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An evaluation of primary water standards by TG/DTA and vapor sorption analysis

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Abstract Sodium tartrate dihydrate, lactose monohydrate, potassium citrate monohydrate, and calcium oxalate monohydrate are commonly used as primary standards for methods that determine water content. Identification of the type of water of hydration (channel, lattice, or ion associated) is provided herein for each standard based upon thermogravimetry/differential thermal analysis (TG/DTA) and dynamic vapor sorption data. Sodium tartrate dihydrate was found to be a mixed hydrate, containing 1 mol of channel water and 1 mol of lattice water. Lactose monohydrate and calcium oxalate monohydrate were both determined to contain lattice water of hydration. Potassium citrate was shown to exist as an ion-associated hydrate. Also provided is a discussion of how hydrate type, thermal properties and hygroscopicity may impact suitability of each compound for use as a standard.

Keywords Channel hydrate · Lattice hydrate · Karl Fischer · Water isotherm

Introduction

As early as 1951, sodium tartrate dihydrate was proposed for use as a primary water standard for Karl Fischer (KF) titrations [1]. In this early article, the authors evaluated, but rejected, several other organic hydrates including lactose monohydrate and potassium citrate monohydrate. By 1960, the American Chemical Society Committee on Analytical Regents included sodium tartrate dihydrate within that year's edition of *Regent Chemicals* noting that the material "is suitable for standardization of Karl Fischer reagent as used for the determination of water [2]." Within that same volume, two methods were described for Karl Fischer reagent standardization. Method 1 for Karl Fischer recommended water as the standard, and Method 2 described the use of sodium tartrate dihydrate.

A critical evaluation of the use of sodium tartrate dihydrate as a primary water standard was published in 1972 [3]. Beasley et al. reported occluded water within the dihydrate crystals they studied (as high as 0.3% absolute) based upon microscopic observations and drying results. For that reason the authors concluded that the material should not be used as a primary water standard. This study was refuted in 1976. Bryan and Rao found no evidence of water occlusions and concluded that sodium tartrate dihydrate was a reliable primary standard [4].

May et al. were the first to report the use of sodium tartrate dihydrate as a reference material for moderate drying conditions [5]. In the publications described in the previous paragraph [3, 4], a drying temperature of 150 °C was used to release both waters of hydration contained within the dihydrate. In the May paper, a lower temperature drying condition was employed. Drying at room temperature, over anhydrous pentoxide resulted in removal of only one of the two waters of hydration. This publication may have been the first to recognize that the two waters of hydration within sodium tartrate dihydrate were not equivalent.

Today, use of sodium tartrate dihydrate as a water standard has become such common practice that it is suggested as a "convenient water reference substance" within the water determination monograph of the US Pharmacopeia and referenced for use in the ASTM standard method E 203-01 "Standard Test Method for Water Using Volumetric Karl Fischer Titration" [6]. It is sold by

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several vendors of Karl Fischer instruments as well as by fine chemical vendors as a primary water standard.

Potassium citrate monohydrate, lactose monohydrate, and calcium oxalate monohydrate are also used as primary water standards. Although not as commonly used as sodium tartrate, both lactose monohydrate and potassium citrate are suggested for use as water standards by vendors of KF instruments as well as vendors of fine chemicals. In particular, the potassium citrate monohydrate is often recommended for oven KF standardization rather than for the more traditional, dissolution KF methods. The European Pharmacopeia suggests calcium oxalate for use as a thermogravimetric standard within its “Thermal Analysis” and sells certified material specifically for that use [7].

