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Research Article

Lemongrass tea consumption and changes in Acid-Base Balance and Electrolyte homeostasis

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Abstract

The consumption of dietary herbs and supplements may be associated with several physiological consequences including, but not limited to disturbances of acid-base homeostasis, minerals and electrolytes wasting, gastrointestinal disturbances as well as hemodynamic changes. Plants food based nutritional studies are important for assessing the effect of plants on human health and wellbeing. The aim of this study was to assess the changes in acid-base status and electrolyte homeostasis following the consumption of lemongrass tea. The acute and sub-chronic effects of infusions prepared from 2, 4, and 8g lemongrass leaf powder on serum and urinary pH, and electrolytes levels were assessed in 105 subjects using an interventional study design. The results post-treatment were compared with baseline values.

Plasma pH decreased from baseline value of 7.37 ± 0.02 to 7.20 ± 0.03, and 7.30 ± 0.02 at days 10 and 30 respectively for participants treated with infusion prepared from 2g of lemongrass leaf powder. For those treated with infusion prepared from 4g of lemongrass leaf powder, plasma pH decreased from baseline value of 7.35 ± 0.02 to 7.22 ± 0.02 and 7.29 ± 0.02 at days 10 and 30 respectively.

Treatment with infusion prepared from 8g of lemongrass leaf powder caused a decrease in plasma pH from baseline value of 7.38 ± 0.02 to 7.15 ± 0.02 and 7.18 ± 0.02 at days 10 and 30 respectively. Corresponding changes in urinary pH were also observed. Furthermore, at days 10 and 30, plasma protein concentrations increased significantly ($p < 0.05$) in subjects treated with infusion prepared from 8g lemongrass leaf extract. There were also significant increases ($p < 0.05$) in urinary volume, urination frequency, and urinary electrolytes levels within the same period.

The consumption of lemongrass tea may be associated with changes in acid-base balance and electrolyte homeostasis due to its varied biological constituents and their activities.

Introduction

Disturbances in acid–base balance and electrolyte homeostasis associated with the consumption of dietary herbs are common [1], but underreported [2]. Such cases, if reported, could be of public health interest, as they may serve to alter both consumers' and healthcare practitioners' opinions. Accordingly, Luyckx et al. [3], report metabolic acidosis in 80.8% and volume depletion with associated electrolyte derangement in 62.8% of patients with renal failure following the consumption of a particular herbal diet. Similarly, Ifudu and Friedman [2], report a case of type 4 renal tubular acidosis with associated hyperkalemia in a patient who ingested a particular herbal medicine. Other reported cases include hyperkalemia induced by noni (*Morinda citrifolia*) juice in a patient with renal insufficiency [4]. Gerson cancer therapy-induced hyperkalemia in patients with Hodgkin lymphoma [5], aristolochic acid-induced hypokalemic paralysis, hypokalemia with renal potassium wasting, hyperchloremic metabolic acidosis, hypophosphatemia with hyperphosphaturia, hypouricemia with hyperuricosuria and glycosuria (i.e., Fanconi syndrome) [6] and licorice-induced hypokalemia in a

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patient with prostate cancer [7]. The abovementioned cases are merely a fraction of all of such cases, as there are likely many more cases unreported by both consumers and practitioners. In addition, they do not include non-hospitalized cases and under-diagnosed cases, particularly in developing countries lacking accurate/advanced diagnostic facilities. According to Ko [8], approximately 32% of 260 alternative medicine products analyzed contained potentially harmful undeclared substances [2]. Moreover, Haller et al. [9], report that only 40% of people who used alternative medicine products inform their primary care physicians. Although the underlying mechanisms by which some alternative medicine products alter acid–base balance and electrolyte homeostasis remain debatable, current evidence suggests the causal roles of various bioactive constituents and their pharmacodynamic and pharmacokinetic interactions with the body's homeostatic mechanisms. For instance, noni juice causes hyperkalemia owing to its high potassium content (56.3 mEq/L) [4], whereas mourning cypress (*Cupressus funebris* Endl.) extract causes acute renal failure, acute hepatic failure, autoimmune hemolytic anemia, and thrombocytopenia owing to its high flavonoids content [10]. Several other herbs with laxative activities also cause hypokalemia with associated metabolic alkalosis [11].

