(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
25 September 2014 (25.09.2014)

WIPO | PCT

(10) International Publication Number
WO 2014/152789 A1

(51) International Patent Classification:
A61P 3/02 (2006.01) *A23L 2/52* (2006.01)
A61P 3/14 (2006.01) *A23L 1/304* (2006.01)
A23L 2/385 (2006.01) *A61K 31/19* (2006.01)

(21) International Application Number:
PCT/US2014/027736

(22) International Filing Date:
14 March 2014 (14.03.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/793,442 15 March 2013 (15.03.2013) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,

[Continued on next page]

(54) Title: CITRATE CONTAINING BEVERAGE

(57) Abstract: Provided are beverage compositions comprising a urine citrate increasing component and a urine oxalate reducing component. The beverage compositions may be provided in a ready-to-drink form or may be provided in a concentrate form. Also provided are kits comprising the beverage compositions and methods for treating various conditions using the beverage compositions.

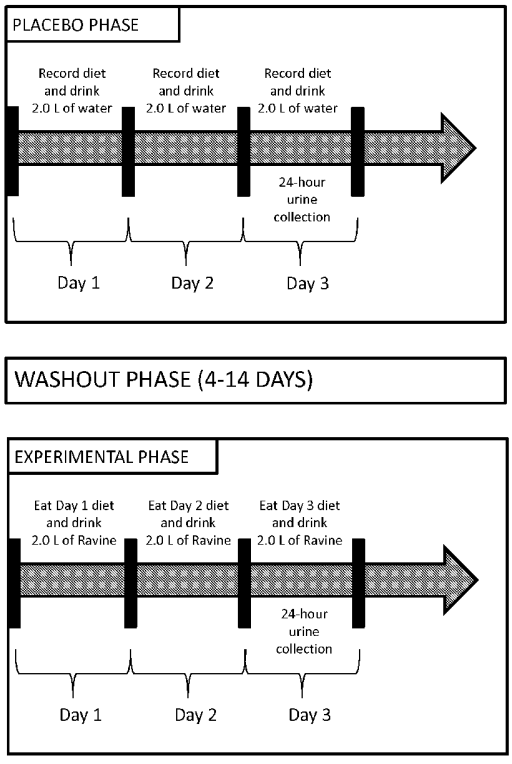

FIGURE 1

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KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

CITRATE CONTAINING BEVERAGE

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional application no. 61/793,442, filed on March 15, 2013, the disclosure of which is incorporated herein by reference in its entirety.

BACKGROUND OF THE INVENTION

[0002] Kidney stones are a common cause of morbidity, with a lifetime worldwide prevalence of 5-10%. In the absence of prevention, recurrence is common, with over 50% of patients having a recurrent stone episode within 5-10 years of their first stone. The most common stone type is calcium oxalate. A second type of stone that may occur is calcium phosphate. Calcium-based stones comprise roughly 80% of all stones. At least 10% of stones are composed of uric acid and about 1% of stones (and 6% of stones in children) are composed of cystine.

[0003] Although it is considered that patients are amenable to modifying their eating and drinking habits in preference to taking prescription pills for the prevention of various conditions, there is no beverage currently available that is designed to increase urine citrate and pH, while reducing urinary calcium.

SUMMARY OF THE DISCLOSURE

[0004] The present invention is based, in part, on the inventors' surprising and unexpected discovery that beverages made in accordance with the invention and comprising a urine citrate increasing component and a urine oxalate reducing component have improved benefits in the management of kidney stones as compared to prior art compositions. The invention encompasses a beverage comprising a urine citrate increasing component and a urine oxalate reducing component. The invention contemplates beverages to be ready to drink or alternatively reconstituted from powdered mixes, concentrated liquid (concentrate) or tablets.

[0005] In a specific embodiment, the urine citrate increasing component comprises sodium citrate, potassium citrate or magnesium citrate, or combinations thereof. In one specific preferred embodiment, the invention provides a beverage comprising sodium citrate, potassium citrate, magnesium citrate, citric acid, pyridoxine and combinations thereof.

[0006] In some embodiments, the oxalate reducing component is a magnesium salt. In one specific preferred embodiment, the magnesium salt is magnesium hydroxide.

[0007] In other preferred embodiments, the oxalate reducing component is selected from the group consisting of a magnesium, pyridoxine and combinations thereof.

[0008] In some embodiments, the beverage of the invention comprises citrate, magnesium and pyridoxine.

[0009] In some embodiments, the beverage of the invention further comprises vitamins, minerals, phytate, amino acids and combinations thereof.

[0010] In one specific embodiment, the beverages of the invention are calorie-free. In another specific embodiment the beverages of the invention are calcium free.

[0011] The invention encompasses methods for management of kidney stone disease in a human in need thereof comprising administration of a beverage comprising a urine citrate increasing component and a urine oxalate reducing component.

[0012] In other embodiments, the invention encompasses methods for management of bone disease in a human in need thereof comprising administration of a beverage comprising a urine citrate increasing component and a urine oxalate reducing component.

[0013] In one specific embodiment, the beverages in accordance with the invention comprise: 1.0 to 4.0 mmol/L sodium citrate; 3.0 to 7.5 mmol/L potassium citrate; 15 to 25 mmol/L citric acid; 1 to 3 mmol/L magnesium hydroxide; and 1.5-3.5 mg/L pyridoxine, wherein the pH of the beverage is 3.3-7.0.

[0014] In another specific embodiment, the beverages in accordance with the invention comprise: 3.33 mmol/L sodium citrate; 5.0 mmol/L potassium citrate; 19.67 mmol/L citric acid; 2.0 mmol/L magnesium hydroxide; and 2.5 mg/L pyridoxine, wherein the pH of the beverage is 3.5.

[0015] The invention also encompasses methods for increasing urinary citrate and reducing urinary oxalate by providing a beverage to an individual, said beverage comprising 1 to 4.0 mmol/L sodium citrate; 3.0 to 7.5 mmol/L potassium citrate; 15 to 25 mmol/L citric acid; 1 to 3 mmol/L magnesium hydroxide; and 1.5-3.5 mg/L pyridoxine, wherein the pH of the beverage is 3.3-7.0.

[0016] In one specific embodiment, the invention provides a method for increasing urinary citrate and reducing urinary oxalate by providing a beverage to an individual, said beverage comprising 3.33 mmol/L sodium citrate; 5.0 mmol/L potassium citrate; 19.67

mmol/L citric acid; 2.0 mmol/L magnesium hydroxide; and 2.5 mg/L pyridoxine, wherein the pH of the beverage is 3.5.

[0017] In another specific embodiment, the invention provides a method for management of kidney stones in a human in need thereof comprising administering a beverage to the human, said beverage comprising 1 to 4.0 mmol/L sodium citrate; 3.0 to 7.5 mmol/L potassium citrate; 15 to 25 mmol/L citric acid; 1 to 3 mmol/L magnesium hydroxide; and 1.5-3.5 mg/L pyridoxine, wherein the pH of the beverage is 3.3-7.0.

[0018] In yet another specific embodiment, the invention provides a method for management of kidney stones in a human in need thereof comprising administering a beverage to the human, said beverage comprising 3.33 mmol/L sodium citrate; 5.0 mmol/L potassium citrate; 19.67 mmol/L citric acid; 2.0 mmol/L magnesium hydroxide; and 2.5 mg/L pyridoxine, wherein the pH of the beverage is 3.5.

[0019] In another specific embodiment, the invention provides a method management of bone disease in a human in need thereof comprising administering a beverage to the human, said beverage comprising 1 to 4.0 mmol/L sodium citrate; 3.0 to 7.5 mmol/L potassium citrate; 15 to 25 mmol/L citric acid; 1 to 3 mmol/L magnesium hydroxide; and 1.5-3.5 mg/L pyridoxine, wherein the pH of the beverage is 3.3-7.0.

[0020] In another specific embodiment, the invention provides a method for management of bone disease in a human in need thereof comprising administering a beverage to the human, said beverage comprising 3.33 mmol/L sodium citrate; 5.0 mmol/L potassium citrate; 19.67 mmol/L citric acid; 2.0 mmol/L magnesium hydroxide; and 2.5 mg/L pyridoxine, wherein the pH of the beverage is 3.5.

[0021] The invention also provides a kit comprising a powdered mix, a concentrate, or a tablet comprising:

(a) sodium citrate, potassium citrate, citric acid, magnesium hydroxide, and pyridoxine in amounts such that a beverage prepared from it will have 1.0 to 4.0 mmol sodium citrate, 3.5 to 7.5 mmol potassium citrate, 15 to 25 mmol citric acid, 1 to 3 mmol magnesium hydroxide, and 1.5 to 3.5 mg pyridoxine per liter;

(b) packaging for a container;

(c) a container; and

(d) a set of instructions, said instructions describing how to prepare and store a beverage using the powdered mix or the tablet and describing the frequency and volume of the beverage to be consumed by an individual.

[0022] In another specific embodiment, the invention provides a kit comprising a powdered mix, a concentrate, or a tablet comprising:

(a) sodium citrate, potassium citrate, citric acid, magnesium hydroxide, and pyridoxine in amounts such that a beverage prepared from it will have 3.33 mmol sodium citrate, 5.0 mmol potassium citrate, 19.67 mmol citric acid, 2.0 mmol magnesium hydroxide, and 2.5 mg pyridoxine per liter;

(b) packaging for a container;

(c) a container; and

(d) a set of instructions, said instructions describing how to prepare and store a beverage using the powdered mix or the tablet and describing the frequency and volume of the beverage to be consumed by an individual

[0023] In one embodiment, the invention provides a kit comprising:

(a) a powdered mix, a concentrate, or a tablet comprising sodium citrate, potassium citrate, citric acid, magnesium hydroxide, and pyridoxine in amounts such that a beverage prepared from it will have 1.0 to 4.0 mmol sodium citrate, 3.5 to 7.5 mmol potassium citrate, 15 to 25 mmol citric acid, 1 to 3 mmol magnesium hydroxide, and 1.5 to 3.5 mg pyridoxine per liter;

(b) a set of instructions, said instructions describing how to prepare and store a beverage using the powdered mix, concentrate or the tablet and describing the frequency and volume of the beverage to be consumed by an individual.

