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Using Low-calorie Orange Juice as a Dietary Alternative to Alkali Therapy

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Abstract

Purpose: The pursuit of a dietary source to increase urine pH and citrate in stone formers has been ongoing for more than 30 years. Early evidence showed that orange juice (OJ) contains alkali and citrate but high sugar and ascorbic acid content limited the use of OJ as a viable daily source of alkali. Recently, novel low calorie OJs have emerged and could potentially be a better option.

Methods: Beverages with high concentrations of alkali citrate and malate were identified using ion chromatography. Two low calorie OJ beverages, in addition to Crystal Light Lemonade (CLLB) were chosen. Healthy volunteers (5 men, 5 women) drank 1L of OJ or CLLB with 1L water daily for 7 days and then completed a 24-hour urinalysis. A washout week was instituted between trial weeks. The study design is a prospective randomized cross over control trial. A paired analysis using comparison of means was used to evaluate low calorie OJ and CLLB. Volunteers had no prior history of kidney stones and maintained a journal with beverage compliance, side effect, and dietary consumption data.

Results: Tropicana 50 (TRP50), Kroger low calorie OJ (KLCO) and CLLB were found to have a total alkali content of 56.60, 47.9, and 17.3 mEq/L, respectively, based on ion chromatography. Consumption of all three beverages raised urinary citrate (116.6 [-118 to 373, 177.9 [-3 to 359], 155.6 [-4 to 237] △mg/d 95% CI) and urinary pH (0.25 [0.08-0.53], 0.74 [0.41-1.07 $p<0.05$], 0.25 [0.25-0.64]) respectively, compared to water phase. Based on journal entries by volunteers, TRP50 had the most side effects (90% participants) felt to be a result of the artificial sweetener (Stevia ®).

Conclusion: Low-calorie orange juice, and to a lesser extent CLLB, have alkali and citrate based on ion chromatography. Daily consumption, by healthy volunteers of KLCO can raise urinary pH.

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Introduction

Dietary alternatives to modify urinary derangements such as hypocitraturia or aciduria have been explored for more than 30 years[1]. Low urinary citrate and pH can promote calcium oxalate and uric acid stone formation, respectively. The current AUA guidelines state that potassium citrate (kcit) therapy should be initiated for patients with recurrent calcium stones and low urinary citrate, and uric acid or cystine stone formers with low urinary pH[2]. Unfortunately, compliance rates with kcit are poor because of gastrointestinal side effects, poor palatability, large pill size[3] and cost[4]. Rampant increases in the price of generic medications, such as kcit, occur when pharmaceutical companies obtain a market share of a drug's production or supply[5]. This has been identified as a relatively new issue affecting kcit compliance rates.

There are multiple publications on dietary sources of alkali and citrate. Wabner et al. published one of the earliest series in 1993 looking at orange juice (OJ) as an alternative source for citrate to prevent kidney stones[6]. Additionally, lemon-based beverages have been evaluated extensively both in both bench[7] and clinical settings[8-10]. Changing urinary citrate and pH levels with concentrated lemon extract, lemonade, grapefruit[11], raspberry and coconut juice[12] have had mixed results. Despite early evidence that OJ harbored excellent alkali potential, valid concerns over the sugar content in OJ, in combination with the promising bench results of concentrated lemon juice led to a focused effort evaluating the efficacy of lemon-based beverages on urinary citrate and pH modulation. Eisner et al. published a summary of the alkali potential of multiple lemon-based beverages[13]. Interestingly, despite its frequent utilization, the paper did not feature Crystal Light Lemonade beverage (CLLB) as there is little to no research on CLLB as an alternative source of alkali therapy. After multiple trials[8-10] evaluating the effectiveness of lemon-based beverages, the results are still inconclusive; supporting continued efforts to find alternative sources of dietary citrate and alkali therapy. One example is the use of novel low calorie OJ drinks with the potential to provide dietary citrate or alkali without large quantities of sugar.

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Our group decided to evaluate the potential for urinary citrate and pH with low calorie OJ beverages. Prior to any clinical application of low calorie OJ in stone patients, we wanted to evaluate the alkali potential in popular consumer beverages; these included low calorie OJ and CLLB. We hypothesized that low calorie OJ and CLLB would have favorable alkali potential based on ion chromatography. After identifying beverages with favorable profiles based on ion chromatograph that were easily accessible and cost effective, we hypothesized that consumption of these specific beverages by healthy volunteers would yield urinary alkalization with concomitant increases in urinary citrate.