Likewise, herbs with known diuretic activity may induce changes in acid–base balance as well as water and electrolyte homeostasis partly because of the interaction of some of their bioconstituents with various physiological systems responsible for the body's acid–base and electrolyte homeostasis. One such herb with known diuretic action but without adequate documented evidence for its effect on acid–base homeostasis and electrolyte balance in human is lemongrass (*Cymbopogon citratus (C. citratus)*, family: Poaceae), it is a widely distributed tall aromatic perennial plant with thin green leaves approximately 90 cm long and 1.5 cm wide [12]. The leaves contain various bioactive substances including phytochemicals, macronutrients, minerals, vitamins, and essential oils. Citral, a monoterpene aldehyde, is the predominant constituent, and pharmacologically and physiologically important component of *C. citratus* essential oil. *C. citratus* has a century-long record of extensive therapeutic, nutritional, and cosmetic usage. It is used in alternative medicine for its anti-inflammatory, anticarcinogenic, antimicrobial, antioxidant, antidiabetic, antidyslipidemic, antiplatelet, antispasmodic, antipyretic, analgesic, sedative, and cardio-protective properties [13]. Meanwhile, it is also used in traditional cuisines including dishes, baked foods, and confections; it is consumed as tea in Brazil and in soft drinks in Peru [14]. It is also preferred by many consumers because of its physiochemical characteristics including taste, lemony aroma, and color [15]. Regarding cosmetic uses, the plant is used in perfumes, soaps, detergents, and body creams [16]. Recent evidence supports its use in food preservation because of its significant broad-spectrum antimycotic potency, which can remain for 210 days of storage [17], as well as its fungitoxic, fungistatic, antimycotoxin, and non-phytotoxic properties [18]. However, whether *C. citratus* leaf infusion interferes with plasma pH, water, and electrolyte balance has not yet been documented despite its long history of edible, therapeutic, and cosmetic uses. Plant food based nutritional studies are important for assessing the effect of plants on human health and well-being. Therefore, the present study aimed to determine the effects of *C. citratus* leaf infusion on acid–base balance and electrolyte homeostasis in normal humans.

Materials and Methods

Selection of participants

One hundred and five participants (55males and 50females) were qualified to participate in this survey. They provided written informed consent to validate their participation. All participants underwent a thorough pre-survey medical screening that was performed by a Medical Doctor to ensure medical fitness and to exclude those who did not meet the inclusion criteria. The exclusion criteria were as follows: previous history of hypersensitivity reaction to any of the lemongrass constituents,

use of drugs that may interfere with the effect of the extract, and history of kidney or liver disease. Other exclusion criteria include disorders of hematopoietic system (such as sickle cell disease), in appropriate age (<18 and >35years), pregnancy or lactation and failure to satisfy the pre-trial clinical and biochemical assessment.

The preliminary medical screening included obtaining past medical history, a life-style assessment (smoking status, drinking, diet, drug history and physical activity status), blood pressure (BP), heart rate (HR), weight, blood glucose level, full blood count and platelet count, and urine and blood indices of renal and hepatic function. The participants were advised to avoid excessive physical activity and ingestion of drugs or alcohol, and to remain on their regular diet, but to avoid high saponins and polyphenol-rich foods/vegetables. The study design and experimental protocols were approved by the Institutional Human Ethics Committee.

Preparation of extract for phytochemical and nutritional analysis

C. citratus leaves were harvested fresh from a local farm in Uyo, Akwa Ibom State, Nigeria few days prior to utilization. The leaves were identified and authenticated by a taxonomist in the Department of Botany at the University of Uyo, Nigeria. The leaves were rinsed, sundried and pulverized into powder using electric blender to yield a weight of 200g. The leaf powder was soaked in a container with 2L of hot water and allowed to stand for approximately 8hrs. Thereafter, the solution was filtered using N_0.2 Whatman filter paper. The filtrate was evaporated by heating in a water bath at 40°C to obtain the solid extract. The solid extract was weighed (ACS-ZE14 Surgifriend Medical Ltd, England) to obtain a yield of 70g (35% w/w) which was then stored in clean bottles at room temperature and later used for phytochemical and nutritional analysis.

