

# **Urolithiasis/Endourology**

**JU Insight** 

# Alkaline Water: Help or Hype for Uric Acid and Cystine Urolithiasis?

Paul Piedras, Andrei D. Cumpanas, Amanda McCormac, et al.

Corresponding Author: Roshan M. Patel (<u>roshanmp@hs.uci.edu</u>). Full-length article available at https://doi.org/10.1097/JU.000000000003767.

Study Need and Importance: Urinary alkalization is a cornerstone in the medical management of patients with low urine pH, usually associated with uric acid or cysteine stones. Given the poor adherence to the mainstay therapy (ie, potassium citrate) finding a more practical, cost-effective therapeutic measure that facilitates an increase in urine pH would be beneficial. We sought to evaluate the impact of alkaline water and 49 other beverages and supplements to evaluate their alkali/citrate content and hence their potential to increase urine pH. Five different brands of "high pH and low mineral" bottled alkaline water were tested at Litholink to determine the electrolyte and alkali content. Additionally, a comprehensive review was done to detail the alkali, sodium, and caloric content of other over-the-counter beverages and supplements. The cost for supplying the daily recommended amount of alkali per month was determined for all studied and reviewed substances, and a handout was created to facilitate distribution of this information in an office setting (Figure).

What We Found: High-pH, low-mineral alkaline water was found to contain less than 1 mEq/L of alkali. Alternatively, we have identified 11 specific beverages or supplements with significantly higher alkali content, among which the most cost-effective would be baking soda. These options are capable of meeting the daily alkali intake recommendations set by the AUA and the

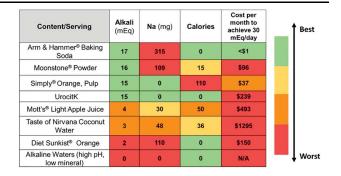


Figure. A preview of the comprehensive Figure in the article that contains organic, diet, and stone prevention supplements/ beverages and their respective alkali content, sodium content, calories, and cost per serving size.

European Association of Urology when consumed in 2 to 3 servings.

**Limitations:** This study is not without limitations as alkaline water was only tested in a laboratory via biochemical analysis and not in human subjects.

**Interpretation for Patient Care**: The handout that was created is intended not only for health care providers, but also for patients. Our aim is to educate the public regarding the optimal beverage and supplement choices that may help increase urine pH and enhance the overall adherence to a therapeutic regimen for patients with uric acid and cystine urolithiasis.

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# Alkaline Water: Help or Hype for Uric Acid and Cystine Urolithiasis?

Paul Piedras,<sup>1</sup> Andrei D. Cumpanas,<sup>1</sup> Amanda McCormac,<sup>1</sup> Seyed Amiryaghoub M. Lavasani,<sup>1</sup> Antonio R. H. Gorgen,<sup>1</sup> Allen Rojhani,<sup>1</sup> Minh-Chau Vu,<sup>1</sup> Rohit Bhatt,<sup>1</sup> John Asplin,<sup>2</sup> Zachary E. Tano,<sup>1</sup> Jaime Landman,<sup>1</sup> Ralph V. Clayman,<sup>1</sup> and Roshan M. Patel<sup>1</sup>

<sup>1</sup>Department of Urology, University of California, Irvine, Orange, California <sup>2</sup>Litholink Corporation, Labcorp, Ithasca, Illinois

**Purpose:** The consumption of alkaline water, water with an average pH of 8 to 10, has been steadily increasing globally as proponents claim it to be a healthier alternative to regular water. Urinary alkalinization therapy is frequently prescribed in patients with uric acid and cystine urolithiasis, and as such we analyzed commercially available alkaline waters to assess their potential to increase urinary pH.

**Materials and Methods:** Five commercially available alkaline water brands (Essentia, Smart Water Alkaline, Great Value Hydrate Alkaline Water, Body Armor SportWater, and Perfect Hydration) underwent anion chromatography and direct chemical measurements to determine the mineral contents of each product. The alkaline content of each bottle of water was then compared to that of potassium citrate (the gold standard for urinary alkalinization) as well as to other beverages and supplements used to augment urinary citrate and/or the urine pH.

**Results:** The pH levels of the bottled alkaline water ranged from 9.69 to 10.15. Electrolyte content was minimal, and the physiologic alkali content was below 1 mEq/L for all brands of alkaline water. The alkali content of alkaline water is minimal when compared to common stone treatment alternatives such as potassium citrate. In addition, several organic beverages, synthetic beverages, and other supplements contain more alkali content than alkaline water, and can achieve the AUA and European Association of Urology alkali recommendation of 30 to 60 mEq per day with  $\leq$  3 servings/d.

**Conclusions**: Commercially available alkaline water has negligible alkali content and thus provides no added benefit over tap water for patients with uric acid and cystine urolithiasis.