[0024] In another embodiment, the invention provides a kit comprising

(a) a powdered mix, a concentrate, or a tablet comprising sodium citrate, potassium citrate, citric acid, magnesium hydroxide, and pyridoxine in amounts such that a beverage prepared from it will have 3.33 mmol sodium citrate, 5.0 mmol potassium citrate, 19.67 mmol citric acid, 2.0 mmol magnesium hydroxide, and 2.5 mg pyridoxine per liter;

(b) a set of instructions, said instructions describing how to prepare and store a beverage using the powdered mix or the tablet and describing the frequency and volume of the beverage to be consumed by an individual.

[0025] In other embodiments, the kit comprises a plurality of portions of powdered mixes, concentrates or tablets and a preselected amount of aqueous liquid (such as water) such that each powdered mix, concentrate or tablet when mixed with the preselected amount of water will provide a beverage as described in the various embodiments herein. Each portion of the powdered mix, concentrate or tablet may be packaged individually in the kit.

[0026] The kits of the invention are contemplated to include ready to drink beverages made in accordance with the invention.

[0027] Additional aspects and advantages of the invention will be set forth in the description which follows and, in part, will be obvious from the description, or may be learned from practicing the invention as set forth herein. The objects and advantages of the invention will be realized and attained by means of the elements and combinations particularly pointed out herein and specified in the claims. It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory and do not restrict the invention as claimed.

BRIEF DESCRIPTION OF THE FIGURES

[0028] Figure 1 is a representation of a scheme for a trial for testing the effect of consumption of a beverage of the present invention.

DETAILED DESCRIPTION OF THE DISCLOSURE

[0029] The present disclosure provides a beverage comprising citrate in an amount that delivers clinically significant citrate to individuals such that the occurrence of kidney stones is prevented or reduced. The beverage comprises a urine citrate-increasing component and a urine oxalate-reducing component. Consumption of the beverage raises the urine citrate levels, raises urine pH, and reduces urine oxalate levels. The terms beverage and drink are used interchangeably in this description. In one embodiment, urine citrate and pH are increased, while urine calcium is decreased.

[0030] In one embodiment, the urine citrate increasing component comprises, consists essentially of, or consists of sodium citrate, potassium citrate, and citric acid, and the urine oxalate reducing component comprises, consists essentially of, or consists of a magnesium salt (such as magnesium hydroxide) and pyridoxine.

[0031] In one embodiment, the beverage of the present disclosure comprises sodium citrate, potassium citrate, citric acid, magnesium hydroxide and pyridoxine. The ingredients are present in such amounts that urine citrate and pH are increased while not altering other

urine chemistries. In one embodiment, the citrate may be magnesium citrate instead of or in addition to sodium citrate and potassium citrate. In one embodiment, the citrate comprises, consists essentially of, or consists of potassium citrate and magnesium citrate.

[0032] While not intending to be bound by any particular theory, it is considered that the sodium cation improves palatability and also provides a delivery vehicle for high levels of citrate that is not exclusively associated with potassium. In one embodiment, the amount of sodium citrate can be from 0.5 to 5 mmol/L and all amounts therebetween to the tenth decimal place and includes all ranges therebetween. In another embodiment, it is present from 1.0 to 4.0 mmol/L. In another embodiment, it is present from 3.0 to 3.5 mmol/L.

[0033] In one embodiment, the beverage is sodium-free. In this embodiment, the beverage may comprise potassium citrate, optionally magnesium citrate, citric acid, magnesium hydroxide, and pyridoxine.

[0034] In one embodiment, more potassium is present than sodium. However, the levels of potassium should not be such that it would result in hyperkalemia. In one embodiment, potassium citrate is present from 3.5 to 7.5 mmol/L and all amounts therebetween to the tenth decimal place and includes all ranges therebetween. In another embodiment, it is present from 4.0 to 6.0 mmol/L. In another embodiment it is present from 4.5 to 5.5 mmol/L.

[0035] The present beverage also comprises citric acid. In one embodiment, the amount of citric acid is from 15 to 25 mmol/L and all amounts therebetween to the tenth decimal place and includes all ranges therebetween. In another embodiment, the citric acid is present from 17 to 23 mmol/L.

[0036] The amount of citrate (calculated from citric acid, sodium citrate, and potassium citrate) is from 20 to 30 mmol/L and all amounts therebetween to the tenth decimal place and includes all ranges therebetween. In one embodiment, the citrate is from 23 to 27 mmol/L.

[0037] In one embodiment, the ratio of sodium to potassium is from 1:1.1 to 1:2. In another embodiment, it is from 1:1.3 to 1:1.7. In another embodiment, it is from 1:1.4 to 1:1.6.

[0038] To further aid in the prevention or amelioration of kidney stones, the present beverage contains magnesium compounds. Magnesium is a cation that can bind with oxalate in the urine and therefore interfere with the complexing of oxalate with calcium. In one embodiment, the magnesium compound is magnesium hydroxide. In one embodiment, in

addition to, or instead of magnesium hydroxide, magnesium citrate may be used. The amount of magnesium hydroxide is from 1 to 3 mmol/L and all amounts therebetween to the tenth decimal place and includes all ranges therebetween. In one embodiment, it is from 1.5 to 2.5 mmol/L.

[0039] The present beverage also comprises pyridoxine (Vitamin B6). The amount of pyridoxine is from 1.5 to 3.5 mg/L and all amounts therebetween to the tenth decimal place, and includes all ranges therebetween. In one embodiment, the amount is from 2 to 3 mg/L.

[0040] In one embodiment, the beverage of the present invention contains no calcium. In other embodiments, it contains less than 0.1, 0.05 or 0.01 mmol/L of calcium. In one embodiment, the calcium may be higher – i.e., up to 2.5 mmol/L.

[0041] The pH of the composition upon mixing of the ingredients is about 3.5. It is generally from 3.4 to 3.7 and all values to the tenth decimal place therebetween. It can be adjusted upward to a pH of from 3.5 to 7.0 and all values to the tenth decimal place therebetween and includes all ranges therebetween. In one embodiment, it is from 3.4 to 4.0.

[0042] In one embodiment, the calorie content of the beverage is less than 1. In one embodiment, the caloric content is 0. In another embodiment, the beverage has less than 5 calories (and can therefore, be considered "calorie free"). In another embodiment, it is a low calorie drink. The term "low calorie" as used herein means 40 calories or less. In other embodiments, the caloric content is from 1 to 40 calories and all integers and ranges therebetween. In other embodiments, the drink may have more than 40 calories.

[0043] A variety of flavors and/or colors can be added to the beverage as desired. In one embodiment, the color, flavor or other additive does not add any caloric value to the drink and does not alter the sodium, potassium or citrate parameters as described herein. Flavors may be natural or artificial. Examples of suitable flavors include lemon, orange, banana, strawberry, other fruits, fruit punch and the like.

[0044] In one embodiment, the composition of the present invention can also include vitamins, minerals, phytate and/or amino acids or other nutrients. Suitable vitamins include vitamin B1, vitamin B2, niacinamide, vitamin B12, folic acid, vitamin C, and vitamin E. Suitable minerals include iron, zinc, vanadium, selenium, chromium, boron, potassium, manganese, copper and magnesium. Suitable amino acids include lysine, isoleucine, leucine, threonine, valine, tryptophan, phenylalanine, methionine and L-selenomethionine, Additionally, wetting agents may also be included to improve mouth feel. In one embodiment, the beverage is a clear drink or a translucent drink.

[0045] While not intending to be bound by any particular theory, it is considered that increase in urine citrate and/or the reduction in urinary calcium is obtained, at least in part, due to the "citrate-as-alkali" effect. The organic anions of the present composition are accompanied by positively charged ions (cations) such as sodium or potassium. Therefore, instead of a proton (as would be the case for organic acids like acetic acid or citric acid), the carboxyl yields a bicarbonate without yielding a proton, and leads to net formation of base, which can neutralize other protons in the body, leading to an increase in blood pH and then urine pH and urine citrate. Because blood bicarbonate is readily excreted by the kidneys the pH of the blood changes only slightly while the urine pH will increase. We refer to this as "citrate-as-alkali" – the form of ingested citrate which leads to increased blood pH, urine citrate, urine pH, and therefore to reduction in kidney stone formation.

[0046] In one embodiment, other agents may be added that contribute to increasing the urinary pH. For example, malate or organic anions can be added.

[0047] In one embodiment, the present beverage may contain agents which can enhance the flavor or appearance of the beverage, but which do not affect the citrate or oxalate content of the urine or the ratio of sodium to potassium. These agents are referred to herein as "non-active" agents. In one embodiment, the non-active agents do not change the sodium or potassium content. In one embodiment, the non-active agents do not change the sodium or potassium content by more than 0.1%.

[0048] The beverage can be packaged in suitable containers such as bottles, cans, cardboard packages or the like in any suitable size including up to 0.5, 1 or 2 liter portions. The beverages can be aseptically packaged and stored at ambient temperatures (generally from 65 to 75 F) or at refrigeration temperatures.