Administration of infusion

The participants were divided into 3groups (n=35/group). Each group received infusions prepared from 2, 4, or 8g of *C. citratus* leaf powder, in 150ml of hot water, given once daily at scheduled time (between 10am-3pm) for 30days. This infusion was prepared in this manner to correspond to the way in which lemongrass tea is usually prepared by the population. The dose range employed was adapted from previous human studies in which participants showed no obvious clinical or biochemical evidence of toxicity [19,20]. Also, a pilot study conducted on 10 volunteers using infusions prepared from 2, 4, 8 and 10g of *C. citratus* leaf powder in 150ml of hot water showed no evidence of adverse/toxic effects, based on the results of the tolerability assessment. These included a range of clinical and laboratory tests, including test for renal function (serum creatinine and clearance rate (Cr), liver function (Aminotransferase activity), serum urea levels and hematological indices. The participants were also examined for presence of jaundice, or pallor (evidence of hepatotoxicity and hemolysis), and for evidence of abnormal skin reactions. The participants were also instructed to report any unusual symptom on the symptomatology and fluid intake assessment questionnaire including lightness of the body, headache, dizziness, sweating, frequent maturation, belching, dyspepsia, diarrhea, constipation, vomiting and palpitation.

Samples collection and biochemical analysis

Venous blood samples were drawn from all participants on the scheduled days (days 0, 10 and 30) in 10ml EDTA and dry tubes for plasma and serum collection respectively. Blood samples were immediately stored in cold boxes and transferred to department of chemical pathology, University of Uyo Teaching Hospital where the biochemical analysis was done using standard procedures.

Twelve-hour urine samples were collected from all participants between the hours of 6 pm and 6 am, at days 0, 10, and 30 after initiation of the study. The volume of the urine was measured with a calibrated cylinder, while the 24-h urination frequency was reported in a chart designed by the authors. The Na^+ and K^+ concentrations in the urine

were determined by Flame Photometry ("Jencon PEP 9", Jencons Scientific Limited, Bedfordshire, UK), Ca^{2+} was measured by atomic absorption spectrophotometry (Jarrel-Arh Model 82-36, UK), and Cl^- was measured using an ion selective meter (Orion 730", Orion Research Inc. Boston, USA). Urinary pH was measured using a digital pH meter (Model E9610, Equiptronics, England), while glucose and protein were measured using urine reagent test strips (Combi 9, Macherey-Negrel, Germany). On the days when urine specimens were collected (i.e., days 0, 10, and 30), fluid and food intake were restricted between the time of administration of the infusion and collection of the final urine sample (6pm to 6am).

Statistical analysis

Data (mean ± SEM) were analyzed using one-way analysis of variance (ANOVA). Differences were considered statistically significant at $P < 0.05$. All analyses were performed using the Statistical Package for the Social Sciences (SPSS 20.0).

Results

The phytochemical constituents of *C. citratus* leaf extract revealed a relatively high concentration of saponins; moderate concentrations of tannins, flavonoids, and phenols; and relatively low concentrations of alkaloids, deoxysugars, and anthraquinones. The nutrient constituents of *C. citratus* leaf extract detected include moisture, crude protein, fiber, fat, carbohydrates, and micronutrients including K^+, Na^+, Ca^{2+}, F^{2+}, Mg^{2+}, Cu, Mn, Se, Zn, vitamin C, and folate. Regarding the baseline demographic and clinical characteristics of the study participants, most (52%) were males and were between 18 and 35 years old.