Methods

Using an ICS 2000 system equipped with an AS-11 analytical column with KOH elutent (Dionex, Sunnyvale, California), ion chromatography was completed on common consumer beverages to evaluate for total citrate, malate, and alkali potential. The pK of tricarboxylic acid citrate was used to calculate anion content was 3.1, 4.7, 6.4 and for dicarboxylic malate the pK was 3.4, and 5.1 respectively. Anion peaks were detected by a conductivity meter with eluent background conductivity suppressed by an ASRS® Ultra II anion self-regenerating suppressor. The pH of each beverage was measured with a pH electrode. Various brands of standard and low-calorie OJ, Crystal Light Lemon and orange, and carbonated flavored water were selected for the initial analysis. Unprotonated citrate and malate anion concentrations were obtained and used to calculate the total alkali content of each beverage expressed in mEq/L.

From the initial analysis, two low-calorie OJ options [Tropicana 50 (TRP50) and Kroger Low Calorie (KLCO) brand] along with CLLB were selected for clinical evaluation. All of the commercial orange beverages had robust concentrations of alkali, however, TRP50 was chosen because it is widely available for purchase at stores such as Target, Walmart, and on Amazon.com. KLCO was selected because it was locally available and the cheapest option of low calorie OJ options. CLLB was included as a zero-calorie option for those who might not tolerate the extra calories of even low calorie OJ. The study was structured as a randomized prospective cross-over study that evaluated the 24-hour urine parameters of 10 healthy volunteers (mean age: 42.1 [24-64] yrs, BMI 25.3 ± 4.1 kg/m^2, 5 female) with no

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history of kidney stones. The volunteers were recruited via word of mouth and flyers posted around the hospital after the study received institutional review board-approval. Each volunteer was assigned a randomized drink order which included: 2L water/day, 1L low-calorie TRP50 OJ and 1L water/day, 1L KLCO and 1L water/day, or 1L CLLB and 1 L water/day. Each beverage was consumed for 7 continuous days. Validation that volunteers were not consuming vitamins or medications that would affect their 24-hour urinalysis occurred upon enrollment. No other dietary restrictions were enforced. After 7 days of each beverage consumption a 24-hour urine collection was completed and sent to Litholink Corporation for testing. Between each trial beverage there was a one-week washout period where volunteers had no dietary restrictions. The trial took 8 weeks to complete for each volunteer. The Litholink urinary panel provides measures including, but not limited to, citrate, calcium, oxalate, phosphate, uric acid and urinary pH. Volunteers maintained a diary where they recorded adherence to the beverage consumption requirements, any side effects from the beverages, and a description of their meals while on a trial week. These journals were reviewed at the conclusion of the trial to ensure consistency in dietary habits between the trial weeks and compliance with beverage consumption at the prescribed volumes. Paired changes in mean citrate excretion, pH, and urine volume were the primary endpoints of the study and were conducted using an ANOVA comparison of means. A p value of <0.05 is considered statistical significance.

Results

Results of the chemical analysis are represented in table 1. We found that Minute Maid pure Squeeze 50 had the highest citrate composition (45 mmol/L) of all the beverages analyzed while LaCroix Orange (<0.2 mmol/L) and Crystal Light Orange (15.5 mmol/L) had the lowest. All the OJ drinks provided a large total alkali and potassium load. CLLB demonstrated an intermediate alkali load with 17.3 mEq/L. In table 2, 24-hour average urine results are listed by drink category. All collections were evaluated for their appropriateness (Cr24/kg) with average baseline values of 25.8 ± 3.8 and 22.1 ± 3.6 respectively for male and female volunteers. The only statistical difference between the groups was change in urinary pH (CLLB, 0.25 [0.08-0.53]; KLCO, 0.74 [0.41-1.07 $p<0.05$]; TRP50, 0.25 [0.25-0.64])) with urinary citrate increased (CLLB, 116.6 [-118 to 373; KLCO,