[0049] In one embodiment, instead of a beverage, all of the above formulations can be provided in the form of powdered mixes, concentrated liquid (concentrate) or tablets. In one embodiment, the present invention provides a kit comprising a powdered mix, concentrated liquid or a tablet, which upon mixing with a suitable liquid (such as water) or diluting (if it is concentrate), will provide the beverage of the present invention. The kit may also contain a set of instruction for preparing the beverage from the powdered mix, concentrate or the tablet and for consumption (such as over a 24 hour period). The set of instructions may provide the frequency and the amount of beverage to be consumed over a 24 hour (or other selected) period. The set of instructions may also provide storage recommendations. The powdered mix, concentrate and the tablets can be packaged in suitable

containments – such as paper packages or pouches for the powdered mix, cartons, bottles, containers, or boxes for the concentrate, and blister packages for tablets. The powdered mix, concentrate or the tablet can be portioned such that they can be made into a preselected volume of beverage. For example, the powdered mix, concentrate or the tablet can be portioned such that it makes up a quart, half liter or a liter of beverage. Further, a kit may contain multiple pouches of the powdered mix and one or more sheets of the blister packaged tablet. The term tablets includes any compacted form of the powdered formulation including pills, caplets and the like. The kit may also contain the liquid for making up the beverage. For example, the kit may contain a measured amount of liquid for adding the powdered mix, concentrate or the tablet. Packaging can be compartmentalized such that the powdered mix, concentrate or the tablet is in one compartment and a measured amount of liquid in the other. The partition between these compartments may be such that it can be pierced or removed with or without exposing the contents to the outside thereby allowing mixing of the contents of the two compartments. The packaging can be in suitable portions allowing packing together of the supply for a day or a week or a month etc.

[0050] In one embodiment, the beverage of the present disclosure provides a calorie-free and calcium-free beverage. One to 2 liters of the beverage can be conveniently consumed over a 24 hour period to increase urinary citrate levels and reduce urinary oxalate levels, while not affecting other chemistries. This drink will be useful for individuals who have been diagnosed with kidney stones, for individuals who are at risk for developing stones, and generally for any individual for the prevention of kidney stones. This drink is also useful for general consumption such as as a thirst quencher. The beverage may be consumed by humans - both adults and children of all ages. It may also be used for consumption by animals. It may be used by individuals who are in need of increasing urine citrate levels, raising urine pH, or reducing urine oxalate levels. It may also be used by individuals with no known diagnosed disease conditions or by individuals having disease conditions (whether diagnosed or not) including individuals with bone diseases.

[0051] In one embodiment, the present disclosure provides a beverage which is organoleptically acceptable to consumers, and in a 1 liter package/container provides to the consumer from 1 to 4 mmol of sodium citrate, 4 to 6 mmol of potassium citrate, 15 to 25 mmol of citric acid, 1.5 to 3.5 mg of pyridoxine, and 1 to 3 mmol of magnesium hydroxide. In one embodiment, the 1 liter beverage does not contain any other salts. In one embodiment, the 1 liter beverage does not contain any other sodium or potassium salts or any other citrate,

and does not contain any other agent that would alter the amount of oxalate in the urine. Non-active agents like color and flavors may be added to the beverage. The beverage may be calorie-free, low calorie or may provide more than 40 calories.

[0052] In another embodiment, the present disclosure provides a beverage which is organoleptically acceptable to consumers, and in a 1 liter package/container provides to the consumer from 3 to 3.5 mmol of sodium citrate, 4.5 to 5.5 mmol of potassium citrate, 18 to 22 mmol of citric acid, 2 to 3 mg of pyridoxine, and 1.5 to 2.5 mmol of magnesium hydroxide. In one embodiment, the 1 liter beverage does not contain any other sodium or potassium salts or any other citrate, and does not contain any other agent that would alter the amount of oxalate in the urine. However, non-active agents like color and flavors may be added to the beverage. The beverage may be calorie-free, low calorie or may provide more than 40 calories.

[0053] The present disclosure also provides a method for preventing or reducing the occurrence of kidney stones. The method comprises providing to an individual a beverage of the present invention in an amount that is sufficient to reduce or prevent the formation of kidney stones. It is considered that the present beverage alters urine composition to make the urine less hospitable for kidney stone formation, by raising urine citrate and urine pH. The present beverage also lowers urine oxalate levels. In one embodiment, an individual consumes from 1 to 2 liters of the beverage per day (24 hour period).

[0054] The present compositions may also be used to improve bone mineral density and therefore, for the treatment, prevention or reduction of osteoporosis, osteopenia and metastatic bone cancer. In one embodiment, the compositions may be used in the treatment, prevention or reduction of chronic renal insufficiency.

[0055] In one embodiment, the beverage may contain from, 0.1% to 10% sweeteners and all percentages to the tenth decimal place therebetween. The sweeteners may be nutritive and non-nutritive, natural and artificial or synthetic. Such sweeteners are well known in the art.

[0056] In some aspects and embodiments, the present disclosure provides the following:

[0057] A calorie-free, calcium-free beverage consisting essentially of a urinary citrate increasing component and a urinary oxalate reducing component.

[0058] A calorie free, calcium free beverage consisting essentially of 1.0 to 4.0 mmol/L sodium citrate, 3.5 to 7.5 mmol/L potassium citrate, 15 to 25 mmol/L citric acid, 1 to

3 mmol/L magnesium hydroxide, and 1.5 to 3.5 mg/L pyridoxine, wherein the pH of the beverage is from 3.3 to 7.0.

[0059] A method for increasing urinary citrate and reducing urinary oxalate by providing a beverage to an individual, said beverage essentially consisting of 1.0 to 4.0 mmol/L sodium citrate, 3.5 to 7.5 mmol/L potassium citrate, 15 to 25 mmol/L citric acid, 1 to 3 mmol/L magnesium hydroxide, and 1.5 to 3.5 mg/L pyridoxine, wherein the pH of the beverage is from 3.3 to 7.0.

[0060] A method of preventing or reducing the occurrence of kidney stones by providing a beverage to an individual, said beverage comprising a urinary citrate increasing component and a urinary oxalate reducing component, wherein said beverage in a volume of 1-2 liters is consumed by the individual over a 24 hour period.

[0061] A kit comprising a powdered mix a concentrate or a tablet comprising sodium citrate, potassium citrate, citric acid, magnesium hydroxide, and pyridoxine in amounts such that a beverage prepared from it will have 1.0 to 4.0 mmol sodium citrate, 3.5 to 7.5 mmol potassium citrate, 15 to 25 mmol citric acid, 1 to 3 mmol magnesium hydroxide, and 1.5 to 3.5 mg pyridoxine per liter, packaged in a containment, and a set of instructions, said instructions describing how to prepare and store a beverage using the powdered mix or the tablet and describing the frequency and volume of the beverage to be consumed by an individual.

[0062] Examples of some specific embodiments of this disclosure are provided below:

[0063] A beverage comprising a urine citrate increasing component and a urine oxalate reducing component.

[0064] A beverage comprising a urine citrate increasing component and a urine oxalate reducing component, wherein the urine citrate increasing component comprises sodium citrate.

[0065] A beverage comprising a urine citrate increasing component and a urine oxalate reducing component, wherein the urine citrate increasing component comprises potassium citrate.

[0066] A beverage comprising a urine citrate increasing component and a urine oxalate reducing component, wherein the urine citrate increasing component comprises magnesium citrate.

[0067] A beverage comprising a urine citrate increasing component and a urine oxalate reducing component wherein the urine citrate increasing component is selected from the group consisting of sodium citrate, potassium citrate, magnesium citrate and combinations thereof.

[0068] A beverage comprising sodium citrate, potassium citrate, magnesium citrate, citric acid, pyridoxine and combinations thereof.

[0069] A beverage comprising a urine citrate increasing component and a urine oxalate reducing component, wherein the oxalate reducing component is a magnesium salt.

[0070] A beverage comprising a urine citrate increasing component and a urine oxalate reducing component, wherein the oxalate reducing component is a magnesium salt and wherein the magnesium salt is magnesium hydroxide.

[0071] A beverage comprising a urine citrate increasing component and a urine oxalate reducing component, wherein the oxalate reducing component is selected from the group consisting of a magnesium, pyridoxine and combinations thereof.

[0072] A beverage comprising a urine citrate increasing component and a urine oxalate reducing component, and further comprising vitamins, minerals, phytate, amino acids and combinations thereof.

[0073] A calorie-free beverage comprising a urine citrate increasing component and a urine oxalate reducing component.

[0074] A calcium-free beverage comprising a urine citrate increasing component and a urine oxalate reducing component.

[0075] A method for management of kidney stone disease in a human in need thereof comprising administration of a beverage comprising a urine citrate increasing component and a urine oxalate reducing component.

[0076] A method for management of bone disease in a human in need thereof comprising administration of a beverage comprising a urine citrate increasing component and a urine oxalate reducing component.

[0077] A beverage comprising citrate, magnesium, and pyridoxine.

[0078] A beverage comprising citrate, magnesium, and pyridoxine, wherein the source of citrate ions is selected from the group consisting of sodium citrate, potassium citrate, magnesium citrate and combinations thereof.

[0079] A beverage comprising citrate, magnesium, and pyridoxine, wherein the source of magnesium is magnesium hydroxide or magnesium citrate.

[0080] A beverage comprising:

(1) 1.0 to 4.0 mmol/L sodium citrate;

(2) 3.0 to 7.5 mmol/L potassium citrate;

(3) 15 to 25 mmol/L citric acid;

(4) 1 to 3 mmol/L magnesium hydroxide; and

(5) 1.5-3.5 mg/L pyridoxine

wherein the pH of the beverage is 3.3-7.0.

[0081] A beverage comprising:

(1) 3.33 mmol/L sodium citrate

(2) 5.0 mmol/L potassium citrate;

(3) 19.67 mmol/L citric acid;

(4) 2.0 mmol/L magnesium hydroxide; and

(5) 2.5 mg/L pyridoxine

wherein the pH of the beverage is 3.5.

[0082] A beverage comprising: 1.0 to 4.0 mmol/L sodium citrate; 3.0 to 7.5 mmol/L potassium citrate; 15 to 25 mmol/L citric acid; 1 to 3 mmol/L magnesium hydroxide; and 1.5-3.5 mg/L pyridoxine, wherein the pH of the beverage is 3.3-7.0 and wherein the beverage is calcium-free.