The participants' basic characteristics were as follows: mean weight, 60.74 ± 1.93 kg; body mass index, 23.46 ± 0.75 kg/m^2; systolic blood pressure, 120.53 ± 1.89 mmHg; diastolic blood pressure, 74.64 ± 1.62 mmHg; mean arterial pressure, 85.69 ± 1.13 mmHg; heart rate, 77.71 ± 1.99 beats/min; mean pulse pressure, 45.89 ± 1.04 mmHg; glomerular filtration rate, 99.88 ± 1.52mlmin; and mean respiratory rate, 18.56 ± 1.52 mL/min. There were no significant changes in serum concentrations of K^+, Na^+, Cl^-, or HCO_3^- at days 10 or 30, (Table 1). In addition, serum Ca^{2+} levels did not differ significantly from baseline, but decreased significantly at day 30 in those treated with infusion prepared from 8 g leaf powder for 30 days ($p < 0.05$).

Plasma pH decreased from baseline value of 7.37 ± 0.02 to 7.20 ± 0.03, and 7.30 ± 0.02 at days 10 and 30 respectively for participants treated with infusion prepared from 2g of *C. citratus leaf* powder. For those treated with infusion prepared from 4g of *C. citratus* leaf powder, plasma pH decreased from baseline value of 7.35 ± 0.02 to 7.22 ± 0.02 and 7.29 ± 0.02 at days 10 and 30 respectively.

Table 1: Acute (10 Days) and sub-chronic (30 days) effects of infusions prepared from C. citratus powder on serum electrolytes and Ph.

Duration/ concentration	K^+ mmol/L	Na^+ mmol/L	Ca^{2+} mmol/L	Cl^- mmol/L	HCO_3 mmol/L	pH	Protein g/dl
Control							
2g	3.98±0.06	138.69±0.83	2.42±0.04	101.80±2.28	24.37±0.25	7.37±0.02	68.26 ± 0.53
4g	3.84±0.04	138.14±0.33	2.54±0.04	102.51±0.42	23.86±0.20	7.35±0.02	68.70 ± 0.62
8g	3.93±0.07	136.66±0.64	2.67±0.06	103.11±0.61	23.77±015	7.38±0.02	68.76 ± 0.66
Acute							
2g	3.99±0.38	138.91±0.46	2.56±0.03	100.86±2.31	24.29±0.24	7.20±0.03	68.29 ± 0.72
4g	4.29±0.07	140.60±0.72	2.57±0.04	102.11±0.49	24.09±0.26	7.22±0.02	68.77 ± 0.70
8g	4.01±0.06	139.26±0.57	2.88±0.015[c]	102.91±0.60	24.01±0.24	7.15±0.02	75.78 ± 0.52[a]
Sub-chronic							
2g	3.89±0.04	138.60±0.21	2.30±0.04	100.29±2.31	24.20±0.28	7.30±0.02	69.46 ± 0.98
4g	3.84±0.05	138.02±0.26[b]	2.37±0.03	101.71±0.25	24.03±0.23	7.29±0.02	69.80 ± 0.75
8g	3.85±0.04	133.91±0.38[b]	2.47±0.05[ab]	103.00±0.36	23.83±0.23	7.18±0.02	77.12 ± 0.51[a]

a = significantly different from control ($p < 0.05$), b = significantly different from 2 g ($p < 0.05$), c = significantly different from 4 g ($p < 0.05$). Values reported as Mean ± SEM.

Treatment with infusion prepared from 8g of *C. citratus* leaf powder caused a decrease in plasma pH from baseline value of 7.38 ± 0.02 to 7.15 ± 0.02 and 7.18 ± 0.02 at days 10 and 30 respectively.

Urinary pH decreased from baseline value of 5.57 ± 0.24 to 4.59 ± 0.19 and 4.02 ± 0.14 at days 10 and 30 respectively for participants treated with infusion prepared from 2g of *C. citratus* leaf powder.

Treatment with infusion prepared from 4g of *C. citratus* leaf powder decreased urinary pH from the baseline value of 5.88 ± 0.19 to 5.00 ± 0.23 and 4.11 ± 0.16 at days 10 and 30 respectively.