In this study the waters of hydration of sodium tartrate dihydrate, lactose monohydrate, potassium citrate monohydrate, and calcium oxalate monohydrate were evaluated to better understand the suitability of each of these compounds as a primary water standard. Specifically, thermogravimetric analysis and dynamic water vapor sorption studies were used to identify the type of water of hydration within each compound. Water of hydration may be classified into one of three different designations: isolated lattice, channel, or ion-associated water [8, 9]. Of these, the lattice-isolated water and ion-associated water of hydration are stoichiometric and stable to changes in humidity. Either could be considered a candidate for use as a primary water standard based upon water stability. The water content of a channel hydrate is dependent upon relative humidity and need not be stoichiometric. Consequently, use of this type of a hydrate as a primary water standard minimally may require extra care or could be inappropriate altogether.

Experimental section

Materials

Sodium tartrate dihydrate was purchased from EMD Chemicals as ACS grade material with a label assay of 99.0–101.0%. The label LOD result for the lot used was 15.61–15.71%.

Lactose monohydrate was purchased as an Aquastar water standard from EMD Chemicals. The label water content was indicated as 5.00–5.20%. An additional note on the label indicated that the uncertainty was extended ±0.05% due to the uncertainty associated with the KF measurement method. Potassium citrate monohydrate prepared by Riedel-de Haën was purchased as a Hydranal® “Water standard for KF-Oven 230 °C” from Sigma–Aldrich. The label water content was identified as 5.55% (±0.05%) based upon loss on drying. Calcium oxalate monohydrate reference standard (Batch 1.2) was purchased from the European Pharmacopeia. The certificate of analysis for this batch indicated a certified mass loss of 12.1% with an uncertainty of 0.2%.

Instrumentation

Simultaneous TG and DTA curves were obtained using a Seiko TG-DTA 220. Approximately 8–10 mg samples were run in aluminum sample pans under a dry nitrogen purge of 200 mL/min. Scans were started at 25 °C and continued at 5 °C min^{-1} until an acceptable baseline could be obtained post transition. The TG/DTA was temperature calibrated using certified using tin and gallium standard materials. The balance performance was confirmed using a certified weight set. DTA curves in for study are plotted with endotherms pointing downward. Water isotherms were obtained using a Surface Measurement System’s DVS-1 unit at 25 °C. Thin layers of samples (no more than 12 mg) were cycled from 0% to 90% RH and back to 0% RH at a rate of 5% RH units/h. The RH calibration of the unit was confirmed using the deliquescence points of LiCl, $Mg(NO_3)_2$, and KNO_3. Balance performance was confirmed using a certified weight set.

Results

Evaluation by TG/DTA

Sodium tartrate dihydrate

As shown in Fig. 1, the TG/DTA profile for sodium tartrate dihydrate indicates the presence of two different types of water of hydration. One mole of the water is driven off prior to the sample reaching 100 °C, consistent with the

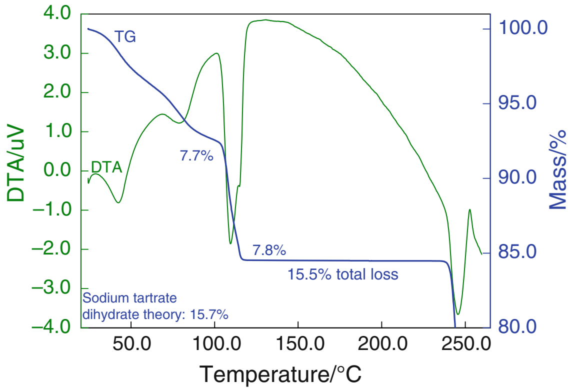

Fig. 1 Simultaneous thermogravimetric analysis and differential thermal analysis curves for sodium tartrate dihydrate showing two distinct hydrate types (endotherms shown pointing *down*)