177.9 [-3 to 359]; TRP50, 155.6 [-4 to 237] △mg/d [95% CI]) by not statistically significant in a paired difference test (table 3). Changes in urinary volume, citrate and urinary pH with TRP50 compared to KCLO were less; likely the result of a reduced beverage consumption at high volumes from gastrointestinal side effects potentially a result, in part, by the artificial sweetener. Volunteers reported side effects (S.E - 90%), including gastrointestinal side effects (bloating, diarrhea, acid reflux) and headaches with TRP50 which were less prevalent (30%) and severe with KLCO. Intestinally, other than 3 patients complaining of the taste, no one reported any side effects associated with CLLB consumption. All participants validated that they were compliant with the volume of water and trial beverage for the trial week, with the exception of one participant who could not complete a week of TRP50 because of headaches and abdominal cramping. CLLB did raise urinary pH by 0.25 (p=0.99), urinary volume almost 200mL (p=0.008), and citrate levels 155mg/day (p=0.05) compared to values obtained during the water phase.

Discussion

Dietary sources of alkali and citrate have been identified. Common consumer beverages have been primarily evaluated because they have more consistent concentrations of bioavailable alkali salts and they provide the potential to increase dietary fluid intake. The AUA guidelines clearly outline that patients being treated for hypocitraturia or aciduria can reduce their risk of recurrent calcium oxalate or uric acid stone disease with supplemental citrate and alkali therapy[(2)]. Potassium citrate has long been the mainstay therapy to restore urinary citrate and pH levels[(14)]. However, there are a number of challenges associated with potassium citrate therapy that negatively impact patient compliance. The typical dose of potassium citrate ranges from 20 – 60 mEq/day which a recent publication estimated to cost up to $5100 annually[(15)]. For most patients, this is unaffordable, especially when insurance denies coverage. The prevalence of stones in the United States is increasing[(16)] and preventative therapies are paramount to minimize patient morbidity and mitigate health costs. Finding a dietary alternative, especially in a beverage, is imperative to reduce or replace our dependence on costly prescription-based medications with known patient compliance issues.

The early evidence that OJ has good alkali potential compared to alternate beverages[6] has largely been overlooked because of valid concerns about the associated sugar and caloric content. To some extent, this aided in the proliferation of lemon-based beverage studies. Lemon-based beverages can be consumed in large volumes and they avoid the introduction of stone substrates such as ascorbic acid. However, lemonade and lemon-based beverages have had mixed results[8,10,15] with urinary citrate modulation or urine alkalization in healthy volunteers or recurrent stone formers (table 4). A recent publication by Eisner et al, explains that dietary citrate exists as a salt coupled with potassium, calcium, sodium, magnesium or as an acid[13]. In the case of lemon-based beverages the predominant cation is hydrogen, which neutralizes any systemic alkali potential from the conversion of citrate to bicarbonate by the liver. Additionally, pure lemon juice has to be diluted to improve its palatability; factors which could be the reason for the variability in urinary citrate and pH modulation with lemon-based beverages. Despite a lower alkali content associated with CLLB compared to all OJ beverages on ion chromotography (table 1), we did see increases in both citrate, urine volume, and urinary pH in healthy volunteers from baseline levels on 24-hour urinalyses with CLLB. Even though the statistical significance may be lacking, our results do align with previous publications (table 4) that in a paired-difference analysis, CLLB, on average, raised urinary volume, citrate and pH compared to baseline.

By comparison, in addition to raising urinary citrate and volume, KCLO did show a statistically significant increase in average paired difference of urinary pH. Wabner et al. demonstrated the same finding in 1993[6] with standard OJ which was further supported by Odvina et al. in 2006[17] (table 4). These studies are limited in that they used high volumes of pure OJ in a controlled environment and dietary regimen which confers large dietary sugar loads and somewhat unrealistic lifestyle expectations of patients. The volunteers in this study demonstrated that consumption of KLCO can raise the urinary pH, with less sugar, within the stresses of daily life and activity. Based on the average paired difference of 0.74 pH units between baseline and KCLO urine samples, KCLO could be implemented into the prevention of uric acid or calcium oxalate stones in patients with aciduria. There are challenges with this intervention, both our data and Odvina et al.

showed increases in urinary oxalate likely resulting from higher dietary consumption of ascorbic acid (table 4). however, these have limited clinical impact and can potentially be mitigated with increased dietary calcium consumption and avoidance of specific foods rich in oxalate. Additionally, based on diary logs, 30% of volunteers had GI S.E. (two described bloating and one suffered abdominal cramps) from consuming KLCO. Although there were no compliance issues with the daily consumption of 1L of KLCO, we did see issues with TRP50. Multiple volunteers (90%) reported S.E. with TRP50 which we hypothesized was caused by the artificial sweetener (Stevia®) resulting in one patient withdrawing from the TRP50 trial week. We feel there is a clinical application of low-calorie OJ in the prevention of nephrolithiasis, however, a specific type and possibly lower daily volume may be required before formal recommendations can be established.