Furthermore, in participants treated with infusion prepared from 8g of *C. citraus* leaf powder, urinary pH decreased from baseline value of 5.20 ± 0.17 to 4.99 ± 0.11 and 5.01 ± 0.18 at days 10 and 30 respectively. Serum protein increased in all groups, but the increases were only significant among those treated with infusion prepared from 8 g for 10 and 30 days (Table 1). Urinary K^+ and Na^+ concentrations increased significantly ($p < 0.05$) at day 10. By day 30, K^+ and Na^+ concentrations decreased, but the decrease in urinary Na^+ concentration was significant only among those treated with infusions prepared from 2 or 8 g *C. citratus* powder. Urinary Ca^{2+} and Cl^- concentrations increased significantly at both days 10 and 30, except in those treated with infusion prepared from 8 g *C. citratus* leaf powder for 10 days, which did not differ significantly from baseline. In addition, 24-hour urination frequency increased significantly in all groups except in participants treated with infusion prepared from 2 g *C. citratus* leaf powder for 30 days. Twelve-hour urine volume increased significantly in all treatment groups by day 10 ($p < 0.05$). After 30 days, urine output remained elevated in the participants treated with infusions prepared from 4 or 8 g *C. citratus* leaf powder (Table 2). The renal fractional excretion of electrolytes (i.e., K^+, Na^+, Ca^{2+}, and Cl^-) and organic substances (i.e., urea, uric acid, and creatinine) generally increased significantly in most of groups in both study phases.

Discussion

Under normal steady-state metabolic conditions, the human body tends to tightly control pH from 7.35–7.45 (mean: 7.4) by respiratory excretion of carbon dioxide and renal excretion of non-carbonic acids or bases [21]. Even slight deviations can lead to serious even life-threatening metabolic derangement [22]. The results of the present study indicate *C. citratus* leaf extract decreased plasma and urinary pH below the baseline values and the limit of the respective reference ranges. Although the mechanism(s) by which *C. citratus* leaf extract causes these changes is unknown, the results of the phytochemical analysis of the extract in the present and previous studies [22-24], show the presence of several phytoactive constituents (i.e., saponins,

Table 2: Acute and sub-chronic effects of infusions prepared from C. citratus powder on urinary electrolytes, pH and 24hr urination frequency

Duration/ Concentration	K^+ mmol/L	Na^+ mmol/L	Ca^{2+} mmol/L	Cl^- mmol/L	pH	24 hr urination frequency
Control						
2g	40.83±1.87	160.63±5.57	11.78±3.87	130.34±6.37	5.57±0.24	6.42±0.24
4g	39.40±1.37	117.94±8.56	16.25±2.97	147.80±6.44	5.88±0.19	5.06±0.20
8g	37.71±1.68	135.63±8.20	11.95±2.84	137.23±7.46	5.20±0.17	6.02±0.28
Acute						
2g	58.57±3.18^a	170.37±8.02^{a*}	13.69±1.83^a	198.80±8.47^a	4.59±0.19^a	7.08±0.22^a
4g	52.87±2.87^a	141.89±5.53^{ab}	20.38±2.30^{ab}	206.97±3.35^a	5.00±0.23^a	7.04±0.37^a
8g	44.06±3.06^{abc}	140.06±7.20^b	12.86±1.86^c	181.51±11.72^{ac}	4.99±0.11	7.02±0.34^a
Sub-chronic						
2g	37.67±0.39	127.14±8.21^a	17.13±2.26^a	190.23±7.43^a	4.02±0.14^a	6.56±0.25
4g	37.40±1.85	116.00±6.73	20.43±2.99^a	174.60±8.44^a	4.11±0.16^a	6.74±0.31^a
8g	36.54±0.65	126.11±7.70^a	17.05±2.54^a	162.94±8.16^{ac}	5.01±0.18^{bc}	8.00±0.22^{abc}

a = significantly different from control ($p < 0.05$), b = significantly different from 2 g ($p < 0.05$), c = significantly different from 4 g ($p < 0.05$). Values reported as Mean ± SEM.

tannins, flavonoids, alkaloids, anthraquinones, etc.) and nutrients (i.e., protein, carbohydrates, electrolytes, and minerals). Several studies show that some of these bioactive constituents interfere either individually or synergistically with enzyme/transport systems (i.e., Na^+–K^+ ATPase and alpha epithelial Na^+ channel [αENaC] mRNA) responsible for the reabsorption of these electrolytes, H^+, and water in the renal tubules, leading to perturbed acid–base and electrolyte homeostasis [25,26].