behavior of channel type water of hydration. The second mole of water is evolved at temperatures above 100 °C as expected for lattice type hydrates. The occurrence of two differing types of hydrates within a single moiety has been described previously in the literature for risedronate sodium hemi-pentahydrate [10, 11]. The TG/DTA curve clearly illustrates the relative mobility for each water type. The initial water loss of the channel type water of hydration is shown as a gradually sloping TG loss curve and shallow, relatively broad DTA endotherm. The water is able to "leak" out of the crystal channels gradually and with a low energy in comparison to the lattice hydrate. Water loss begins almost as soon as heating is initiated. In comparison, the lattice hydrate is dehydrated immediately upon reaching a temperature that presumably corresponds to destruction of the crystal lattice. The mass loss curve shows a sudden sharp step and the DTA shows a corresponding sharp endotherm that is much larger than that observed for loss of the channel water. In short, the TG/DTA curves illustrate how channel water can readily leak out of an intact crystal while lattice water remains in place until an event occurs that destroys the crystal lattice. The total weight loss observed 15.5%, is in agreement with the theory of 15.66% for the dihydrate.

Following the mass loss due to dehydration, the TG baseline is flat until onset of rapid weight loss associated with degradation near 250 °C. The clear separation of the dehydration mass loss and the degradation mass loss make this compound a suitable candidate for water determination by loss on drying or an oven based Karl Fischer system.

Lactose monohydrate

The TG/DTA curves as shown in Fig. 2 are consistent with a lattice hydrate. Little to no water loss is observed below 100 °C. The dehydration loss of 4.9% is in agreement with theory for monohydrate (5.00%). The DTA portion of the thermal curve is consistent with earlier descriptions of differential scanning calorimetry results. A sharp endotherm is observed concurrent with dehydration of the monohydrate. The dehydration endotherm is followed by a smaller endotherm/exotherm that is reported in the literature as due to the melting of a meta-stable anhydrate formed during dehydration and the subsequent exothermal crystallization to a stable anhydrate [12, 13]. The endotherm above 200 °C has been previously assigned to the melt and concurrent degradation of the most stable anhydrous lactose form. Of greater importance to this study is the appearance of the TG portion of the curve. The TG trace indicates little to no water loss prior to 100 °C indicating lattice type water of hydration. Immediately following dehydration of the monohydrate, a gradual mass loss is observed until a more rapid loss is observed concurrent with the final melt and sample degradation. It is generally agreed that the first step in thermal degradation of carbohydrates under dry conditions is the formation of anhydro sugars via loss of water [14]. The proximity of the initial thermal degradation to the monohydrate dehydration would be expected to cause difficulty in using either a loss on drying or an oven-based Karl Fischer system for water determination of this material. At temperature required to remove the lattice water of hydration, chemical dehydration might also be expected to occur.

Potassium citrate monohydrate

The TG/DTA profile for potassium citrate monohydrate consists of a single mass loss and single endotherm related to the dehydration. The observed loss of 5.4% is in agreement with the expected value of 5.55% for monohydrate. As shown in Fig. 3, water loss occurs well above 100 °C, consistent with ion-associated hydrate. No mass

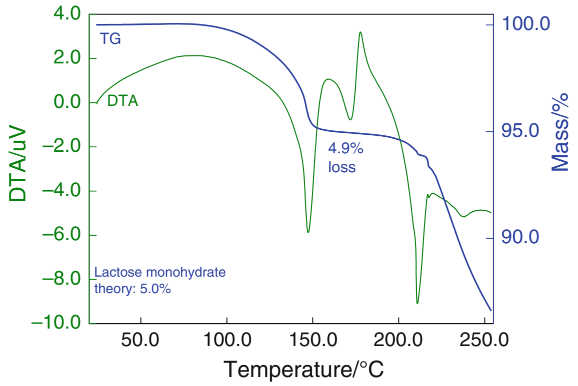

Fig. 2 Simultaneous thermogravimetric analysis and differential thermal analysis curves for lactose monohydrate (endotherms shown pointing *down*)