Key Words: urolithiasis, uric acid stones, alkalization, complimentary therapies

ALKALINE water is an electrolyzed, mineral-filled water that can be found naturally in springs where water passage over rocks results in the dissolution of minerals and an increase in alkalinity. This natural process is intricate and costly thereby precluding commercial production. As such, manufacturers have transitioned to using electrolysis to alkalinize water, a mechanism through which ionizers use electricity to separate acidic and alkaline substitutes from pure water. Upon the decomposition of pure water, hydrogen and oxygen gas are formed on the cathode side and anode side, respectively.<sup>1</sup> The cathode and anode compartments are separated by an impermeable membrane that prevents the mixing of the hydroxide ions on the cathode side and Submitted August 2, 2023; accepted October 20, 2023; published January 9, 2024.

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Ethics Statement: This research adhered to the ethical guidelines and regulation despite not involving human subjects or animals. The study solely focused on data analysis and did not involve any direct interaction with a living organism. In lieu of a formal ethics committee, the principles of the Helsinki Declaration were followed.

Author Contributions: P.P., A.D.C., J.A., R.V.C., and R.M.P. conceived the project, P.P., A.D.C., J.A., J.L., R.V.C., and R.M.P. were involved in editing the manuscript. A.M., S.A.M.L., A.R.H.G., A.R., M.V., and R.B. compiled and extracted the data and were involved in drafting the manuscript. Z.E.T., J.A., and R.M.P. were involved in reviewing the data for accuracy. All authors were involved in the writing, editing, and approval of the final manuscript.

\*Co-first authors.

Corresponding Author: Roshan M. Patel, MD, Department of Urology, University of California, Irvine, 3800 Chapman Ave, Suite 7200, Orange, CA 92868 (<u>roshanmp@hs.uci.edu</u>).

Editor's Note: This article is the fourth of 5 published in this issue for which Category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 337 and 338.

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**Table 1.** Summary of Ingredient Lists of 5 Brands of BottledAlkaline Water

Brand	Summary of ingredient lists
Essentia	NaHCO <sub>3</sub> , K <sub>2</sub> HPO <sub>4</sub> , MgSO <sub>4</sub> , and CaCl <sub>2</sub>
Smart Water Alkaline	KHCO <sub>3</sub> , CaCl <sub>2</sub> , and MgCl <sub>2</sub>
Great Value	K <sub>2</sub> CO <sub>3</sub> , KHCO <sub>3</sub> , MgSO <sub>4</sub> , and Na
Body Armor SportWater	KHCO <sub>3</sub> , CaCl <sub>2</sub> , and MgCl
Perfect Hydration	K <sub>2</sub> CO <sub>3</sub> , KHCO <sub>3</sub> , and MgSO <sub>4</sub>

the hydrogen ions from the anode side, allowing for the isolation of water with a pH between 8 and  $10.^2$ 

High pH water, also referred to as alkaline water, consumption has risen an average of 12.2% a year globally since 2013; consumption is expected to increase from 635 million L in 2018 to 2.2 billion L by 2023.<sup>3</sup> Its rise in popularity can be attributed to multiple research studies reporting potential advantages associated with the intake of alkaline water. In murine models, these benefits encompass heightened antioxidant response, elevated telomerase activity, elongated telomere length, and a reduction in the number of reactive oxygen species.<sup>4</sup> Regardless, the exploration of alkaline water's effects on human subjects remains limited, with only a handful of studies conducted. Notably, some of these studies have suggested improved hydration, an increase in postexercise urine pH and increase in urine pH with high mineral alkaline water.<sup>5,6</sup> As a result of these studies many companies and online platforms have capitalized on marketing all forms of alkaline water (eg, commercially produced as well as true mineral water) as having the ability to raise urine pH.<sup>7,8</sup> To the best of our knowledge, no study has previously evaluated the potential use of commercially produced alkaline water for alkalinizing the urine pH to benefit uric acid and cystine urolithiasis.

The formation of stones in urolithiasis patients can be heavily influenced by changes in urinary pH. Uric acid stones invariably require a pH below 6 in order to form, whereas cystine stones double in solubility as the urine becomes more alkaline.<sup>9</sup> Potassium citrate is most often prescribed to patients with uric acid and cystine stone urolithiasis to raise the urine pH.<sup>10</sup> Due to the frequency of administration, number and size of tablets, cost and side effects, adherence to potassium citrate tablet therapy is challenging for many patients.<sup>11</sup> Finding a more practical, cost-effective approach toward therapeutic measures that can both facilitate an increase in urine pH while increasing fluid intake is of great interest.

Accordingly, we sought to evaluate the potential impact of 5 commercially available alkaline waters to provide alkali content and potentially alkalinize the urine pH. The alkali content of these 5 commercially available alkaline waters was then contrasted with the alkali content of previously studied beverages and supplements.

#### **METHODS**

Five brands of bottled alkaline water were tested at Litholink/Labcorp in Itasca, Illinois: Essentia, Smart Water Alkaline, Great Value Hydrate Alkaline Water, Body Armor SportWater, and Perfect Hydration (Table 1). One bottle from each brand of bottled alkaline water underwent testing twice over the span of a week to determine the physiologic alkali content. The pH of each beverage was measured using a pH electrode. Citrate and bicarbonate were measured using ion chromatography (Table 2).

