studied in this work. Since from ternary mixtures consisting of HKGA, NaCl, and water, only

HKGA · H₂O and NaCl precipitate, the composition of the saturated liquid phase in equilibrium is expressible in concentrations of HKGA, NaCl, and water. The experimental results of this work satisfy this condition with excellent agreement since the symbols indicating the liquid phase composition of all samples consisting of HKGA, NaCl, and water in SLE lie on the diagonal connecting the corners of HKGA and NaCl in Figure 2.

When mixing NaKGA, HCl, and water, the model predicts three possible solids: NaKGA · H₂O, HKGA · H₂O, and NaCl, as well as combinations of them. This is shown in Figure 2, in which the diagonal connecting the corners of NaKGA and HCl passes through the regions indicating the presence of these three solids in equilibrium. When considering the respective phase diagram in the ternary projection shown in Figure 3 d), it should be noted that, however, only SLEs with the solid NaKGA · H₂O can be visualized there. The reason for this is as follows: as soon as HKGA · H₂O or NaCl precipitated from a mixture created by mixing NaKGA, HCl, and water, the liquid supernatant has a stoichiometric composition that cannot be obtained anymore by mixing NaKGA, HCl, and water (the composition of the liquid phase is shifted from the diagonal connecting the corners of NaKGA and HCl in Figure 2), and thus cannot be visualized in the ternary diagram of NaKGA, HCl, and water. Therefore, both the shown experimental data and the model results in Figure 3 d) are restricted to SLEs with a solid that is pure NaKGA · H₂O. However, in Figure 2, this system can be studied more comprehensively. Since at high concentrations of NaKGA, only pure NaKGA · H₂O precipitates, the symbols representing the liquid phase composition of the experimental samples in SLE must lie on the diagonal connecting the corners of NaKGA and HCl. This is satisfied for all samples in the region of pure solid NaKGA · H₂O whereas a deviation from the diagonal is observed if HKGA · H₂O is the precipitating species. The experimentally studied concentration range in the system NaKGA + HCl + water was limited due to degradation processes at high concentrations of HCl and the resulting very low pH values, which is indicated by the light gray area in Figure 3 d). Also the dark gray area in Figure 3 d) was not studied in this work since only solid phases are expected in this region.

Overall, excellent agreement of the experimental data and the results of the model for the composition of the liquid phase and the coexisting solid phase in SLE is found for all ternary subsystems, cf. also Table 2.

In Figure 4, experimental results for the solid-liquid equilibrium in the ternary system HKGA + NaKGA + water at 303 K and ambient pressure from a previous work of our group [10] are shown as symbols. In our previous work, a rather simple model based on an extension of the Debye-Hückel theory was used to model the SLE in this system at 303 K and found to yield good results. In Figure 4, the solid line denotes the results from the model of this work, which is based on the Pitzer approach, extrapolated to 303 K. The relevant equilibrium constants for 303 K, i.e. the sol-

228 ubility products of $\text{HKGA} \cdot \text{H}_2\text{O}$ and $\text{NaKGA} \cdot \text{H}_2\text{O}$ and the dissociation constant of HKGA, were
 229 calculated from the solubility of pure HKGA in water and pure NaKGA in water at 303 K and the
 230 results of a study of the pH value in an aqueous solution of known HKGA concentration from the
 231 previous work, respectively. The equilibrium constant for the autoprotolysis of water was taken
 232 from the literature [22]. Again, the model shows an excellent agreement with the experimental
 233 results, although the Pitzer parameters were fitted to experimental data at 298 K. This indicates
 234 that the model can also be extrapolated to other temperatures, at least if they are not too far
 235 away from 298 K.

Figure 4: Solid-liquid phase diagram of the ternary system HKGA + NaKGA + water at 303 K and ambient pressure. Symbols: experimental liquid phase composition [10]. Solid lines: modeled liquid phase composition, this work. L: unsaturated solution. L+A: SLE, the solid phase is $\text{HKGA} \cdot \text{H}_2\text{O}$. L+B: SLE, the solid phase is $\text{NaKGA} \cdot \text{H}_2\text{O}$. L+A+B: SLE with two solid phases ($\text{HKGA} \cdot \text{H}_2\text{O}$ and $\text{NaKGA} \cdot \text{H}_2\text{O}$). The shaded area was not studied in this work.

236 5. Conclusion

237 2-keto-L-gulonic acid (HKGA) is the key intermediate in the L-ascorbic acid process and is
 238 mainly produced by fermentation. Crystallization is a promising method to separate and purify
 239 HKGA from fermentation broths, which are diluted aqueous solutions containing electrolytes. The
 240 presence of electrolytes and the pH value of the solution have a significant influence on the solubility
 241 of HKGA. Furthermore, different crystal species can precipitate from the solution depending on
 242 the composition of the solution, such as sodium-2-keto-L-gulonate monohydrate ($\text{NaKGA} \cdot \text{H}_2\text{O}$) if
 243 sodium ions (Na^+) are present. For the conceptual process design, the solubility of HKGA in such
 244 complex aqueous solutions as well as the crystallizing species in equilibrium have to be known. In
 245 this work, the solid-liquid equilibrium (SLE) in the quinary system 2-keto-L-gulonic acid (HKGA)
 246 + sodium-2-keto-L-gulonate (NaKGA) + hydrochloric acid (HCl) + sodium chloride (NaCl) +

247 water was investigated experimentally at 298 K and ambient pressure. At these conditions, HKGA
248 and NaKGA crystallize exclusively as monohydrates $\text{HKGA} \cdot \text{H}_2\text{O}$ and $\text{NaKGA} \cdot \text{H}_2\text{O}$, respectively,
249 whereas NaCl crystallizes in the pure form. A thermodynamic model of the SLE, which is based
250 on the Pitzer model to calculate the activity coefficients in the liquid phase, was developed and
251 unreported Pitzer parameters for the interaction of undissociated HKGA with hydrogen ions (H^+)
252 and of undissociated HKGA with chloride ions (Cl^-) were fitted to the experimental data. The
253 equilibrium constants were calculated from data reported in the literature for the autoprotolysis of
254 water and the solubility of NaCl and from experimental data from this and an earlier work of our
255 group for the dissociation of HKGA and the solubility of $\text{HKGA} \cdot \text{H}_2\text{O}$ and $\text{NaKGA} \cdot \text{H}_2\text{O}$. The
256 agreement of the model with the experimental data is excellent, both regarding the composition
257 of the liquid phase as well as the coexisting solid phase in equilibrium.

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261 **Declarations of interest**

262 none

263 **Nomenclature**

264 *Symbols*

A	solid HKGA · H ₂ O
a	activity
B	solid NaKGA · H ₂ O
C	solid NaCl
C^ϕ	Pitzer interaction parameter
i	species
J	Jänecke index
K	equilibrium constant
L	liquid phase
M	molar mass / g/mol
m	molality / mol/kg
R	universal gas constant / J/(mol·K)
T	temperature / K
w	mass fraction / g/g

265 *Greek letters*

β	Pitzer interaction parameter
γ	activity coefficient
Δ	difference
θ	Pitzer interaction parameter
λ	Pitzer interaction parameter
Ψ	Pitzer interaction parameter

266 *Sub- and Superscripts*

0	reference
diss	dissociation
i	species
j	equilibrium reaction
SP	solubility product

HKGA	2-keto-L-gulonic acid
KGA ⁻	2-keto-L-gulonate ion
HPLC	high-performance liquid chromatography
IC	ion chromatography
NaKGA	sodium-2-keto-L-gulonate
RI	refractive index
SLE	solid-liquid equilibrium
W	water

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