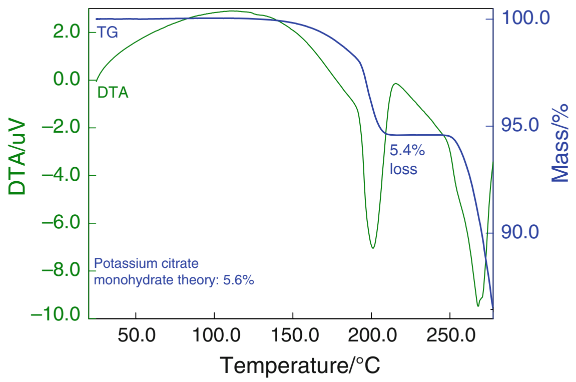

Fig. 3 Simultaneous thermogravimetric analysis and differential thermal analysis curves for potassium citrate monohydrate (endotherms shown pointing *down*)

loss or evidence of water loss is observed at temperatures below 150 °C. Following the dehydration, the TG curve continues to remain flat until the onset of degradative mass loss near 250 °C. There is sufficient separation between the temperature required for dehydration and onset of degradation to enable water determination by heating to selectively remove the water of hydration.

Calcium oxalate monohydrate

Calcium oxalate monohydrate is a material of interest for study as a common component of kidney stones and as the naturally occurring mineral whewelitte. Thermal analytical studies have been reported at least as early as 1947 and it is widely accepted that the material undergoes three separate thermal transitions: dehydration, carbonate formation and lastly, oxide formation [15, 16]. Studies have examined the dehydration kinetics under varying conditions [17, 18]. Based upon these earlier studies, it has been demonstrated repeatedly that the dehydration of calcium oxalate monohydrate occurs as a single, cleanly marked step loss by TG (under a dry purge gas). Dehydration begins above 100 °C, consistent with a lattice type hydrate. As reported in the earlier studies, there is a clear separation between temperature for dehydration and the onset of mass loss due to carbonate formation, hence the selection of this material as reference material for TG.

Shown in Fig. 4 is a TG/DTA profile for the current EP standard. The observed mass loss of 12.1% is in excellent agreement with the label claim of 12.1% but slightly low compared to the 12.33% theory for monohydrate. The cause for this difference is not known but it must be assumed, since this material was obtained from the European Pharmacopeia, that there may be some difficulty in obtaining calcium oxalate monohydrate of sufficient purity for the water content to exactly match theory.

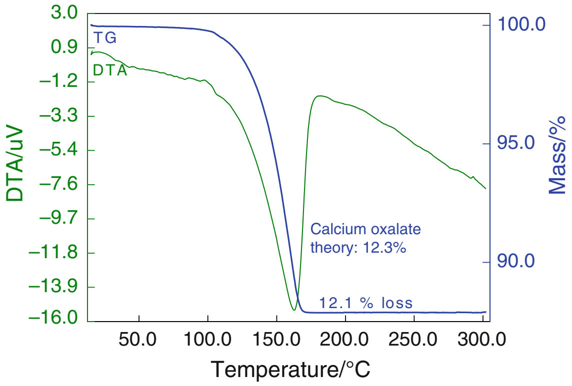

Fig. 4 Simultaneous thermogravimetric analysis and differential thermal analysis curves for calcium oxalate monohydrate (endotherms shown pointing *down*)

Water isotherms

Sodium tartrate dihydrate

The water isotherm for sodium tartrate dihydrate is shown in Fig. 5. As described by May et al., 1 mol of channel type water of hydration is removed at upon desiccation [5]. As expected, the second water of hydration is resistant to dehydration under desiccation. The sorption portion of the curve shows the ease with which the material rehydrates back to the dihydrate. At relative humidities of approximately 1% and higher, the material spontaneously rehydrates. Over a wide relative humidity range (1–90%), at 25 °C, the water content of sodium tartrate dihydrate is stable. Only under desiccating conditions could water mobility become an issue. Should the material inadvertently be desiccated, exposure to moderate humidity would restore the hydration level.