The concerns over our dependence on potassium citrate as the primary source for alkali and citrate is prompting multiple parallel studies of dietary alternatives[18-19]. Aside from lemon and orange-based beverages, other drinks, including grapefruit juice and coconut water have shown similar changes in urinary citrate and pH after controlled consumption in healthy volunteers[11-12]. Compared to controls, after 4-7 days of grapefruit juice or coconut water consumption, urinary pH and citrate did increase, but these changes were all non-significant except for the increase in urinary citrate concentration after coconut water consumption (table 4). By comparison, all beverage trials that used OJ (including this study for pH), showed statistical increases in urinary pH and citrate after 7 days of consumption (table 3,4). Concerns over the sugar, ascorbic acid, and artificial sweetener load with the consumption of low calorie OJ on overall gut microbiome health, stone metabolite absorption and any underlying metabolic syndrome will persist with the use of OJ, however, a better alternative to increase urinary pH is still lacking. For example, Lytholyte ® asserts 45mEq of alkali therapy for $2.25 per day[18] with no guaranteed fluid volume consumption compared to KCLO which confers an average increase of 400mL of urine at $1.46 per day for the same amount of alkali. To providers, we would recommend trying different brands of low calorie OJ if patients report poor palatability. The findings reported here are promising, but further studies are needed to evaluate if daily low-calorie

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OJ is safe to consume in patients with a history of nephrolithiasis, hypocitraturia, aciduria and potentially metabolic syndrome.

This study is not without limitations. Despite being a prospective randomized, cross-over trial, the sample size of volunteer participants is small. Nevertheless, we were able to demonstrate a statistical difference in urinary pH when volunteers consumed KLCO. We realize that in the study design we did not control diet, environment, and activity, however, we did review the volunteer journals and could not identify any noteworthy variances in beverage compliance or diet variability amongst the volunteers. We feel this study design is still representative of how urinary modulation can be achieved despite the inherent variability when research is conducted in a *real-world* setting. Additionally, the external validity of our results may have a limited potential when applied to patients with hypocitraturic or aciduric nephrolithiasis. These patients typically have comorbidities, for instance: metabolic syndrome, that may limit their ability to safely consume daily low-calorie OJ because of the additional sugar intake. Additionally, it is unclear in a diseased state such a hypocitratic nephrolitahsis with comorbidities like metabolic syndrome how low-calorie OJ consumption will translate into systemic or urinary alkalinization. Further research is underway to evaluate the potential positive urinary changes daily low-calorie OJ consumption can have in patients with hypocitraturic or aciduric nephrolithiasis.

Conclusion

There are a variety of options to introduce natural sources of alkali and citrate salts into the diet. In healthy volunteers, our study supports the use of both low-calorie OJ and CLLB to modulate urinary characteristics; namely urinary pH. Additional work is underway to evaluate if the same outcomes can be achieved in patients with nephrolithiasis, hypocitraturia and low urinary pH.

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Abbreviations

AUA = American Urologic Association

BMI = Body Mass Index

CLLB = Crystal Light Lemonade Beverage

kcit = Potassium Citrate

KLCO = Kroger Low Calorie Orange Juice

L = Liter

Miliequivalents = mEq

OJ = Orange Juice

TRP50 = Tropicana 50 Orange Juice

S.E. = Side Effect

△ = Change in

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Table Legends:

Table 1: Results from ion chromatography on common consumable beverages completed with the assistance of Litholink Lab Corp.