In addition, using the PubMed and Scopus databases, a comprehensive review of the literature was performed using the following keywords and phrases: "citrus fruit juice," "orange juice," "lemonade," "sodas," "diet sodas," "sport drinks," "coconut water," "nephrolithiasis," "kidney stones," "urolithiasis," "supplements," and "over-the-counter therapies" in order to review the previously determined alkali content of various beverages and supplements promoted for reducing the risk of lithogenesis (Supplementary Appendix A, https:// www.jurology.com). The alkali content of these beverages and supplements was previously reported by outside literature using similar laboratory techniques (ie, ion chromatography and direct chemical measurements). As such, these values were compared to the tested samples of bottled alkaline water. The cost of beverages, serving size, sodium load, and caloric intake values for each drink were acquired through each manufacture's website and according to each respective nutrition label. For those beverages where the price was not listed on the manufacture's website, prices were obtained through retail websites such as Walmart and Target. Since the price of products can differ based on geographical location, this investigation lists prices specifically for Orange, California. Costs were reported in US dollars with an index to March 2023. These determined market prices were interpolated to calculate the cost to achieve 30 mEq daily per month.

To account for the different factors within these beverages that have an impact on stone formation, a visual guide, in the form of a heat map, was created (Figure and Supplementary Appendix B, <u>https://www.jurology.com</u>). The color code used (green, yellow, orange, and red) comprises 4 distinct groups, based on their beneficial role on

 Table 2. The pH and Organic Anions in 5 Brands of Bottled Alkaline Water

	Essentia	Smart Water	Great Value	Body Armor	Perfect Hydration
pН	9.85	9.69	9.98	10.15	9.87
Citrate (µM)	<4	<4	<4	6	<4
HCO <sub>3</sub> (mM)	<1	<1	<1	<1	<1

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**B-Sodas** 

#### **A-Organic Beverages**

Content/Serving	Alkali (mEq)	Na (mg)	Calories	Cost per month to achieve 30 mEq/day
1. Simply <sup>®</sup> Orange, Pulp <sup>1</sup>	15	0	110	\$37
2. Tropicana® 50 OJ, Some Pulp <sup>1</sup>	14	10	50	\$34
3. Tropicana® OJ, No Pulp1	13	0	110	\$44
4. Trop50 <sup>®</sup> OJ, No Pulp <sup>1</sup>	13	10	50	\$44
6. Kroger <sup>®</sup> Low Cal OJ <sup>1</sup>	11	5	60	\$43
7. Simply <sup>®</sup> Grapefruit Juice <sup>2</sup>	9	10	100	\$59
8. Mott's <sup>®</sup> Apple Juice*	5	30	120	\$78
9. Lakewood <sup>®</sup> Pure Cranberry Juice <sup>2</sup>	4	15	120	\$720
10. Mott's <sup>®</sup> Light Apple Juice	4	30	50	\$493
11. Taste of Nirvana Coconut Water <sup>3</sup>	3	48	36	\$1295
12. Welch's <sup>©</sup> White Grape Juice'	2	15	140	\$207
13. MinMaid <sup>®</sup> Lite Lemonade <sup>4</sup>	2	15	0	\$191
14. MinMaid® Lemonade4	1	35	140	\$135
15.Ocean Spray <sup>®</sup> Cranberry Juice Cocktail <sup>2</sup>	1	5	110	\$260
16. GTS Gingerade <sup>®</sup> Kombucha	<1	10	50	\$2532
17.Braggs <sup>®</sup> Apple Cider Vinegar <sup>2</sup>	<1 °	0 °	0 °	\$4161°
17. Alkaline Waters (high pH, low mineral)*	<1	0	0	N/A

#### **C-Synthetic Beverages**

Content/Serving	Alkali (mEq)	Na (mg)	Calories	Cost per month to achieve 30 mEq/day
1. Crystal Light Lemonade On the Go <sup>1</sup>	8‡	75‡	10‡	\$62 ‡
2. Shaklee Performance <sup>®</sup> Lime <sup>5</sup>	5	130	100	\$212
<ol> <li>Crystal Light Orange On the Go<sup>1</sup></li> </ol>	2‡	0‡	5‡	\$273 <b>‡</b>
4. Gatorade <sup>®</sup> Lime*	2	107	53	\$205
5. Gatorade® Orange*	1	107	53	\$288

Standard serving = 8 oz cup = 240 mL

• serving = 1 Tablespoon

**‡ serving** = 16 oz = 480 mL

∆ serving = tablet/capsule

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* = Original Data
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Content/Serving	Alkali (mEq)	Na (mg)	Calories	Cost per month to achieve 30 mEq/day
1.Diet Sunkist <sup>®</sup> Orange <sup>6</sup>	2	110	0	\$150
2. Diet 7 Up®6	2	45	0	\$148
3. Diet Canada Dry <sup>®8</sup>	2	120	0	\$158
4. Sierra Mist <sup>®</sup> Free <sup>6</sup>	<2	35	0	\$659
5. Sprite <sup>®</sup> Zero <sup>s</sup>	<2	35	0	\$194
6. Diet Orange Crush®s	<2	75	0	\$230
7. Fresca <sup>®6</sup>	<2	50	0	\$227
8. Diet Mt Dew <sup>®6</sup>	<2	70	0	\$270
9. Fanta <sup>®</sup> Orange Zero <sup>6</sup>	1	35	0	\$416
10. Diet Squirt <sup>®6</sup>	<1	55	0	\$416
11. Diet Mug <sup>®</sup> Root Beer <sup>6</sup>	<1	65	0	\$716
13. Diet Pepsi <sup>®</sup> No Caffeine <sup>s</sup>	<1	35	0	\$15,406
14. Coke® Zero <sup>6</sup>	<1	40	0	\$15,406