De Souza et al. [27], report that saponin inhibits Na^+–K^+ ATPase in a manner similar to but stronger than furosemide, a standard loop diuretic. Rhiouani et al. [28], studied the effects of saponins from *Hermiaria glabra* on blood pressure and renal function in rats and conclude chronic oral administration of saponins decreases arterial blood pressure and affects salt and water transport in renal tubules. Meanwhile, Jouad et al. [29], report that flavonoids significantly increase urinary Na^+, K^+, and $2Cl^-$ concentrations in a manner similar to that of furosemide. Recent experimental studies by Hiwatashi et al. [30] and Chen et al. [31], demonstrate the inhibitory effect of saponins on the renin–angiotensin–aldosterone system (RAAS), a key regulator of blood pressure, acid–base balance, and fluid volume in the body [32]. Such inhibitory actions could have extended to affect the aldosterone-sensitive Na^+ channels located on the renal cortical collecting tubules; this would consequently decrease the number of open Na^+ channels, which would increase Na^+ excretion, K^+ retention, and associated acid-base and electrolyte changes observed in the present study. This notion is supported in a study by Aoi et al. [33], who report that quercetin, a flavonoid (also found in *C. citratus*) inhibits αENaC mRNA expression in the kidneys. Lee and Chen [10], report biochemical and clinical evidence of flavonoid-induced biochemical and metabolic derangement after ingestion of a flavonoid-rich extract of *C. funebris* (mourning cypress). Furthermore, the consumption of *C. citratus* leaf extract is reported to be associated with metabolic derangement [12].

Tarkang et al. [12], report increased blood urea nitrogen and mild tubular distortion in the kidneys after the administration of *C. citratus* ethanol extract for 28 days. Compared to the controls, serum creatinine levels suggested a non-renal cause of the derangement; this further implicates the action of *C. citratus* phytoactive compounds including saponins and flavonoids, which are known for their adverse metabolic effects. Collectively, considering this consistent empirical evidence, it can be concluded that the metabolic derangement observed in the present study is corollary of the bioactive constituents in the lemongrass leaf extracts. This is supported by previous studies evaluating these compounds and reporting similar results. However, it is noteworthy that these effects are not universal. Besides the aforementioned mode of action, available evidence also implicates the pathophysiological role of some of *C. citratus* leaf extracts' acid-forming constituents including the biologically active-peptides derived from its high protein content. Interestingly, the high protein content in *C. citratus* leaf extracts has been repeatedly acknowledged by several investigators. In parallel studies, Oloyede [24], Akande et al. [34] and Arhoghro and Kpomah [35], report high protein concentrations in lemongrass leaf extracts. Furthermore, Tarkang et al. [12] report a significant increase in plasma protein in experimental animals fed with *C. citratus* leaf extract for 28 days.

The detection of a substantial amount of protein in our experimental leaf extract and the increase in plasma protein in participants treated with infusions prepared from 8 g *C. citratus* leaf powder for 10 and 30 days in the present study corroborate the results of the abovementioned studies. Therefore, without any contrary evidence, the changes in acid-base balance observed in the present study could be partly associated with the high protein content of the lemongrass leaf extract. This assertion is supported by the fact that relatively high dietary protein intake can generate substantial fixed acids, leading to acidemia due to the excess of sulfuric anions produced by the catabolism of the sulfur amino acids[36] Indeed, Aftab et al. [26] report high levels of sulfur,

iron, phosphate, and aluminum (>1%) in their lemongrass sample compared to other trace elements (<1%); in the present study, we obtained a pH of 4.5–5.35 for our experimental sample. These results collectively indicate the acidogenic potential of lemongrass leaf extract.