[0083] A beverage comprising: 1.0 to 4.0 mmol/L sodium citrate; 3.0 to 7.5 mmol/L potassium citrate; 15 to 25 mmol/L citric acid; 1 to 3 mmol/L magnesium hydroxide; and 1.5-3.5 mg/L pyridoxine, wherein the pH of the beverage is 3.3-7.0 and wherein the beverage is calorie-free.

[0084] A beverage comprising 3.33 mmol/L sodium citrate; 5.0 mmol/L potassium citrate; 19.67 mmol/L citric acid; 2.0 mmol/L magnesium hydroxide; and 2.5 mg/L pyridoxine, wherein the pH of the beverage is 3.5 and wherein the beverage is calcium-free.

[0085] A beverage comprising 3.33 mmol/L sodium citrate; 5.0 mmol/L potassium citrate; 19.67 mmol/L citric acid; 2.0 mmol/L magnesium hydroxide; and 2.5 mg/L pyridoxine, wherein the pH of the beverage is 3.5 and wherein the beverage is calorie-free

[0086] A method for increasing urinary citrate and reducing urinary oxalate by providing a beverage to an individual, said beverage comprising 1 to 4.0 mmol/L sodium citrate; 3.0 to 7.5 mmol/L potassium citrate; 15 to 25 mmol/L citric acid; 1 to 3 mmol/L magnesium hydroxide; and 1.5-3.5 mg/L pyridoxine, wherein the pH of the beverage is 3.3-7.0.

[0087] A method for increasing urinary citrate and reducing urinary oxalate by providing a beverage to an individual, said beverage comprising 3.33 mmol/L sodium citrate; 5.0 mmol/L potassium citrate; 19.67 mmol/L citric acid; 2.0 mmol/L magnesium hydroxide; and 2.5 mg/L pyridoxine, wherein the pH of the beverage is 3.5.

[0088] A method for management of kidney stones in a human in need thereof comprising administering a beverage to the human, said beverage comprising 1 to 4.0 mmol/L sodium citrate; 3.0 to 7.5 mmol/L potassium citrate; 15 to 25 mmol/L citric acid; 1 to 3 mmol/L magnesium hydroxide; and 1.5-3.5 mg/L pyridoxine, wherein the pH of the beverage is 3.3-7.0.

[0089] A method for management of kidney stones in a human in need thereof comprising administering a beverage to the human, said beverage comprising 3.33 mmol/L sodium citrate; 5.0 mmol/L potassium citrate; 19.67 mmol/L citric acid; 2.0 mmol/L magnesium hydroxide; and 2.5 mg/L pyridoxine, wherein the pH of the beverage is 3.5.

[0090] A method for management of bone disease in a human in need thereof comprising administering a beverage to the human, said beverage comprising 1 to 4.0 mmol/L sodium citrate; 3.0 to 7.5 mmol/L potassium citrate; 15 to 25 mmol/L citric acid; 1 to 3 mmol/L magnesium hydroxide; and 1.5-3.5 mg/L pyridoxine, wherein the pH of the beverage is 3.3-7.0

[0091] A method for management of bone disease in a human in need thereof comprising administering a beverage to the human, said beverage comprising 3.33 mmol/L sodium citrate; 5.0 mmol/L potassium citrate; 19.67 mmol/L citric acid; 2.0 mmol/L magnesium hydroxide; and 2.5 mg/L pyridoxine, wherein the pH of the beverage is 3.5.

[0092] A kit comprising a powdered mix a concentrate or a tablet comprising:

(a) sodium citrate, potassium citrate, citric acid, magnesium hydroxide, and pyridoxine in amounts such that a beverage prepared from it will have 1.0 to 4.0 mmol sodium citrate, 3.5 to 7.5 mmol potassium citrate, 15 to 25 mmol citric acid, 1 to 3 mmol magnesium hydroxide, and 1.5 to 3.5 mg pyridoxine per liter;

(b) packaging for a container;

(c) a container; and

(d) a set of instructions, said instructions describing how to prepare and store a beverage using the powdered mix or the tablet and describing the frequency and volume of the beverage to be consumed by an individual.

[0093] A kit comprising a powdered mix a concentrate or a tablet comprising:

(a) sodium citrate, potassium citrate, citric acid, magnesium hydroxide, and pyridoxine in amounts such that a beverage prepared from it will have 3.33 mmol sodium citrate, 5.0 mmol potassium citrate, 19.67 mmol citric acid, 2.0 mmol magnesium hydroxide, and 2.5 mg pyridoxine per liter;

(b) packaging for a container;

(c) a container; and

(d) a set of instructions, said instructions describing how to prepare and store a beverage using the powdered mix or the tablet and describing the frequency and volume of the beverage to be consumed by an individual.

[0094] A beverage concentrate comprising a urine citrate increasing component and a urine oxalate reducing component.

[0095] A beverage concentrate comprising a urine citrate increasing component and a urine oxalate reducing component wherein the urine increasing component is selected from the group consisting of sodium citrate, potassium citrate, magnesium citrate and combinations thereof.

[0096] The following examples are provided as illustrative examples and are not intended to be restrictive in any way.

EXAMPLE 1

[0097] This example provides results obtained from ingestion of the beverage on urine composition. A placebo controlled trial was performed in which 24 hour urine samples were collected while drinking 2 L of water (placebo) and then a subsequent 24-hour urine sample was collected while drinking 2 L of the present beverage. The protocol followed for the trial is shown in Figure 1. The Washout phase is between the placebo phase and the experimental phase. During the washout phase, the diet was ad lib (meaning the individuals consumed what they wanted.). The beverage had the following composition.

Sodium Citrate	3.33 mmol/liter
Potassium Citrate	5.0 mmol/liter
Citric Acid	19.67 mmol/liter
$Mg(OH)_2$	2.0 mmol/liter
Pyridoxine	2.5 mg/liter

[0098] The pH of the composition was 3.5. Ten participants have completed the trial and for each, significant increase in pH, citrate, and potassium and significant decrease in

calcium and supersaturation of uric acid (SSUA) was observed. Data (average values) are provided in the table below.

Urine Parameter	Placebo	Present formulation	Statistical significance
Calcium	206.1 mg/day	158.6 mg/day	0.04
Citrate	616.4 mg/day	945.1 mg/day	<0.0001
pH	6.33	6.97	0.0003
Supersaturation of uric acid (SSUA)	0.37	0.12	0.02
Potassium	74.7 mEq/day	96.7 mEq/day	0.001

[0099] It is considered that the increase in citrate and decrease in calcium both indicate that the drink decreases the likelihood of producing a calcium oxalate stone if given to a calcium stone former. The increase in pH and the decrease in SSUA indicate that the drink decreases the likelihood of making a uric acid stone if given to a uric acid stone former. The increase in pH indicates that the drink decreases the likelihood of producing a cystine stone if given to a cystine stone former. The increase in potassium indicates that the participants did "absorb" the potassium in the drink and were compliant during the trial (If they didn't drink the drink in the right amounts, the potassium would not have changed).

What is claimed is:

1. A beverage comprising sodium citrate, potassium citrate, citric acid, magnesium salt and pyridoxine.

2. The beverage of claim 1, wherein the pH of the beverage is from 3.3 to 7.0

3. The beverage of claim 1, wherein the magnesium salt is magnesium citrate or magnesium hydroxide.

4. The beverage of claim 1, wherein the ratio of potassium citrate to sodium citrate is 1.1:1.0, 1.2:1.0, or 1.3:1.0 to 1.7:1.0.

5. The beverage of claim 1, further comprising vitamins, minerals, phytate, amino acids, or combinations thereof.

6. The beverage of claim 1, wherein the beverage is calorie-free.

7. The beverage of claim 1, wherein the beverage is calcium-free.

8. The beverage of claim 1, wherein the beverage is calorie-free and calcium-free.

9. The beverage of claim 1, wherein the pH is from 3.4 to 3.7.

10. A beverage comprising:

(1) 1.0 to 4.0 mmol/L sodium citrate;

(2) 3.0 to 7.5 mmol/L potassium citrate;

(3) 15 to 25 mmol/L citric acid;

(4) 1 to 3 mmol/L magnesium hydroxide; and

(5) 1.5-3.5 mg/L pyridoxine,

wherein the pH of the beverage is 3.3-7.0.

11. The beverage of claim 10 where the pH is 3.4 to 3.7.

12. A beverage comprising:

(1) 3.33 mmol/L sodium citrate

(2) 5.0 mmol/L potassium citrate;

(3) 19.67 mmol/L citric acid;

(4) 2.0 mmol/L magnesium hydroxide; and

(5) 2.5 mg/L pyridoxine,

wherein the pH of the beverage is 3.5.

13. The beverage of claims 9 or 11 wherein the beverage is calcium-free.

14. The beverage of claims 9 or 11 wherein the beverage is calorie-free.

15. A method for management of kidney stone disease in a human in need thereof comprising administration of a beverage comprising sodium citrate, potassium citrate, citric acid, magnesium hydroxide and pyridoxine.

16. A method for increasing urinary citrate and/or reducing urinary oxalate by providing a beverage to an individual, said beverage comprising 1 to 4.0 mmol/L sodium citrate; 3.0 to 7.5 mmol/L potassium citrate; 15 to 25 mmol/L citric acid; 1 to 3 mmol/L magnesium hydroxide; and 1.5-3.5 mg/L pyridoxine, wherein the pH of the beverage is 3.3-7.0.

17. A method for increasing urinary citrate and/or reducing urinary oxalate by providing a beverage to an individual, said beverage comprising 3.33 mmol/L sodium citrate; 5.0 mmol/L potassium citrate; 19.67 mmol/L citric acid; 2.0 mmol/L magnesium hydroxide; and 2.5 mg/L pyridoxine, wherein the pH of the beverage is 3.5.