#### **D-Over-the-Counter and Medical Food Supplements**

Content/Serving	Alkali (mEq)	Na (mg)	Calories	Cost per month to achieve 30 mEq/day
1. Arm & Hammer® Baking Soda*	17 †	315 †	0†	< \$1 †
2. Moonstone <sup>®</sup> Powder <sup>7</sup>	16‡	109 ‡	15‡	\$96‡
3. UrocitK*	15 <b>Δ</b>	0Δ	0Δ	\$239 <b>A</b>
4. KSP tabs™7	14 ‡	224 ‡	10‡	\$57 <b>‡</b>
5. NOW <sup>®</sup> Potassium Citrate <sup>7</sup>	12	1.0	0	\$5
6. LithoBalance <sup>™ 2,7</sup>	12	15	4	\$43
7. KSP <sup>™</sup> Very Berry Tablets <sup>2</sup>	9	219	10	\$60
8. KSP™ Key Lime tablets <sup>2</sup>	9	223	10	\$62
9. TheraLith XR <sup>® 7</sup>	7Δ	4 Δ	0Δ	<b>\$51</b> Δ
10. Litholyte <sup>®</sup> Powder <sup>7</sup>	7‡	67 ‡	0‡	\$68‡
11. Litholyte <sup>®</sup> Coffee7	6	28	0	\$146
12. Kidney COP <sup>® 7</sup>	3 Δ	<1 <b>Δ</b>	0 Δ	\$116 ∆
13. Horbäach® Potassium Citrate <sup>7</sup>	2 🛆	<1 <b>Δ</b>	0 Δ	\$205 ∆
14. Stone Breaker <sup>2</sup>	0	0	0	N/A

Figure. A list of organic, diet, sports, and stone prevention supplements/beverages and their respective alkali content, sodium content, calories, and cost per serving size. This table can be downloaded as a patient handout via the QR code.

lithogenesis prophylaxis (scaling from high to low/green to red). Servings required per day was based on the number of servings needed to achieve the 30 mEq/day minimum as recommended by the AUA and the European Association of Urology (EAU): green = 2 to 3 servings per day, yellow = 4to 6 servings per day, orange = 7 to 10 servings, and red => 10 servings per day. Sodium (Na) load values per serving were separated by determining the following quartile ranges: green = fourth quartile (<10 mg), yellow = third quartile (10-35 mg), orange = second quartile (35-65 mg), and red = first quartile (>66 mg). The caloric intake per serving in each group were divided as follows: green = 0 cal, yellow = < 50 cal, orange = 50 to 100 cal, and red = > 100 cal. Costs were then color coded to highlight the least expensive to the most expensive options available: green (<\$1), yellow (<\$10), orange (<\$100), and red (>\$100).

#### RESULTS

The pH of the 5 brands of alkaline water all had a similar pH in a narrow range around 10 (Table 2) with Body Armor SportWater having the highest pH (10.15) and Smart Water Alkaline having the lowest pH (9.69). Ingredient lists of each alkaline bottled water are displayed in Table 1. No organic anions that could be metabolized to alkali were identified in the alkaline water other than a small amount of citrate in Body Armor alkaline water. This result was unexpected given the bottle did not list citrate as an ingredient. Nonetheless, the physiological alkali content in all brands remained below 1. It is worth noting that although stated on the ingredient labels for 4 out

Worst

Best



<sup>†</sup> serving = ¼ Teaspoon

the 5 brands of alkaline water, none of the waters tested above the detection threshold for citrate.

Several of the reviewed alternative beverages and supplements did contain the AUA and EAU recommended daily alkali content of 30 to 60 mEq in 2 to 3 servings (highlighted in green in the Figure) with the synthetic supplement sodium bicarbonate (ie, household baking soda) having the highest amount of potential alkali of 17.4 mEq per serving; however, it also had the highest sodium content at 400 mg per serving. Welch's white grape juice and MinMaid Lite Lemonade were found to have the most calories at 140 calories per serving. UrocitK, the most commonly prescribed urolithiasis medication, had the highest cost, \$3.93 per serving. A list of all beverages and a summary of their alkali content, sodium load, caloric intake, and cost per serving are presented in the Figure.

