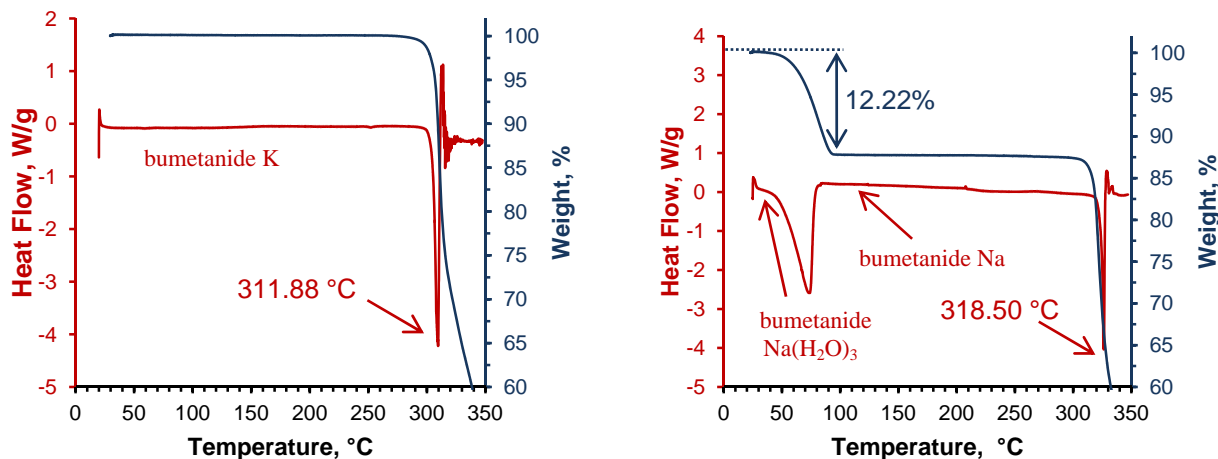
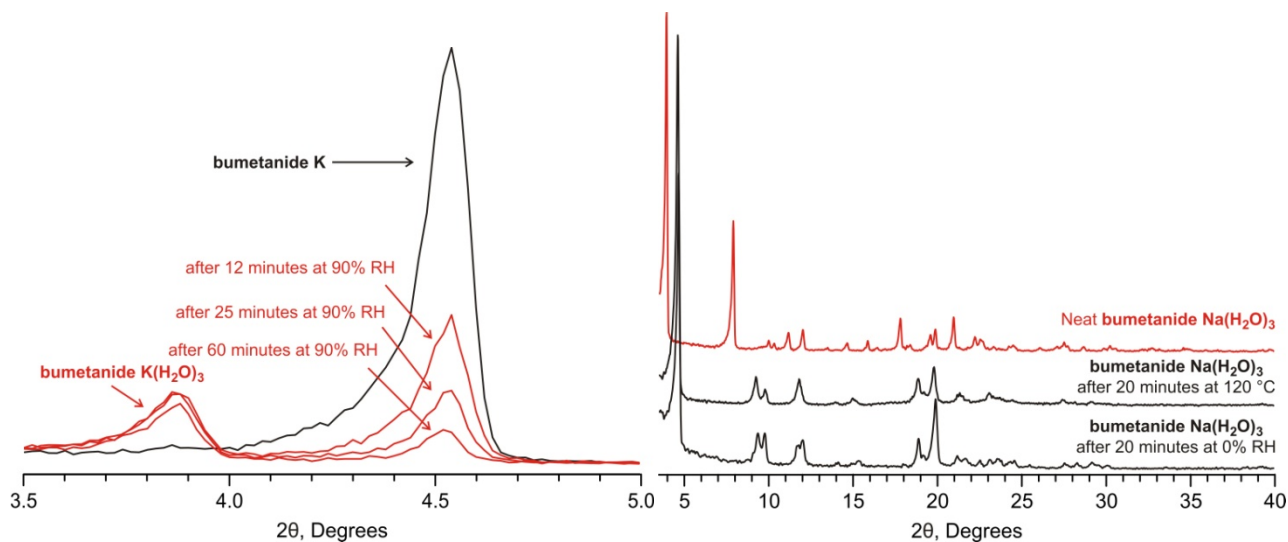