Table 1	pH	Citrate (mmol/L)	Malate (mmol/L)	Total Alk (mEq/L)	K (mmol/L)	Sugar (g/L)	Calories Liter
Crystal Light Orange	3.246	15.5	< 0.2	9.1	<2	0	10
Crystal Light Lemonade	3.218	30.4	< 0.2	17.3	6.4	0	10
Minute Maid Pure Squeezed 50 Calories, No Pulp	3.964	45.2	8.6	52.8	53.4	42	208
Trop50, No Pulp	3.894	37.4	24.7	56.1	51.6	42	208
Trop50, Some Pulp (SUP)	3.824	37.1	23.5	57.6	48.5	42	208
LaCroix Orange	5.200	< 0.2	< 0.2			0	0
Tropicana, No Pulp	3.903	42.8	18.4	56.4	51.9	96.1	458
Kroger Low-calorie OJ	3.978	41.8	6.6	47.9	26.3	37.5	250
Simply Orange, Pulp (SUP)	3.924	42.6	19.4	63.5	52.9	85	667

Table 2: Averages of 24-hr urinalysis for common urinary parameters for each beverage. Statistical significance set at p<0.05, pH (bolded) was the only variable that showed statistical significance between the groups on ANOVA.

Table 2	Control	CLLB	KLCO	TRP50
Number of participants	10	10	10	9
Volume (L/day)	2.5 ± 1.2	2.7 ± 1.1	2.9 ± 1.3	2.2 ± 1.0
Calcium (mg/day)	178 ± 101	189 ± 71	148 ± 61	184 ± 114
Oxalate (mg/day)	38.5 ± 11.4	36.8 ± 7.7	46.4 ± 8.2	42.2 ± 18.3
Citrate (mg/day)	735 ± 294	891 ± 424	913 ± 422	861 ± 325
pH	**6.19 ± 0.45**	**6.44 ± 0.33**	**6.93 ± 0.41**	**6.63 ± 0.42**
Uric acid (g/day)	0.71 ± 0.24	0.66 ± 0.15	0.65 ± 0.28	0.68 ± 0.34
Sodium (mmol/day)	180 ± 93	182 ± 60	187 ± 79	140 ± 68
Potassium (mmol/day)	79.3 ± 21.8	78.1 ± 30.3	104.1 ± 42.1	94.2 ± 52.2
Ammonium (mmol/day)	47.7 ± 18.6	42.3 ± 12.6	32.2 ± 17.5	33.2 ± 13.3
Magnesium (mg/day)	118 ± 55	111 ± 34	104 ± 27	110 ± 46
Phosphorus (g/day)	1.15 ± 0.41	0.94 ± 0.33	0.97 ± 0.46	1.01 ± 0.39
Sulfate (mEq/day)	55.8 ± 24.3	49.7 ± 23.1	42.4 ± 25.1	49.4 ± 33.1
Creatinin24/kg (mg/kg/day) - Male	25.1 ± 4.2	26.4 ± 2.3	25.5 ± 3.2	26.1 ± 6.6
Female	22.5 ± 4.2	23.8 ± 2.7	19.4 ± 4.1	22.7 ± 6.1

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Table 3: Average of the paired difference between trial beverage and control. Statistical significance set at p<0.05, change pH (bolded) was the only variable that showed statistical significance between the groups on ANOVA. △ represents change in.

* When KCLO is compared to TRP50 for △Vol (mL) p= 0.012 and for △Cit24 (mg/day) p= 0.011

Table 3	△ Vol (mL)	△ Ca24 mg (mg/day)	△ Ox24 (mg/day)	△ Cit24 (mg/day)	△ pH	△ Na24 (mmol/day)	△ K24 (mmol/day)
CLLB (n=10)	196	11.6	-1.71	155.65	+0.25	2.87	-1.22
KLCO (n=10)	387*	-29.43	7.90	177.98*	**+0.74**	7.10	24.28
TRP50 (n=9)	-341	11.88	5.84	116.6	+0.25	-15.67	15.01
P significance	0.080	0.212	0.452	0.863	0.033	0.691	0.217

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Table 4: Summary of published literature evaluating the urinary changes seen with the consumption of beverages hypothesized to have high concentrations of bioavailable alkali and citrate. # Comparison was conducted between a baseline metabolic evaluation and therapeutic intervention- significant differences in paired differences are reported as bolded value. Bolded values indicate significant differences between control and trial beverage, $p<0.05$