#### DISCUSSION

With an unmodifiable genome and resultant metabolic alterations, targeting the dietary aspect of lithogenesis has become an important part of the complex management of stone disease.<sup>10,12</sup> An adequate fluid intake that promotes production of at least 2.5 L/d of urine, an increased intake of fruits and vegetables with a limited intake of nondairy animal protein, a normal calcium diet (ie, 1-1.3 g/d) and a low salt diet (ie, 2-3 g/d) are several of the dietary recommendations included in the AUA and/ or the EAU guidelines.<sup>9,13</sup> Furthermore, Betz and Penniston go into detail about the various classifications of food and their influence on potential renal acid load and net acid production among individuals with urolithiasis.<sup>14</sup> This study along with others regarding diet holds significance for uric acid and cystine urolithiasis as it can provide valuable insights into raising urine pH levels mitigating stone formation risks through diet.<sup>14,15</sup> More commonly, potassium citrate has become widely prescribed due to its ability to alkalinize the urine.<sup>12</sup> Unfortunately. the cumbersome thrice daily treatment regimen, large tablets, gastrointestinal side effects, and cost has led to a long-term adherence rate as low as 61%.4,11

It is easy to understand that the lay stone-forming public might surmise that drinking an alkaline fluid, with a pH around 10, would cause urinary alkalinization; however, pH of the beverage is only one of the determinants of the physiologic alkali load. At a pH of 10, water will have a hydroxyl (alkali) concentration of 0.1 mEq/L, trivial as compared to the typical daily metabolic acid production of humans, which is in the range of 40 to 100 mEq/d.<sup>14,16</sup> In order to provide a clinically significant alkali load, a beverage or food must contain organic anions that create alkali when metabolized.<sup>16,17</sup> The alkaline waters we tested had trace amount of minerals and organic anions, thus the alkali load is limited to that provided as hydroxyl ions. Although alkaline water contains little alkali content, it may exhibit a more pleasant taste in comparison to other types of water. Platikanov et al have demonstrated that water with a moderate level of dissolved solids and a higher pH was perceived as more favorable by participants when compared to tap water.<sup>18</sup> As such, while there seems to be no discernible advantage in terms of increasing alkali content for uric acid or cystine stone formers from consuming relatively expensive alkaline water vs regular spring water, one might argue that the increased palatability of alkaline waters leads to an increased fluid intake, which has been proven advantageous for those at risk of developing kidney stones.<sup>9,13</sup> This is, however, beyond the scope of the present study.

If alkaline water is of little benefit regarding increasing the urine pH, is there a viable alternative to potassium citrate tablets? Citrus fruit juices are an effective and cost-efficient alternative to potassium citrate, as they not only provide sufficient alkali, but also increase fluid intake.<sup>19</sup> Specifically, orange juice consumption is associated with significant increases in urine citrate and pH.<sup>20,21</sup> Indeed, prior studies have shown that among tested organic beverages, the alkali content is highest in orange juice (Figure). Odvina previously demonstrated that although lemonade may be similar in terms of citric acid content, only orange juice ingestion results in significant urine alkalinization.<sup>21</sup> Citrate in its protonated form of citric acid, as it exists in lemonade, does not exert the alkalinizing effect on the serum pH and as such, its effect on the proximal convoluted tubule sodium-citrate cotransporter and urine alkalinization is minimal.<sup>10,19</sup> It is important to note that many of the organic beverages reported in the Figure have a high caloric load and hence the recommendation for diet orange juice.<sup>20</sup>

With sales of \$166 billion in 2022, energy and sport drinks are among the most popular beverages consumed. Goodman et al evaluated the impact of 2 sport drinks, Performance and Gatorade on a group of 9 healthy subjects (Figure).<sup>22</sup> They found that while both energy drinks increase the urinary pH, the change was only statistically significant in the Performance group; however, the study group consisted of only 16 participants none of whom ever had urolithiasis.<sup>22</sup> As such, Performance is far from being an ideal drink for treating uric acid or cystine nephrolithiasis, especially given its high salt (ie, 130 mg sodium per serving) and calorie (ie, 100 cal per serving) load.<sup>22</sup>

Coconut water has been shown to inhibit crystal deposition in the renal tissue of rats pretreated with ethylene glycol mixed water to promote crystal formation.<sup>23</sup> Saat et al showed that consuming coconut water was more readily achieved in high quantities as opposed to water or energy drinks for after-exercise rehydration.<sup>24</sup> These combined findings

made coconut water a tempting supplement to consider for nephrogenesis prophylaxis. In an earlier study at our institution, coconut water consumption among nonstone-forming adults had no alkalinizing effect on the urine (Figure).<sup>25</sup> To date, no study on the effects of coconut water consumption on urolithiasis patients has been reported.

Lastly, there are recent developments in the area of over-the-counter alkali solutions. These synthetic powders usually include a combination of different alkali salts that are meant to dissolve in water for subsequent consumption as a beverage. Laboratory analysis in previous papers demonstrated moderate to high amounts of alkali content for multiple overthe-counter supplements including KSP tabs and Litho Balance (Figure).<sup>26-28</sup>

Of particular interest as a potential alkali solution is the common household item, baking soda (ie, sodium bicarbonate). Laboratory tests performed at Litholink/ LabCorp showed that a quarter teaspoon (315 mg) of baking soda provides the highest mean alkali load of 17.4 mEq (Figure). At the same time, while the alkali content of sodium bicarbonate shows great potential for urinary alkalinization, the associated sodium load raises concern (Figure). Over-the-counter supplements containing a high sodium load, may not only cause an increase in calcium excretion but also a decrease in urinary citrate, thus potentially promoting lithogenesis.<sup>26</sup> Contrary to the foregoing hypothetical concerns, Pinheiro et al reported that consumption of sodium bicarbonate did not increase calcium levels in the urine while providing for significant urinary alkalinization.<sup>29</sup> Of note, a full teaspoon of baking soda has 1.259 g sodium; as such, the commonly recommended regimen of one-quarter teaspoon in the morning and one-half teaspoon in the evening

would add just under 1 g salt to an individual's daily diet. While it is widely accepted that a low sodium diet is an intake of less than 2.0 g per day, according to the Figure, patients may be able to potentially manage a 30 mEq alkali intake of sodium bicarbonate (630 mg sodium) for treatment of urine alkalinization without potential ill effects.<sup>30</sup>