18. A method for management of kidney stones in a human in need thereof comprising administering a beverage to the human, said beverage comprising 1 to 4.0 mmol/L sodium citrate; 3.0 to 7.5 mmol/L potassium citrate; 15 to 25 mmol/L citric acid; 1 to 3 mmol/L magnesium hydroxide; and 1.5-3.5 mg/L pyridoxine, wherein the pH of the beverage is 3.3-7.0, wherein said beverage is provided in a volume of 1-2 liters for administration to the individual over a 24 hour period.

19. The method of claim 17, wherein the beverage comprises 3.33 mmol/L sodium citrate; 5.0 mmol/L potassium citrate; 19.67 mmol/L citric acid; 2.0 mmol/L magnesium hydroxide; and 2.5 mg/L pyridoxine, wherein the pH of the beverage is 3.5.

20. A kit comprising:

(a) a composition provided as a powdered mix, a concentrate or a tablet, said composition comprising sodium citrate, potassium citrate, citric acid, magnesium hydroxide, and pyridoxine in amounts such that a beverage prepared from it will have 1.0 to 4.0 mmol sodium citrate, 3.5 to 7.5 mmol potassium citrate, 15 to 25 mmol citric acid, 1 to 3 mmol magnesium hydroxide, and 1.5 to 3.5 mg pyridoxine per liter, and a pH of 3.3 to 7.0;

(b) a set of instructions, said instructions describing how to prepare a beverage using the powdered mix, concentrate or the tablet, and describing the frequency and volume of the beverage to be consumed by an individual.

21. The kit of claim 19, wherein the prepared beverage will have 3.33 mmol sodium citrate, 5.0 mmol potassium citrate, 19.67 mmol citric acid, 2.0 mmol magnesium hydroxide, and 2.5 mg pyridoxine per liter, and a pH of from 3.4 to 3.7.

22. A kit comprising:

a) a plurality of individually portioned powdered mixes, concentrate or tablet, wherein the contents of each portion when mixed with a preselected amount of water, will make a beverage having 1.0 to 4.0 mmol sodium citrate, 3.5 to 7.5 mmol potassium citrate, 15 to 25 mmol citric acid, 1 to 3 mmol magnesium hydroxide, and 1.5 to 3.5 mg pyridoxine per liter;

b) the preselected amount of water for making the beverage from the contents of each individual portion or instructions on how much water is required to make said beverage and directions for making said beverage.

23. The kit of claim 21, wherein each portion is present in a paper package, pouch, or blister package.

24. A beverage concentrate comprising sodium citrate, potassium citrate, citric acid, magnesium salt and pyridoxine.

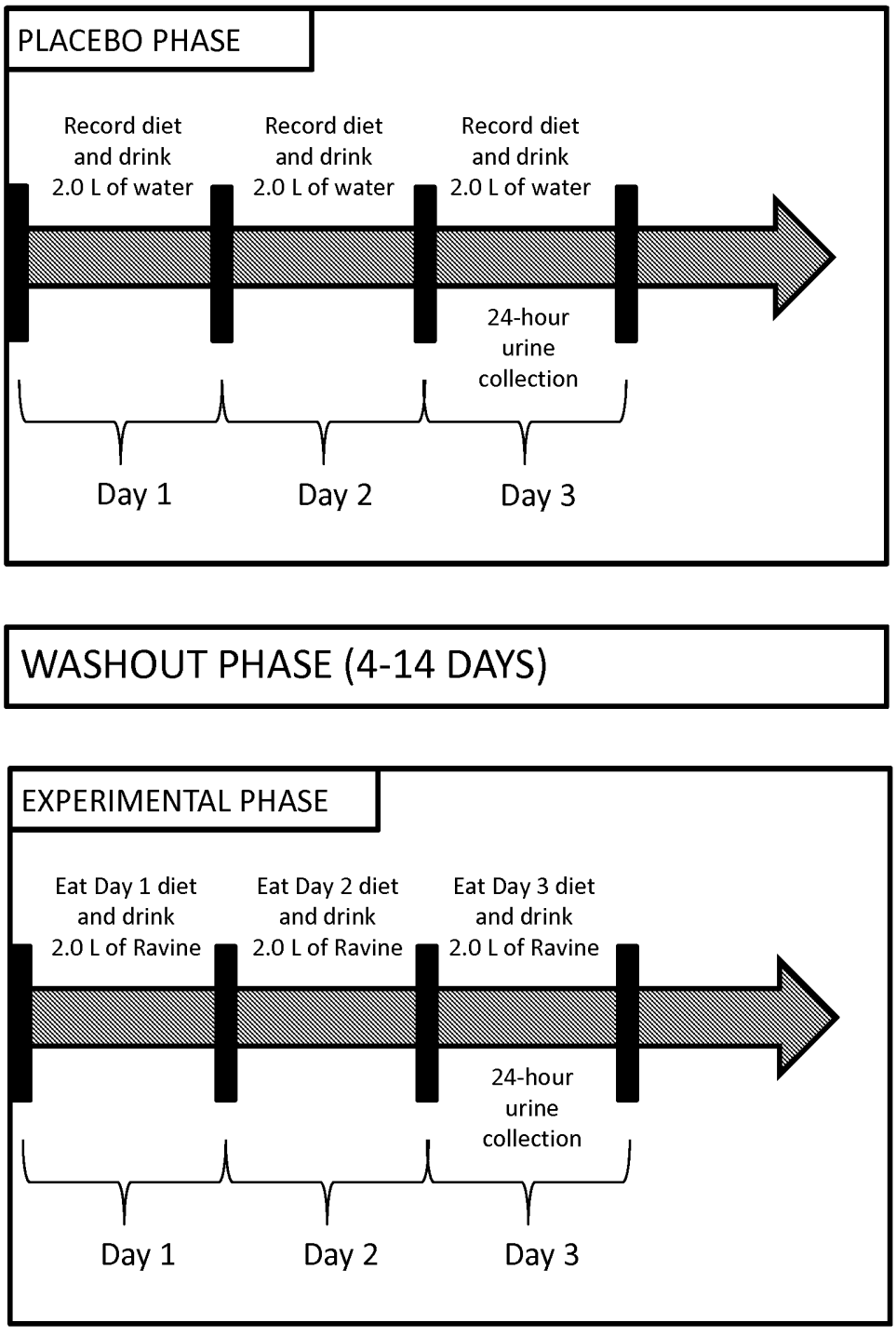
PLACEBO PHASE
Record diet and drink 2.0 L of water
Record diet and drink 2.0 L of water
Record diet and drink 2.0 L of water
24-hour urine collection
Day 1
Day 2
Day 3
WASHOUT PHASE (4-14 DAYS)
EXPERIMENTAL PHASE
Eat Day 1 diet and drink 2.0 L of Ravine
Eat Day 2 diet and drink 2.0 L of Ravine
Eat Day 3 diet and drink 2.0 L of Ravine
24-hour urine collection
Day 1
Day 2
Day 3

FIGURE 1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US14/27736

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61P 3/02, 3/14; A23L 2/385, 2/52, 1/304; A61K 31/19 (2014.01)
USPC - 514/891; 426/72, 74, 330.3, 590; 424/692, 677
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8): A61P 3/00, 3/02, 3/14; A23L 2/00, 2/385, 2/52, 1/304; A61K 31/19 (2014.01)
USPC: 514/891; 426/72, 74, 330.3, 590; 424/692, 677

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
MicroPatent (US-G, US-A, EP-A, EP-B, WO, JP-bib, DE-C,B, DE-A, DE-T, DE-U, GB-A, FR-A); ProQuest; IP.com; Google/Google Scholar; Key Words: beverage, drink, concentrate, powder*, sodium citrate, potassium citrate, magnesium hydroxide, citric acid, pyridoxine, vitamin B6, pH, mmol*, mM*, meq, mg, kidney, renal, stone*, calcium, calorie, administ*, kit, pouch*, instruction*, information

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	WO 2012/013975 A1 (MARTYN, GP) 02 February 2012; abstract; page 8, lines 12-26; page 13, lines 17-30; page 15, lines 17-18; page 18, lines 5-10, 14-16; page 21, lines 7-10;	1-5, 9, 24 --- 6-8, 10-12, 13/9, 13/11, 14/9, 14/11, 16-23
Y	US 2003/0203072 A1 (O'MAHONY, JS et al.) 30 October 2003; abstract; paragraph [0009]; table 1	6-8, 13/9, 13/11, 14/9, 14/11
Y	US 2005/0276839 A1 (RIFKIN, CH) 15 December 2005; table 1	10-12, 13/11, 14/11, 16-23
Y	US 4,966,776 A (PAK, CYC) 30 October 1990; abstract; figure 4; column 3, lines 50-55; column 4, lines 5-8; column 5, lines 24-35	15-17, 19
Y	US 5,108,767 A (MULCHANDANI, RP et al.) 28 April 1992; column 5, lines 14-16; table 1	15
Y	US 2001/0002269 A1 (ZHAO, IG) 31 May 2001; paragraph [0158]-[0159]; claim 16	18
Y	WO 01/93831 A2 (HEISEY, MT et al.) 13 December 2001; example 1	22-23
A	US 2007/0077314 A1 (PAK, CYC et al.) 05 April 2007; entire document	1-12, 13/9, 13/11, 14/9, 14/11, 15-24
A	US 2012/0128815 A1 (POULOS, SP et al.) 24 May 2012; entire document	1-12, 13/9, 13/11, 14/9, 14/11, 15-24

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
12 June 2014 (12.06.2014)	25 JUL 2014
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