## Sodium and potassium salts of bumetanide trihydrate: Impact of counterion on structure, aqueous solubility and dehydration kinetics

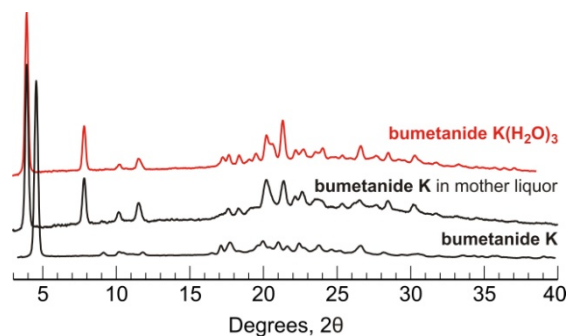
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**Fig. S1** Left: DSC and TGA thermograms of **bumetanide K** are featureless prior to melt-decomposition at 300 °C. Right: TGA thermogram of **bumetanide Na(H<sub>2</sub>O)<sub>3</sub>** showed a 12.2% mass loss due to dehydration to produce **bumetanide Na**, which melted and decomposed at >300 °C. The DSC thermogram of **bumetanide Na(H<sub>2</sub>O)<sub>3</sub>** was recorded using a pinhole pan.



**Fig. S2** PXRD patterns of **bumetanide K** and **bumetanide Na(H<sub>2</sub>O)<sub>3</sub>** following exposure to extreme humidity conditions (i.e., 90% RH or <10% RH) and elevated temperature. Left: exposure of **bumetanide K** to 90% RH resulted in the disappearance of the reflection at 4.5 degrees at the expense of the emerging reflection at 3.9 degrees, which corresponds to **bumetanide K(H<sub>2</sub>O)<sub>3</sub>**. Prolonged exposure at 90% RH to achieve quantitative conversion was not attempted due to moisture build-up in the equipment. Right: **bumetanide Na** was produced after exposure of **bumetanide Na(H<sub>2</sub>O)<sub>3</sub>** to 120 °C or 0% RH for 20 minutes.



**Fig. S3** PXRD pattern of neat **bumetanide K** (bottom) and its suspension in mother liquor (middle). PXRD of suspension was acquired within a minute after **bumetanide K** was suspended in the mother liquor. PXRD of **bumetanide K(H<sub>2</sub>O)<sub>3</sub>** (top), which was recorded from freshly harvested crystals grown in H<sub>2</sub>O, is shown for comparison.

**Table S1** Solubility of bumetanide salts starting from **bumetanide K** and **bumetanide Na(H<sub>2</sub>O)<sub>3</sub>** at various pH values. Hydrochloric acid was used to acidify the suspensions. To raise alkalinity, sodium hydroxide was used for **bumetanide Na(H<sub>2</sub>O)<sub>3</sub>**, while potassium hydroxide was used for **bumetanide K**. Solubility values are reported as the free-acid equivalent.

<b>bumetanide K</b>		<b>bumetanide Na(H<sub>2</sub>O)<sub>3</sub></b>	
pH	Concentration (mg mL <sup>-1</sup> )	pH	Concentration (mg mL <sup>-1</sup> )
1.62	0.00016	2.42	0.00014
2.77	0.0017	2.52	0.0012
5.71	0.55	3.13	0.0018
6.27	2.0	5.64	0.46
6.87	7.7	6.38	2.4
7.96	27	6.46	3.0
8.19	27	6.55	5.3
9.69	27	8.33	5.6
9.90	26	8.48	5.5
10.6	28	10.4	6.2