Table 4 - Study	Cntrl	Trial Beverage	N	Cntrl diet	Volume (L/d)	pH	Citrate (mg/d)	Calcium (mg/d)	Oxalate (mg/d)	Sodium (mmol/d)	K^+ (mmol/d)
Koff 2007[8]	H_2O		21	Yes	1.8 ± 0.6	5.5 ± 0.4	476 ± 467			213 ± 93	53 ± 20
	H_2O	Real Lemon	21	Yes	1.9 ± 0.7	5.6 ± 0.5	446 ± 376			180 ± 73	48 ± 19
Cheng 2018[15]	H_2O		12	Yes	1.9 ± 0.4	6.3 ± 0.3	657 ± 234	161 ± 59	25 ± 4	126 ± 32	63 ± 13
	H_2O	Min maid lemonade	12	Yes	**2.6 ± 0.6**	6.1 ± 0.3	**581 ± 234**	171 ± 59	26 ± 5	115 ± 15	**51 ± 12**
	H_2O	Diet min maid lemonade	12	Yes	**2.8 ± 0.7**	6.2 ± 0.2	**761 ± 342**	161 ± 53	25 ± 4	130 ± 36	63 ± 11
Odvina	H_2O		1	Ye	2.5	~ 5.7	~	159	31	70 ±	38 ±

2006[17]			4	s	± 0.5		520	± 42	± 10	37	11
	H_2O	Lemonade	14	Yes	2.6 ± 0.3	~ 5.6	~ 590	154 ± 58	30 ± 7	58 ± 31	39 ± 7
	H_2O	OJ	14	Yes	2.5 ± 0.4	**~ 6.3**	**~ 950**	146 ± 52	**35 ± 6**	66 ± 48	**85 ± 21**
Seltzer 1996[19]	Fluid		12	Yes	2.7 ± 2.5		142 ± 99	131 ± 119	53 ± 33		
	Fluid	Lemonade	12	Yes	2.9 ± 2.4		**346 ± 197**	92 ± 78	42 ± 12		
Patel 2017[12]	H_2O		8	No	3.0 ± 0.6	6.3 ± 0.3	557 ± 207	139 ± 74	27 ± 9	174 ± 33	64 ± 15
	H_2O	Coconut water	8	No	3.0 ± 0.7	6.4 ± 0.3	**718 ± 278**	137 ± 91	27 ± 7	177 ± 46	**143 ± 30**
Goldfarb 2001[11]	H_2O		10	No	1.7 ± 1.0	6.28 ± 0.3	505 ± 226	122 ± 102	41 ± 9	142 ± 34	59 ± 21
	H_2O	Grapfruit Juice	10	No	1.6 ± 0.8	6.5 ± 0.4	591 ± 220	104 ± 83	52 ± 13	136 ± 56	77 ± 26

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Wabner 1993[6]	H_2O		11	Yes	2.6 ± 0.2	5.7 ± 0.4	571 ± 300	173 ± 56	25 ± 6	88 ± 17	43 ± 16
	H_2O	OJ	11	Yes	2.4 ± 0.4	**6.5 ± 0.3**	**952 ± 508**	159 ± 61	**34 ± 6**	99 ± 28	**94 ± 26**
Our Data 2018	H_2O		10	No	2.5 ± 1.2	6.2 ± 0.5	735 ± 294	189 ± 71	39 ± 11	180 + 93	79 + 22
	H_2O	Crystal Light Lemon	10	No	2.7 ± 1.2	6.4 ± 0.3	446 ± 367	189 ± 71	36 ± 8	182 + 60	78 + 30
	H_2O	Kroger low cal OJ	10	No	**2.9 ± 1.2**	**6.9 ± 0.4**	**913 ± 422**	148 ± 61	**46 ± 8**	186 ± 79	**103 ± 42**
Aras 2008[10]	H_2O		10	Yes	1.5 ± 0.9	5.8 ± 0.4	123 ± 65	187 ± 89	25 ± 29		
	H_2O	Lemon Juice	10	Yes	**2.0 ± 0.9**	6.0 ± 0.3	**303 ± 75**	119 ± 87	27 ± 20		
	H_2O	Potassium Citrate	10	Yes	**2.0 ± 0.8**	**6.5 ± 0.3**	**324 ± 114**	152 ± 119	35 ± 13		
Pennisto n 2007[9]	Base line[#]	Potassium Citrate	37	No	**1.9 ±**	**6.1 ± 0.1**	**683 ± 41**				**62 ± 3**

	Baseline	Lemon Juice	63	No	**0.1 2.0 ± 0.1**	**6.0 ± 0.1**	364 ± 45	53 ± 8

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