(19)中华人民共和国国家知识产权局

(12)发明专利申请

(10)申请公布号 CN 105209120 A
(43)申请公布日 2015.12.30

(21)申请号 201480027995.9

(22)申请日 2014.03.14

(30)优先权数据
61/793,442 2013.03.15 US

(85)PCT国际申请进入国家阶段日
2015.11.13

(86)PCT国际申请的申请数据
PCT/US2014/027736 2014.03.14

(87)PCT国际申请的公布数据
WO2014/152789 EN 2014.09.25

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(51)Int.Cl.
A61P 3/02(2006.01)
A61P 3/14(2006.01)
A23L 2/385(2006.01)
A23L 2/52(2006.01)
A23L 1/304(2006.01)
A61K 31/19(2006.01)

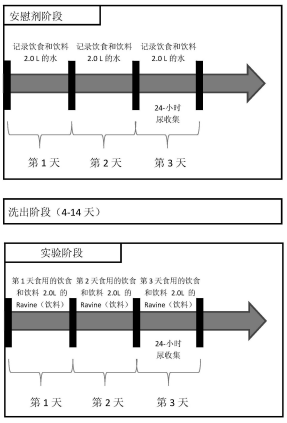
权利要求书2页 说明书10页 附图1页

(54)发明名称

含有柠檬酸盐的饮料

(57)摘要

提供了包括增加的尿柠檬酸盐组分和降低的尿草酸盐组分的饮料组合物。所述饮料组合物可以以立即可饮的形式提供,或者可以以浓缩的形式提供。还提供了包括所述饮料组合物的试剂盒以及用于利用所述饮料组合物治疗多种症状的方法。



CN 105209120 A

1.一种饮料，包括柠檬酸钠、柠檬酸钾、柠檬酸、镁盐和吡哆醇。

2.根据权利要求1所述的饮料，其中所述饮料的pH为3.3-7.0。

3.根据权利要求1所述的饮料，其中所述镁盐为柠檬酸镁或氢氧化镁。

4.根据权利要求1所述的饮料，其中柠檬酸钾与柠檬酸钠的比例为1.1:1.0、1.2:1.0、或1.3:1.0至1.7:1.0。

5.根据权利要求1所述的饮料，还包括维生素、矿物质、植酸盐、氨基酸或它们的组合。

6.根据权利要求1所述的饮料，其中所述饮料是无卡路里的。

7.根据权利要求1所述的饮料，其中所述饮料是无钙的。

8.根据权利要求1所述的饮料，其中所述饮料是无卡路里并且无钙的。

9.根据权利要求1所述的饮料，其中所述pH为3.4至3.7。

10.一种饮料，包括：

(1)1.0至4.0mmol/L的柠檬酸钠；

(2)3.0至7.5mmol/L的柠檬酸钾；

(3)15至25mmol/L的柠檬酸；

(4)1至3mmol/L的氢氧化镁；和

(5)1.5-3.5mg/L的吡哆醇，

其中所述饮料的所述pH为3.3-7.0。

11.根据权利要求10所述的饮料，其中所述pH为3.4至3.7。

12.一种饮料，包括：

(1)3.33mmol/L的柠檬酸钠；

(2)5.0mmol/L的柠檬酸钾；

(3)19.67mmol/L的柠檬酸；

(4)2.0mmol/L的氢氧化镁；和

(5)2.5mg/L的吡哆醇，

其中所述饮料的所述pH为3.5。

13.根据权利要求9或11所述的饮料，其中所述饮料是无钙的。

14.根据权利要求9或11所述的饮料，其中所述饮料是无卡路里的。

15.一种用于管理有需要的人类体内肾结石疾病的方法，包括给药包括柠檬酸钠、柠檬酸钾、柠檬酸、氢氧化镁和吡哆醇的饮料。

16.一种用于通过向个体提供饮料来增加尿柠檬酸盐和/或降低尿草酸盐的方法，所述饮料包括1至4.0mmol/L的柠檬酸钠；3.0至7.5mmol/L的柠檬酸钾；15至25mmol/L的柠檬酸；1至3mmol/L的氢氧化镁；和1.5-3.5mg/L的吡哆醇，其中所述饮料的所述pH为3.3-7.0。

17.一种用于通过向个体提供饮料来增加尿柠檬酸盐和/或降低尿草酸盐的方法，所述饮料包括3.33mmol/L的柠檬酸钠；5.0mmol/L的柠檬酸钾；19.67mmol/L的柠檬酸；2.0mmol/L的氢氧化镁；和2.5mg/L的吡哆醇，其中所述饮料的所述pH为3.5。

18.一种用于管理有需要的人类体内肾结石的方法，包括将饮料给药至所述人类，所述饮料包括1至4.0mmol/L的柠檬酸钠；3.0至7.5mmol/L的柠檬酸钾；15至25mmol/L的柠檬酸；1至3mmol/L的氢氧化镁；和1.5-3.5mg/L的吡哆醇，其中所述饮料的所述pH为

3.3-7.0，其中提供 1-2 升体积的所述饮料以用于在 24 小时的时间内向所述个体给药。

19. 根据权利要求 17 所述的方法，其中所述饮料包括 3.33mmol/L 的柠檬酸钠；5.0mmol/L 的柠檬酸钾；19.67mmol/L 的柠檬酸；2.0mmol/L 的氢氧化镁；和 2.5mg/L 的吡哆醇，其中所述饮料的所述 pH 为 3.5。

20. 一种试剂盒，包括：

(a) 以粉末状混合物、浓缩物或片剂提供的组合物，所述组合物包括柠檬酸钠、柠檬酸钾、柠檬酸、氢氧化镁和吡哆醇的量使得每升由它所制备的饮料会具有 1.0 至 4.0mmol 的柠檬酸钠、3.5 至 7.5mmol 的柠檬酸钾、15 至 25mmol 的柠檬酸、1 至 3mmol 的氢氧化镁和 1.5 至 3.5mg 的吡哆醇，并具有 3.3 至 7.0 的 pH；

(b) 一套指令，所述指令描述了如何利用所述粉末状混合物、浓缩物或所述片剂制备饮料，并描述了所述饮料被个体消耗的频率和体积。

21. 根据权利要求 19 所述的试剂盒，其中每升所制备的饮料会具有 3.33mmol 的柠檬酸钠、5.0mmol 的柠檬酸钾、19.67mmol 的柠檬酸、2.0mmol 的氢氧化镁和 2.5mg 的吡哆醇，并具有 3.4 至 3.7 的 pH。

22. 一种试剂盒，包括：

a) 多个独立分部分的粉末状混合物、浓缩物或片剂，其中当与预选量的水混合时，各个部分的内容物会使每升饮料具有 1.0 至 4.0mmol 的柠檬酸钠、3.5 至 7.5mmol 的柠檬酸钾、15 至 25mmol 的柠檬酸、1 至 3mmol 的氢氧化镁和 1.5 至 3.5mg 的吡哆醇；

b) 用于从各个独立部分的内容物制备所述饮料的所述预选量的水或制备所述饮料需要多少水的指令和用于制备所述饮料的指导。

23. 根据权利要求 21 所述的试剂盒，其中各个部分存在于纸包装、小袋、或泡罩包装。

24. 一种饮料浓缩物，包括柠檬酸钠、柠檬酸钾、柠檬酸、镁盐和吡哆醇。

含有柠檬酸盐的饮料

[0001] 相关申请的交叉引用

[0002] 本发明要求于 2013.03.15 提交的申请号为 61/793,442 的美国临时申请的优先权，该申请的公开在此通过引用将其全部内容引入。

背景技术

[0003] 肾结石是一生全球盛行的 5-10％发病率的常见原因。在缺乏预防的情况下，复发是常见的，超过 50％的患者在他们第一次结石的 5-10 年内具有结石复发症状。最常见的结石类型是草酸钙。可能发生的第二类结石是磷酸钙。钙基结石约占所有结石的 80％。至少 10％的结石由尿酸组成和大约 1％的结石（和儿童中的 6％的结石）由胱氨酸组成。

[0004] 虽然人们认为患者服从于调整他们的饮食习惯胜于服用处方药以预防各种症状，但目前还没有可用的旨在增加尿柠檬酸盐和 PH，同时降低尿钙的饮料。

发明内容

[0005] 本发明部分基于发明人的令人惊讶的和意想不到的发现，相比于现有的组合物，即按照本发明制备的且包括增加的尿柠檬酸盐组分和降低的尿草酸盐组分的饮料管理肾结石的方面具有改善的益处。本发明包含包括增加的尿柠檬酸盐组分和降低的尿草酸盐组分的饮料。本发明预期了可以立即饮用的饮料或者可选地由粉末状混合物、浓缩液（浓缩物）或片剂重组的饮料。

[0006] 在具体的实施方案中，所述增加的尿柠檬酸盐组分包括柠檬酸钠、柠檬酸钾或柠檬酸镁，或者它们的组合。在一个具体优选的实施方案中，本发明提供了一种饮料，其包括柠檬酸钠、柠檬酸钾、柠檬酸镁、柠檬酸、吡哆醇和它们的组合。

[0007] 在一些实施方案中，所述降低的草酸盐组分为镁盐。在一个具体优选的实施方案中，所述镁盐为氢氧化镁。

[0008] 在其他优选的实施方案中，所述降低的草酸盐组分选自由镁、吡哆醇和它们的组合组成的组。

[0009] 在一些实施方案中，本发明的饮料包括柠檬酸盐、镁和吡哆醇。

[0010] 在一些实施方案中，本发明的饮料还包括维生素、矿物质、植酸盐、氨基酸及它们的组合。

[0011] 在一个具体的实施方案中，本发明的饮料是无卡路里的。在另一个具体的实施方案中，本发明的饮料是无钙的。

[0012] 本发明包含用于管理有需要的人类体内肾结石疾病的方法，包括给药包括增加的尿柠檬酸盐组分和降低的尿草酸盐组分的饮料。

[0013] 在一些实施方案中，本发明包含用于管理有需要的人类体内骨疾病的方法，包括给药包括增加的尿柠檬酸盐组分和降低的尿草酸盐组分的饮料。

[0014] 在一个具体的实施方案中，按照本发明的饮料包括：1.0 至 4.0mmol/L 的柠檬酸钠；3.0 至 7.5mmol/L 的柠檬酸钾；15 至 25mmol/L 的柠檬酸；1 至 3mmol/L 的氢氧化镁；和