The present study is not without limitations. Specifically, the bottled alkaline waters herein reviewed via biochemical analysis, may produce dissimilar effects when administered to uric acid or cystine stoneforming patients. Clearly this would require a focused clinical study to discern. Also of note, the charted values need to be taken with "a grain of salt" as they are largely based on bench top laboratory analysis of the listed supplements and beverages. Lastly, even in the case of a clinical setting, observations on the tested supplements were based on a healthy patient cohort rather than on documented uric acid or cystine stone-forming individuals.

#### CONCLUSIONS

All 5 analyzed samples of commercially available alkaline water provided scant alkali. Given this finding, alkaline water should have a negligible effect on urinary pH and on urinary citrate levels. Additionally, among a broad range of alkali-containing beverages and supplements, sodium bicarbonate was found to provide the highest amount of alkali at the lowest cost, albeit with a mild increase in dietary sodium load.

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### REFERENCES

- Kurniawan E. Development of electrolysis process and designing the instrument with energy source of solar cell module for the production of alkaline and acidic waters. *ECS Meeting Abstracts*. 2021;MA2021-01(45):1811.
- Navarro RM, Guil-Lopez R, Fierro JLG. Introduction to hydrogen production. *Compendium of Hydrogen Energy*. 2015;1:21-61.
- Global alkaline water market to treble by 2023. Zenith Global. September 17, 2019. Accessed July 11, 2022. <u>https://www.zenithglobal.com/news/</u> global-alkaline-water-market-to-treble-by-2023-1
- Logozzi M, Mizzoni D, Di Raimo R, et al. In vivo antiaging effects of alkaline water supplementation. *J Enzyme Inhib Med Chem.* 2020;35(1):657-664.
- Chycki J, Zając T, Maszczyk A, Kurylas A. The effect of mineral-based alkaline water on hydration status

and the metabolic response to short-term anaerobic exercise. *Biol Sport.* 2017;34(3):255-261.

- Zhang G, Deng T, Deng R, Sun X, He Y, Liu Z. Baseline urine pH is related to effective urine alkalization by short-term alkaline water supplementation: data from a self-controlled study in healthy Chinese volunteers following a systematic review and meta-analysis of literature. *Transl Androl Urol.* 2022;11(5):710-719.
- Reid R. Alkaline water and urine. TyentUSA. March 12, 2019. Accessed July 7, 2023. <u>https://www.</u> tyentusa.com/blog/alkaline-water-and-urine/
- 8. How can alkaline water affect bladder health?. His Therapy. Accessed July 7, 2023. <u>https://</u> <u>histherapy.net/blog/uncategorized/how-can-</u> alkaline-water-affect-bladder-health/

- Pearle MS, Goldfarb DS, Assimos DG, et al. Medical management of kidney stones: AUA guideline. J Urol. 2014;192(2):316-324.
- Eisner BH, Asplin JR, Goldfarb DS, Ahmad A, Stoller ML. Citrate, malate and alkali content in commonly consumed diet sodas: implications for nephrolithiasis treatment. J Urol. 2010;183(6):2419-2423.
- Manzo BO, Cabrera JD, Emiliani E, Sánchez HM, Eisner BH, Torres JE. Impact of the adherence to medical treatment on the main urinary metabolic disorders in patients with kidney stones. *Asian J Urol.* 2021;8(3):275-279.
- Bek-Jensen H, Fornander AM, Nilsson MA, Tiselius HG. Is citrate an inhibitor of calcium oxalate crystal growth in high concentrations of urine?. *Urol Res.* 1996;24(2):67-71.
- 13. EAU Guidelines. Edn. presented at the EAU Annual Congress Amsterdam. 2022.

- Betz MV, Penniston KL. Primary contributors to dietary acid load in patients with urolithiasis. *J Ren Nutr.* 2023;33(1):53-58.
- Goraya N, Munoz-Maldonado Y, Simoni J, Wesson DE. Treatment of chronic kidney diseaserelated metabolic acidosis with fruits and vegetables compared to NaHCO<sub>3</sub> yields more and better overall health outcomes and at comparable five-year cost. J Ren Nutr. 2021;31(3):239-247.
- Halperin ML, Jungas RL. Metabolic production and renal disposal of hydrogen ions. *Kidney Int.* 1983;24(6):709-713.
- Remer T, Manz F. Potential renal acid load of foods and its influence on urine pH. J Am Diet Assoc. 1995;95(7):791-797.
- Platikanov S, Garcia V, Fonseca I, Rullán E, Devesa R, Tauler R. Influence of minerals on the taste of bottled and tap water: a chemometric approach. *Water Res.* 2013;47(2):693-704.
- Koff SG, Paquette EL, Cullen J, Gancarczyk KK, Tucciarone PR, Schenkman NS. Comparison between

lemonade and potassium citrate and impact on urine pH and 24-hour urine parameters in patients with kidney stone formation. *Urology*. 2007;69(6):1013-1016.