Another potential mechanism by which the high protein content of *C. citratus* extract could derange acid–base balance is through its inhibitory action on the RAAS. Several studies show angiotensin-converting enzyme inhibitory peptides derived from food, particularly those with high protein contents, can act as potential inhibitors of angiotensin II-mediated secretion of aldosterone from the adrenal cortex [30,31,37] Such actions could interfere with aldosterone-sensitive Na^+ channels and by extension, impede Na^+ reabsorption, and K^+ and H^+ secretion. Retention of H^+ and K^+ could lead to acidosis and hyperkalemia with associated natriuresis as was observed in the present study. Similarly, the decrease in K^+ in the subchronic phase to almost baseline levels signifies the adaptive role of the kidneys to acute K^+ loading. Surprisingly, despite the changes in serum H^+ concentration, serum HCO_3^- levels remained unchanged, and urinary HCO_3^- was below detection limit, whereas urinary pH decreased below baseline.

These findings are probably indicative of the adaptive changes in renal function in response to acid insult [38]. In acidosis, the kidneys do not excrete HCO_3^- into urine but reabsorb all of it and even produce new HCO_3^-, which is added to the extracellular fluid. The kidneys consequently reduce the extracellular fluid H^+ concentration through 3 functional mechanisms: hydrogen secretion, re-absorption of filtered HCO_3^-, and production of new HCO_3^-. These mechanisms occur in virtually all parts of the renal tubules except the ascending thin limbs of the loops of Henle. These could explain the non-significant changes in plasma HCO_3^- levels in both phases of the present study and are consistent with previous studies suggesting plasma HCO_3^- levels may be normal even when acidosis is present [39]. The slight increase in plasma pH in the subchronic phase of the study (although still below baseline) is consistent with a previous study showing that acute acid loading may only temporarily disrupt acid–base equilibrium, while the body acid–base maintenance mechanisms (i.e., buffers, respiratory, and renal) attempt to restore a steady-state condition [39]. However, chronic perturbation occurs when metabolism of the diet repeatedly releases non-carbonic acids into the systemic circulation in amounts exceeding the amount of base released concomitantly. This hypothesis explains the partial reversal of plasma pH to baseline level in the sub-chronic phase of the present study.

The decrease in urinary pH levels in both study phases demonstrates the kidneys' role in urine acidification to rid the body of excess acid load. This response includes the reduction if not the elimination of all HCO_3^- from the urine as well as increases in titratable acids (i.e., phosphoric acid, creatinine, and uric acid) and ammonium excretion as observed in the present study. Changes in the electrolyte composition of urine in the present study indicate K^+ and Na^+ concentrations increased and decreased in the acute and sub-chronic phases, respectively, whereas Ca^{2+} and Cl^- remained increased in both study phases. The fluctuation in urinary K^+ levels parallels the changes observed in plasma K^+ levels in both study phases and may signify the effect of the high K+ content of the extract as detected in the present and previous studies [27,29,45] and the role of the kidneys in an adaptive response to a high-K^+ diet. In an excellent functional state, the excretory response to acute K^+ load by the kidneys is enhanced, and the associated increase in plasma K^+ level is mitigated by the preceding period of high K^+ intake. This adaptive response mechanism is controlled by aldosterone, because such an effect is absent in adrenalectomized animals and is restored by administration of an exogenous mineralocorticoid [40].

Similarly, the patterns of fluctuations in plasma and urinary Na^+ levels in the present study are consistent with changes in individuals on a high-K^+ diet as well as electrolyte patterns in animal studies following high K^+ loading [47], accordingly,

Young et al. [41], assessed the chronic effect of K^+ loading on Na^+ balance and found that increasing daily K^+ intake increases the plasma K^+ concentration with a 56% increase in Na^+ excretion despite a 58% increase in plasma aldosterone concentration. The result of the aforementioned study is paradoxical, because an increase in plasma aldosterone caused by increased K^+ it would be expected to cause Na^+ re-absorption, thereby reducing excretion.