1.5-3.5mg/L 的吡哆醇，其中所述饮料的所述 pH 为 3.3-7.0。

[0015] 在另一个具体的实施方案中，按照本发明的饮料包括 :3.33mmol/L 的柠檬酸钠 ;5.0mmol/L 的柠檬酸钾 ;19.67mmol/L 的柠檬酸 ;2.0mmol/L 的氢氧化镁 ;和 2.5mg/L 的吡哆醇，其中所述饮料的所述 pH 为 3.5。

[0016] 本发明还包含用于通过向个体提供饮料来增加尿柠檬酸盐和降低尿草酸盐的方法，所述饮料包括 1 至 4.0mmol/L 的柠檬酸钠 ;3.0 至 7.5mmol/L 的柠檬酸钾 ;15 至 25mmol/L 的柠檬酸 ;1 至 3mmol/L 的氢氧化镁 ;和 1.5-3.5mg/L 的吡哆醇，其中所述饮料的所述 pH 为 3.3-7.0。

[0017] 在一个具体的实施方案中，本发明提供一种通过向个体提供饮料来增加尿柠檬酸盐和降低尿草酸盐的方法，所述饮料包括 3.33mmol/L 的柠檬酸钠 ;5.0mmol/L 的柠檬酸钾 ;19.67mmol/L 的柠檬酸 ;2.0mmol/L 的氢氧化镁 ;和 2.5mg/L 的吡哆醇，其中所述饮料的所述 pH 为 3.5。

[0018] 在另一个具体的实施方案中，本发明提供一种用于管理有需要的人类体内肾结石的方法，包括将饮料给药至所述人类，所述饮料包括 1 至 4.0mmol/L 的柠檬酸钠 ;3.0 至 7.5mmol/L 的柠檬酸钾 ;15 至 25mmol/L 的柠檬酸 ;1 至 3mmol/L 的氢氧化镁 ;和 1.5-3.5mg/L 的吡哆醇，其中所述饮料的所述 pH 为 3.3-7.0。

[0019] 在另一个具体的实施方案中，本发明提供一种用于管理有需要的人类体内肾结石的方法，包括将饮料给药至所述人类，所述饮料包括 3.33mmol/L 的柠檬酸钠 ;5.0mmol/L 的柠檬酸钾 ;19.67mmol/L 的柠檬酸 ;2.0mmol/L 的氢氧化镁 ;和 2.5mg/L 的吡哆醇，其中所述饮料的是所述 pH 为 3.5。

[0020] 在另一个具体的实施方案中，本发明提供一种用于管理有需要的人类体内骨疾病的方法，包括将饮料给药至所述人类，所述饮料包括 1 至 4.0mmol/L 的柠檬酸钠 ;3.0 至 7.5mmol/L 的柠檬酸钾 ;15 至 25mmol/L 的柠檬酸 ;1 至 3mmol/L 的氢氧化镁 ;和 1.5-3.5mg/L 的吡哆醇，其中所述饮料的所述 pH 为 3.3-7.0。

[0021] 在另一个具体的实施方案中，本发明提供一种用于管理有需要的人类体内骨疾病的方法，包括将饮料给药至所述人类，所述饮料包括 3.33mmol/L 的柠檬酸钠 ;5.0mmol/L 的柠檬酸钾 ;19.67mmol/L 的柠檬酸 ;2.0mmol/L 的氢氧化镁 ;和 2.5mg/L 的吡哆醇，其中所述饮料的所述 pH 为 3.5。

[0022] 本发明还提供一种包括粉末状混合物、浓缩物或片剂的试剂盒，包括 :

[0023] (a) 柠檬酸钠、柠檬酸钾、柠檬酸、氢氧化镁和吡哆醇的量使得每升由它所制备的饮料会具有 1.0 至 4.0mmol 的柠檬酸钠、3.5 至 7.5mmol 的柠檬酸钾、15 至 25mmol 的柠檬酸、1 至 3mmol 的氢氧化镁和 1.5 至 3.5mg 的吡哆醇 ;

[0024] (b) 用于容器的包装 ;

[0025] (c) 容器 ;和

[0026] (d) 一套指令，所述指令描述了如何利用粉末状混合物或片剂制备并储存饮料，并描述了所述饮料被个体消耗的频率和体积。

[0027] 在另一个具体的实施方案中，本发明提供一种包括粉末状混合物、浓缩物或片剂的试剂盒，包括 :

[0028] (a) 柠檬酸钠、柠檬酸钾、柠檬酸、氢氧化镁和吡哆醇的量使得每升由它所制备的

饮料会具有 3.33mmol 的柠檬酸钠 ;5.0mmol 的柠檬酸钾 ;19.67mmol 的柠檬酸 ;2.0mmol 的氢氧化镁 ;和 2.5mg 的吡哆醇 ;

[0029] (b) 用于容器的包装 ;

[0030] (c) 容器 ;和

[0031] (d) 一套指令,所述指令描述了如何利用粉末状混合物或片剂制备并储存饮料,并描述了所述饮料被个体消耗的频率和体积。

[0032] 在一个实施方案中,本发明提供了一种试剂盒,包括 :

[0033] (a) 粉末状混合物、浓缩物或片剂,该粉末混合物、浓缩物或片剂包括柠檬酸钠、柠檬酸钾、柠檬酸、氢氧化镁和吡哆醇的量使得每升由它所制备的饮料会具有 1.0 至 4.0mmol 的柠檬酸钠、3.5 至 7.5mmol 的柠檬酸钾、15 至 25mmol 的柠檬酸、1 至 3mmol 的氢氧化镁和 1.5 至 3.5mg 的吡哆醇 ;

[0034] (b) 一套指令,所述指令描述了如何利用粉末状混合物、浓缩物或片剂制备并储存饮料,并描述了所述饮料被个体消耗的频率和体积。

[0035] 在另一个实施方案中,本发明提供了一种试剂盒,包括 :

[0036] (a) 粉末状混合物、浓缩物或片剂,该粉末混合物、浓缩物或片剂包括柠檬酸钠、柠檬酸钾、柠檬酸、氢氧化镁和吡哆醇的量使得每升由它所制备的饮料会具有 3.33mmol 的柠檬酸钠 ;5.0mmol 的柠檬酸钾 ;19.67mmol 的柠檬酸 ;2.0mmol 的氢氧化镁 ;和 2.5mg 的吡哆醇 ;

[0037] (b) 一套指令,所述指令描述了如何利用粉末状混合物或片剂制备并储存饮料,并描述了所述饮料被个体消耗的频率和体积。

[0038] 在另一些实施方案中,所述试剂盒包括多个部分的粉末状混合物、浓缩物或片剂和预选量的水溶性溶液 (例如水) 以使各个部分的粉末状混合物、浓缩物或片剂当与预选量的水混合时会提供如本文各种实施方案中所描述的饮料。各个部分的粉末状混合物、浓缩物或片剂可以独立包装在试剂盒中。

[0039] 本发明的试剂盒被预期包括按照本发明所制成的可以立即饮用的饮料。

[0040] 本发明的其方面和优点将在以下描述中阐述,和部分地将从描述中变得明显,或者可以从实践如本文所阐述的本发明中获知。本发明的目的和优点可以通过在本文中特别指出的和在权利要求中指定的要素和组合来实现和获得。应当理解的是,前面的一般性描述和下面的详细描述都是示例性和解释性的,并不限制所要求保护的发明。

附图说明

[0041] 图 1 是用于测试消耗本发明饮料的效果的试验方案的示意图。

具体实施方式

[0042] 本发明提供了一种饮料,其包括向个体递送临床上显著的柠檬酸盐的量以预防或降低肾结石的发生。该饮料包括增加的尿柠檬酸盐组分和降低的尿草酸盐组分。该饮料的消耗提高了尿柠檬酸盐的水平、提高了尿的 pH,降低了尿草酸盐的水平。术语饮料 (beverage) 和饮料 (drink) 在本说明书中可交替地使用。在一个实施方案中,尿柠檬酸盐和 pH 值增加,而尿钙降低。

[0043] 在一个实施方案中，增加的尿柠檬酸盐组分包括、基本上由、或由柠檬酸钠、柠檬酸钾和柠檬酸组成，同时降低的尿草酸盐组分包括、基本上由、或由镁盐（如氢氧化镁）和吡哆醇组成。

[0044] 在一个实施方案中，本发明的饮料包括柠檬酸钠、柠檬酸钾、柠檬酸、氢氧化镁和吡哆醇。各成分存在的量使尿柠檬酸盐和 pH 值增加而不改变其他尿的化学物质。在一个实施方案中，柠檬酸盐可以是柠檬酸镁，而不是柠檬酸钠和柠檬酸钾或除了柠檬酸钠和柠檬酸钾之外还可以是柠檬酸镁。在一个实施方案中，柠檬酸盐包括、基本上由、或由柠檬酸钾和柠檬酸镁组成。

[0045] 尽管不希望受到任何特定理论的束缚，可以认为，钠阳离子改善适口性，并且还为高水平的柠檬酸盐提供递送载体，其并非仅仅与钾相关。在一个实施方案中，柠檬酸钠的量可以为从 0.5 到 5mmol/L 且其间的所有量到小数点第十位并包含其间的所有范围。在一个实施方案中，存在从 1.0 到 4.0mmol/L 的柠檬酸钠。在另一个实施方案中，存在从 3.0 到 3.5mmol/L 的柠檬酸钠。