- Large T, Williams J Jr, Asplin JR, Krambeck A. Using low-calorie orange juice as a dietary alternative to alkali therapy. *J Endourol.* 2020;34(10):1082-1087.
- Odvina CV. Comparative value of orange juice versus lemonade in reducing stone-forming risk. *Clin J Am Soc Nephrol.* 2006;1(6):1269-1274.
- Goodman JW, Asplin JR, Goldfarb DS. Effect of two sports drinks on urinary lithogenicity. Urol Res. 2009;37(1):41-46.
- Gandhi M, Aggarwal M, Puri S, Singla SK. Prophylactic effect of coconut water (Cocos nucifera L.) on ethylene glycol induced nephrocalcinosis in male Wistar rat. Int Braz J Urol. 2013;39(1):108-117.
- Saat M, Singh R, Sirisinghe RG, Nawawi M. Rehydration after exercise with fresh young coconut water, carbohydrate-electrolyte beverage and plain water. J Physiol Anthropol Appl Hum Sci. 2002;21(2):93-104.

- Patel RM, Jiang P, Asplin J, et al. Coconut water: an unexpected source of urinary citrate. *Biomed Res Int.* 2018;2018:3061742.
- Dai JC, Maalouf NM, Hill K, Antonelli JA, Pearle MS, Johnson BA. Alkali citrate content of common over-the-counter and medical food supplements. *J Endourol.* 2023;37(1):112-118.
- Joshi A, Tallman JE, Calvert JK, et al. Complementary and alternative medicine use in first-time and recurrent kidney stone formers. *Urology*. 2021;156:58-64.
- Canvasser NE, Rivera M, Bechis SK. Over-the-Counter alkali agents to raise urine pH and citrate excretion: a prospective crossover study in healthy adults. *Urology.* 2022;168:72-78.
- Pinheiro VB, Baxmann AC, Tiselius HG, Heilberg IP. The effect of sodium bicarbonate upon urinary citrate excretion in calcium stone formers. *Urology*. 2013;82(1):33-37.
- 30. Guidelines for a low sodium diet. May 2, 2023. https://www.ucsfhealth.org/education/guidelines-fora-low-sodium-diet

# EDITORIAL COMMENTS

Undoubtedly, many urologists have been asked to comment on alkaline water in their clinic. It is a good question, and to a patient, it makes perfect sense. "The pH of my urine is too low. You prescribed me something to raise it? Why can't I drink this? The pH is 10!" Prescription alkalinizing agents, while the cornerstone of medical stone therapy, have poor long-term adherence (as low as 13%).<sup>1</sup> It is fair for patients to seek an alternative.

As the authors point out, the marketing of alkaline water has outpaced its demonstrable efficacy.<sup>2</sup> Its limited benefit is a mere matter of chemistry. Key to body's citraturic response is the ingestion of organic anions with their accompanying cations.<sup>3</sup> Patients and providers alike may fail to understand the difference between pH (log measurement of H<sup>+</sup> concentration) and alkalinity. Alkalinity measures the ability of solution to resist acidification and is dependent on a buffer composed of weak acids and their conjugate bases. Alkaline water can be extremely basic (high concentration of OH<sup>-</sup>) with poor alkalinity due to the lack of buffer anion/cations like citrate. Following ingestion, the basicity of the solution would be immediately neutralized in the stomach due to an abundance of  $H^+$  ions joining  $OH^-$  ions to produce  $H_2O$  (with no weak acids to absorb the excess  $H^+$  ions).

Another common office question is related to apple cider vinegar. While it has a high concentration of organic anion (acetate), the low pH of vinegar means that it mostly exists as acetic acid limiting its alkalinizing potential. However, Zhu et al have presented preclinical data suggesting daily vinegar ingestion causes epigenetic changes in tubule ion transporters generating a citraturic response.<sup>4</sup>

Ultimately, the provider must understand the mechanisms behind alkalinization to guide the patient through the unscrupulous and obfuscating world of complementary health product marketing.

> Brett A. Johnson<sup>1</sup> <sup>1</sup>Department of Urology, University of Texas Southwestern Dallas, Texas

# REFERENCES

- Dauw CA, Yi Y, Bierlein MJ, et al. Factors associated with preventive pharmacological therapy adherence among patients with kidney stones. *Urology*. 2016;93:45-49.
- Piedras P, Cumpanas AD, McCormac A, et al. Alkaline water: help or hype for uric acid and cystine urolithiasis?. J Urol. 2024;211(2):276-284.
- 3. Doizi S, Poindexter JR, Pearle MS, et al. Impact of potassium citrate vs citric acid on urinary stone

risk in calcium phosphate stone formers. *J Urol.* 2018;200(6):1278-1284.