The plausible explanation for this is the suppressive effect of chronic K^+ intake on rennin activity [42,43]. Moreover, the diuretic and natriuretic effect of a high-K^+ diet could explain the urinary electrolyte changes observed in the present study [44]. The decrease of urinary Na^+ levels in the sub-chronic phase corresponds to a return of plasma Na^+ to baseline levels within the same period and signifies the transient inhibitory effect of a high-K^+ diet on the RAAS due to the phenomenon of aldosterone escape [45]. This interaction between K^+ load (i.e., high-K^+ diet) and Na^+ was the focus of Von Bunge's studies in Germany in the mid-1870s and remains a topic of interest to date [46], he was concerned that the natriuresis produced by K^+ would lead to serious disease. However, the natriuresis fortunately lasted only a few days to one week before Na^+ balance was restored.

Similarly, Michelson et al. [47] observed that although initial natriuresis occurred as a result of K^+ administration, Na^+ balance was generally restored within one week. This effect of K^+ on Na^+ excretion is exploited in the management of several diseases associated with high plasma Na^+ concentrations, including heart failure and hypertension [48]. Increase in urinary Ca^{2+} concentration indicates impaired re-absorption. Approximately 50% of plasma Ca^{2+} is freely filtered via the renal glomeruli, and 99% of the filtered Ca^{2+} is reabsorbed along the renal tubules [49]. In addition, approximately 50–60% of the filtered Ca^{2+} is reabsorbed along with Na^+ and H_2O [49]. Therefore, *C. citratus* may impede Ca^{2+} reabsorption via 2 potential pathways: (1) through its diuretic actions (i.e., loop-active-like and potassium sparing actions) [50-52] and (2) through associated metabolic acidosis. As a diuretic agent through its bioactive constituents, *C. citratus* interferes with Na^+ and H_2O re-absorption by inhibiting the 3-ion co-transport system ($Na^+/K^+/2Cl^-$) [52] and also by blocking the aldosterone-sensitive Na^+ channels located on the cortical collecting tubules [52]. Irrespective of the mechanism, the inhibitory actions of diuretics on Na^+ and H_2O re-absorption interfere with the trans-epithelial potential differences associated with the re-absorption of Na^+ and water, which are required for Ca^{2+} re-absorption, leading to hypercalciuria [53].

A recent study suggests acidic pH increases calciuria by inhibiting the renal epithelial apical Ca^{2+} channel transient receptor potential V_5- ($TRPV_5$) and $TRPV_6$-mediated Ca^{2+} re-absorption in the distal nephron [54]. We previously reported that *C. citratus* possesses both loop-active and K-sparing diuretic actions in humans [52], which corroborates previous hypotheses [50,51] and provides empirical evidence in support of the changes in plasma and urinary pH and electrolyte excretion observed in the present study. As a loop-active diuretic, *C. citratus* could impair Na^+, Cl^-, and H_2O re-absorption and secondarily impairs Ca^{2+} reabsorption. Meanwhile, as a K-sparing diuretic, *C. citratus* could cause metabolic acidosis, hyper-kalemia, natriuresis, and chloruresis [52]. Therefore, the increases in urination frequency, urinary volume, and other diuretic indices including increased fractional excretion of electrolytes in the present study are corollaries of the diuretic actions of *C. citratus*. The strength of this study lies in the careful selection of study participants, including the population size, age (18–35 years), which excludes the confounding effect of age-related changes in renal function, equal sex distribution, which excludes sex-related effects on the examined variables, and study design (interventional design), which controls for individual differences in baseline characteristics. Nevertheless, there are some limitations that warrant recognition, including the inability to measure the plasma activities of the alleged affected enzymes systems involved in acid–base and electrolyte homeostasis, including renin, aldosterone, Na^+–K^+ ATPase activity and αENC mRNA. Thus, future studies should address these concerns to confirm the present findings.

Conclusion

The consumption of lemongrass tea may be associated with acid–base derangement and electrolyte wastage in normal individuals through the interactions of some of its phyto-constituents with the body's acid–base and electrolytes homeostatic mechanisms.

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