Lactose monohydrate

At 25 °C, over a relative humidity range of 0–90%, no change was observed in the water content for lactose monohydrate. This is in agreement with earlier reports that fully crystalline, α-lactose monohydrate is not hygroscopic, adsorbing as little as 0.02% water by weight up to 80% RH [19]. Based upon the vapor sorption data (Fig. 6), the water content of crystalline lactose monohydrate is expected to remain stable over a wide relative humidity range. Lactose monohydrate containing small impurities of amorphous and/or anhydrous components would not be expected to as stable as pure monohydrate. Both the anhydrate and amorphous forms have been reported to spontaneously pick up water and convert to the stable monohydrate at moderate relative humidities [19–21].

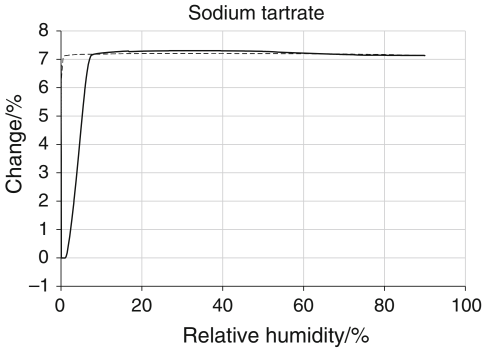

Fig. 5 Water vapor isotherm for sodium tartrate dihydrate with water sorption is shown as a *solid line* and desorption as a *dashed line*

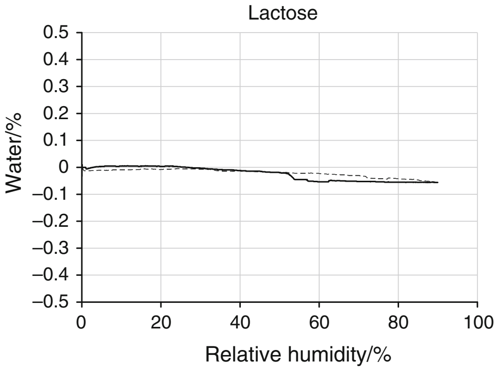

Fig. 6 Water vapor isotherm for lactose monohydrate with sorption is shown as a *solid line* and desorption as a *dashed line*

Potassium citrate monohydrate

As shown in Fig. 7, the water of hydration for potassium citrate monohydrate is stable against desiccation. However, at a relative humidity near 65%, the material deliquesced. This is consistent with a general recognition in the literature that the material is hygroscopic [22]. Significant hysteresis was observed in the isotherm because of the amount of the large water gain upon deliquescence. Evaporation from the deliquesced sample was slow in comparison to the drying ramp. Based upon the vapor sorption data, the water of hydration for potassium citrate is expected to remain constant between 0% and 60% RH. To maintain the water content of this standard material, care would be required to store, handle and weigh potassium citrate monohydrate below 60% RH.

Calcium oxalate monohydrate

As expected for an ion-associated hydrate, no change in water content was observed for calcium oxalate monohydrate upon desiccation (Fig. 8). Upon exposure to higher humidities, no water uptake was observed. The water content of calcium oxalate monohydrate was found to be stable over the entire range of humidity studied (0–90% RH).

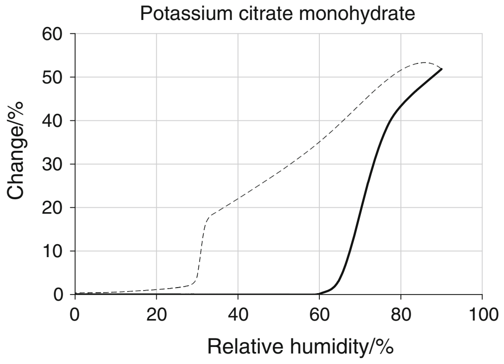

Fig. 7 Water vapor isotherm for potassium citrate monohydrate showing deliquescence occurring above 60% RH