 Zhu W, Liu Y, Lan Y, et al. Dietary vinegar prevents kidney stone recurrence via epigenetic regulations. *EBioMedicine*. 2019;45:231-250. In the mid-19th century, the French biologist Claude Bernaud conducted an experiment during which the urine of rabbits became acidic after a boiled beef diet.<sup>1</sup> The pH of the beef itself had little to do with its effects on urine pH. Muscle tissue, after all, is not acidic while in the body nor upon extraction, after which it might reach a pH nadir of 5.6 to 5.7. If it were only about the pH of foods, acidic foods (ranging from approximately 2-4 on the pH scale) such as vinegars, kimchi, and plants from the genera *Ribes* (currants, cranberries) and *Citrus* (oranges, lemons) would be associated with overly acidic urine. But they are not.

It turns out that the pH of a food or beverage matters little in its ability to affect urine pH. Rather, what matters is the effect on renal acid-base homeostasis of the conglomerate of a food's specific amino acids, organic acids, and other food factors.<sup>2</sup> But science has not stopped the massive "health" food and bottled beverage industries from promoting high-pH waters to people seeking better health. People are drawn to these waters for various reasons, including to alkalinize urine to prevent uric acid and cystine kidney stones. Postpandemic sales of so-called alkaline waters will exceed \$1.3 billion in 2023.<sup>3</sup>

The current study demonstrates that high-pH waters are not necessarily alkaline nor capable of raising urine pH.<sup>4</sup> Only waters providing significant amounts of bicarbonate precursors in the form of certain organic anions can do so. The authors assessed 5 popular brands of bottled "alkaline" waters for ingredients, pH, and organic anions and used the results as a platform for a larger and much-needed discussion on urinary alkalinization. These data, along with the authors' downloadable beverage "guide" will be helpful in discussing the concept of alkaline waters with patients.

#### Kristina L. Penniston<sup>1,2</sup>

<sup>1</sup>Department of Urology, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin

<sup>2</sup>Department of Clinical Nutrition Services, University of Wisconsin University Hospital and Clinics, Madison, Wisconsin

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# REFERENCES

- Arunachalam C, Woywodt A. Turbid urine and beefeating rabbits: Claude Bernard (1813-78)—a founder of modern physiology. NDT Plus. 2010;3(4):335-337.
- Remer T, Manz F. Potential renal acid load of foods and its influence on urine pH. J Am Diet Assoc. 1995;95(7):791-797.

3. Within the water trend: sales of alkaline water sales rising high. News release. NetworkNews-Wire. 2021. Accessed October 16, 2023. <u>https://</u> www.prnewswire.com/news-releases/within-thewater-trend-sales-of-alkaline-water-sales-risinghigh-301397840.html  Piedras P, Cumpanas AD, McCormac A, et al. Alkaline water: help or hype for uric acid and cystine urolithiasis?. J Urol. 2024;211(2):276-284.

The cost of prescription medication therapy for urinary alkalinization continues to rise and is one factor that contributes to poor long-term adherence for kidney stone prevention.<sup>1</sup> Patients are interested in nonprescription over-the-counter alternatives, and it is important for urologists to be familiar with them.<sup>2</sup> It is necessary to determine the benefit of these products since advertised claims are not monitored by the Food and Drug Administration. Alkaline water has gained popularity in recent years, with claims of health benefits and a common assumption is the capability to alkalinize urine. The authors analyzed commercially available alkaline water for alkali content and concluded that they contain negligible alkali content (<1 mEq/L) that is inadequate for urinary alkalinization for kidney stone prevention, especially for uric acid and cystine stone formers who typically need 30 to 60 mEq/d.<sup>3</sup> This article is a significant contribution, and the authors should be applauded for providing evidence that alkaline water does not provide benefit over tap water in this regard.

As pointed out by the authors, some patients may prefer the taste of alkaline water and it will help

those patients reach fluid intake goals; however, they should be advised there is no additional preventive benefit. There are several other alternative over-thecounter options available for urinary alkalinization, and in the Figure in the article the authors have provided an excellent resource of different beverages/ supplements (alkali content, sodium content, calories, and cost per month for 30 mEq/d alkali).<sup>3</sup> We should counsel patients to limit beverages with calories and high sodium chloride content. Another consideration is the environmental impact of single-use plastic water bottles, and patients should be encouraged to use reusable containers to meet hydration goals. This article highlights that tap water should be encouraged, especially when it comes to bottled alkaline water as it has been determined to be hype for urinary alkalinization and kidney stone prevention.

**Necole M. Streeper<sup>1</sup>** <sup>1</sup>Department of Urology, Medical College of Wisconsin, Milwaukee, Wisconsin

# REFERENCES

- Dauw CA, Yi Y, Bierlein MJ, et al. Factors associated with preventive pharmacological therapy adherence among patients with kidney stones. *Urology.* 2016;93:45-49.
- Stern KL, Canvasser N, Borofsky M, et al. Alkalinizing agents: a review of prescription, overthe-counter, and medical food supplements. *J Endourol.* 2020;34(1):1-6.
- Piedras P, Cumpanas AD, McCormac A, et al. Alkaline water: help or hype for uric acid and cystine urolithiasis?. J Urol. 2024;211(2):276-284.

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