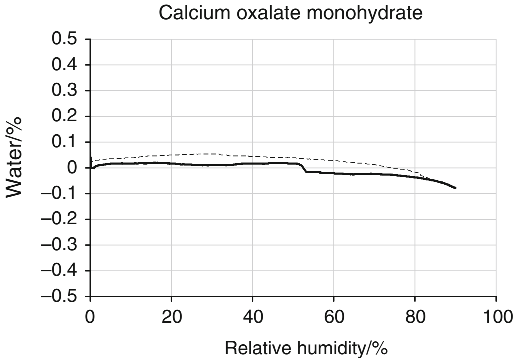

Fig. 8 Water vapor isotherm for calcium oxalate monohydrate with water sorption is shown as a *solid line* and desorption as a *dashed line*

Discussion

Sodium tartrate dihydrate

As shown by both the TG/DTA and vapor sorption results, sodium tartrate dihydrate is a mixed hydrate containing 1 mol of channel water of hydration and 1 mol of lattice water of hydration. The mobility of the channel water of hydration does not pose a concern for use of this material as a primary water standard under routine laboratory use conditions. Inadvertent exposure of the standard material to moderate heat or to desiccation could result in partial dehydration, however, so some care in handling and storage is required for appropriate maintenance of the water content. The separation in temperature between mass losses due to hydrate dehydration and degradative weight loss is sufficient to consider this material appropriate for use in loss on drying or oven-based Karl Fischer methods.

Lactose monohydrate

Lactose monohydrate crystallizes as a lattice type hydrate as evidenced by TG/DTA and vapor sorption data. The water of hydration is stable to RH conditions ranging from desiccation to 90% RH and is stable to moderate heat. Based upon the stability of the water of hydration, this compound would be expected to serve as a very robust primary water standard. Use of lactose monohydrate as a water standard would be best confined to applications that do not require heating to remove the water of hydration. As evidenced by the TGA curve, loss of water due to dehydration is not clearly separated from loss of water due to chemical degradation.

Potassium citrate monohydrate

Based upon by a high dehydration temperature, potassium citrate monohydrate may be classified as an ion-associated hydrate. The water of hydration was stable to desiccation conditions as expected for this type of hydrate. Although the water of hydration was shown to be stable to moderate heat and desiccation, the compound deliquesced at approximately 60% RH. Maintenance of the water of hydration for this standard requires protection from humidity. Handling or storage of this standard material under uncontrolled humidity conditions could result in inadvertent water content changes. Following dehydration, the TG baseline exhibits a flat line that clearly separates the dehydration weight loss from degradative weight loss at higher temperatures and supports the popular use of this material as a standard for oven KF applications.

Calcium oxalate monohydrate

Based upon the well-reported dehydration profile for calcium oxalate monohydrate, the water of hydration can be assigned to lattice type hydration. Additionally, the separation in dehydration temperature from that of the first degradative weight loss is well documented making this compound an excellent candidate for oven KF or loss on drying applications. As expected, the water of hydration was stable to desiccation. No changes in water content were observed for the compound throughout the humidity range studied. The stability of the water of hydration to desiccation, humidity, and to moderate heat indicates that this material may be expected to serve as a particularly robust primary water standard, requiring no special care for storage or handling.

Conclusions

Three different hydration types were observed within the four primary water standard materials studied. Lactose monohydrate and calcium oxalate monohydrate were both determined to be lattice type hydrates and potassium citrate monohydrate, an ion-associated hydrate. Sodium tartrate dihydrate was found to be a mixed hydrate system containing one channel type and one lattice type water of hydration.

Based upon the hydrate assignment, thermal properties and hygroscopicity the following materials were determined appropriate for use as primary water standards in methods that require either room temperature or elevated temperature extraction of water. Lactose monohydrate would be most appropriately used only in room temperature applications.

Of the four materials studied, only two require special care in handling or storage. Sodium tartrate dihydrate should be protected from desiccation and potassium citrate monohydrate from relative humidities of 60% or higher to maintain constant water content.

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