[0046] 在一个实施方案中，所述饮料是无钠的。在这个实施方案中，所述饮料可以包括柠檬酸钾、任选柠檬酸镁、柠檬酸、氢氧化镁和吡哆醇。

[0047] 在一个实施方案中，存在的钾比钠多。然而，钾的水平不应为会导致高钾血症的水平。在一个实施方案中，柠檬酸钾的存在从 3.5 到 7.5mmol/L 且其间的所有量到小数点第十位并包含其间的所有范围。在另一个实施方案中，存在从 4.0 到 6.0mmol/L 的柠檬酸钾。在另一个实施方案中，存在从 4.5 到 5.5mmol/L 的柠檬酸钾。

[0048] 本发明的饮料还包括柠檬酸。在一个实施方案中，柠檬酸的量为从 15 到 25mmol/L 且其间的所有量到小数点第十位并包含其间的所有范围。在另一个实施方案中，存在从 17 到 23mmol/L 的柠檬酸。

[0049] 所述柠檬酸盐的量（由柠檬酸、柠檬酸钠和柠檬酸钾计算而来）为从 20 到 30mmol/L 且其间的所有量到小数点第十位并包含其间的所有范围。在一个实施方案中，存在从 23 到 27mmol/L 的所述柠檬酸盐。

[0050] 在一个实施方案中，钠与钾的比例为 1:1.1 到 1:2。在另一个实施方案中，其为从 1:1.3 到 1:1.7。在另一个实施方案中，其为从 1:1.4 到 1:1.6。

[0051] 为了进一步帮助预防或改善肾结石，本饮料含有镁化合物。镁是可以与尿中草酸盐结合并因此干扰草酸盐与钙络合的阳离子。在一个实施方案中，所述镁化合物为氢氧化镁。在一个实施方案中，除了氢氧化镁之外还可以利用柠檬酸镁，或以利用柠檬酸镁代替氢氧化镁。所述氢氧化镁的量为从 1 到 3mmol/L 且其间的所有量到小数点第十位并包含其间的所有范围。在一个实施方案中，氢氧化镁的量为从 1.5 到 2.5mmol/L。

[0052] 本发明饮料还包括吡哆醇（维生素 B6）。所述吡哆醇的量为从 1.5 到 3.5mg/L 且其间的所有量到小数点第十位并包含其间的所有范围。在一个实施方案中，该量为从 2 到 3mg/L。

[0053] 在一个实施方案中，本发明的饮料不包含钙。在其他实施方案中，其包含低于 0.1、0.05 或 0.01mmol/L 的钙。在一个实施方案中，钙可以更高 - 即高达 2.5mmol/L。

[0054] 将各成分混合后所述组合物的 pH 约为 3.5。其通常为从 3.4 到 3.7 且其间的所有值到小数点第十位。其可以上调至从 3.5 到 7.0 的 pH 且其间的所有值到小数点第十位并

包含其间的所有范围。在一个实施方案中，其为从 3.4 到 4.0。

[0055] 在一个实施方案中，所述饮料的卡路里含量低于 1。在一个实施方案中，所述卡路里含量为 0。在另一个实施方案中，所述饮料的卡路里低于 5（并因此可以被认为是“无卡路里”的）。在另一个实施方案中，其为低卡路里饮料。本文中所用的术语“低卡路里”意味着 40 卡路里或更低。在另一些实施方案中，所述卡路里含量从 1 到 40 卡路里及其间的所有的整数和范围。在另一些实施方案中，所述饮料可以具有高于 40 卡路里。

[0056] 可以根据需要向饮料中加入各种香料和 / 或颜色。在一个实施方案中，颜色、香料或其它添加剂不对饮料增加任何热量值也不改变如本文所述的钠、钾或柠檬酸盐参数。香料可以是天然的或人造的。合适的香料的示例包括柠檬、橙子、香蕉、草莓、其它水果、果汁饮料等。

[0057] 在一个实施方案中，本发明的组合物还可以包含维生素、矿物质、植酸盐和 / 或氨基酸或其他营养物质。合适的维生素包括维生素 B1、维生素 B2、烟酰胺、维生素 B12、叶酸、维生素 C 和维生素 E。合适的矿物质包括铁、锌、钒、硒、铬、硼、钾、锰、铜和镁。合适的氨基酸包括赖氨酸、异亮氨酸、亮氨酸、苏氨酸、缬氨酸、色氨酸、苯丙氨酸、甲硫氨酸和 L- 硒代蛋氨酸。此外，还可以包括润湿剂以改进口感。在一个实施方案中，所述饮料是透明饮料或半透明饮料。

[0058] 尽管不希望受到任何特定理论的束缚，可以认为，至少部分由于“柠檬酸盐作为碱”的作用，实现了尿柠檬酸盐的增加和 / 或尿钙的降低。本发明组合物的有机阳离子伴随有带正电荷的离子（阳离子），如钠或钾。因此，不是质子（如乙酸或柠檬酸的有机酸的情况下），羧基产生碳酸氢盐而不产生质子，并导致碱网的形成，它可以中和体内的其他质子，导致血液 pH 值和然后尿 pH 和尿柠檬酸盐的增加。因为血液中的碳酸氢盐很容易被肾脏排出，血液的 pH 值只有轻微的变化而尿 pH 将增加。我们称此为“柠檬酸盐作为碱”- 摄入的柠檬酸盐的形式，摄入的柠檬酸盐的形式导致增加的血液 pH 值、尿柠檬酸盐、尿 pH 和因此降低肾结石形成。

[0059] 在一个实施方案中，可以加入其他有助于增加尿 pH 的试剂。例如，可以加入苹果酸盐或有机阴离子。

[0060] 在一个实施方案中，本发明的饮料可以包含能够增强饮料的风味或外观而不影响尿中柠檬酸盐或草酸盐含量或钠于钾比例的试剂。这些试剂在本文中被称为“非活性”试剂。在一个实施方案中，所述非活性试剂不改变钠含量或钾含量。在一个实施方案中，所述非活性试剂不改变超过 0.1％的钠含量或钾含量。

[0061] 可以将所述饮料包装在合适的容器中，如包含高达 0.5、1 或 2 升部分的任何合适尺寸的瓶、罐、纸板包装等。可以将所述饮料无菌包装并常温（一般从 65 至 75F）或制冷温度下储存。

[0062] 在一个实施方案中，除了饮料以外，所有上述制剂可以以粉末状混合物、浓缩液（浓缩物）或片剂的形式提供。在一个实施方案中，本发明提供一种包括粉末状混合物、浓缩液或片剂的试剂盒，与合适的液体混合或稀释（如果其为浓缩物）后将该试剂盒提供本发明的饮料。所述试剂盒还可以包含一套用于由粉末状混合物、浓缩物或片剂制备饮料并用于（如在 24 小时期间）进行消耗的指令。该套指令可以提供 24 小时的时间内所消耗饮料的频率和量。该套指令还可以提供储存建议。可以将所述粉末状混合物、浓缩物或片

剂包装在合适的容器－如用于粉末状混合物的纸包装或包装袋，用于浓缩物的纸箱、瓶、容器、或盒子和用于片剂的泡罩包装。可以对所述粉末状混合物、浓缩物或片剂进行分份以使它们可以被制成预选体积的饮料。例如，可以对粉末状混合物、浓缩物或片剂进行分份以使其构成一夸脱、半升或一升的饮料。进一步地，试剂盒可以包含多袋粉末状混合物和一板或多板泡罩包装的片剂。术语片剂包含任何压缩形式的包含丸剂、囊片等的粉末状制剂。所述试剂盒还可以包含用于组成所述饮料的液体。例如，所述试剂盒可以包含测定量的用于加入粉末状混合物、浓缩物或片剂的液体。可以对包装进行划分以使粉末状混合物、浓缩物或片剂在一个隔室并且测定量的液体在其他隔室。这些隔室之间的隔板可以被刺穿或去除，使内容物暴露或未暴露到外部从而使两个隔室的内容物混合。该包装可以为容许日供、或周供或月供等而包装在一起的合适的部分。

[0063] 在一个实施方案中，本发明的饮料提供一种无卡路里并且无钙的饮料。可以在 24 小时的时间内便利地消耗掉 1 至 2 升的饮料以增加尿柠檬酸盐水平并降低尿草酸盐水平，而不影响其他化学物质。这种饮料对于已被诊断患有肾结石的个体来说，对于具有发展结石风险的个体来说，和通常对于预防肾结石的任何个体来说将是有用的。这种饮料还对如作为解渴的一般消耗来说是有用的。该饮料可以被人类消耗－所有年龄的成年人和儿童。其也可用于动物消耗。其可以用于需要增加尿柠檬酸盐水平、提高尿 pH 值或降低尿草酸盐水平的个体。其还可以用于不具有已知诊断疾病症状或包含患有骨疾病的个体在内的具有疾病症状（无论是否诊断）的个体。

[0064] 在一个实施方案中，本发明提供一种饮料，该饮料是消耗者感受器可以接受的，并且 1 升包装 / 容器的饮料向给消耗者提供 1 至 4mmol 的柠檬酸钠，4 至 6mmol 的柠檬酸钾，15 至 25mmol 的柠檬酸，1.5 至 3.5mg 的吡哆醇，和 1 至 3mmol 的氢氧化镁。在一个实施方案中，该 1 升饮料不包含任何其他的盐。在一个实施方案中，该 1 升饮料不包含任何其他钠盐或钾盐或任何其他柠檬酸盐，且不包含任何会改变尿中草酸盐量的其他试剂。可以向饮料中加入如颜料和香料的非活性试剂。所述饮料可以是无卡路里的、低卡路里的或者可以提供超过 40 卡路里。

[0065] 在另一个实施方案中，本发明提供一种饮料，该饮料对消耗者是感受器可以接受的，且 1 升包装 / 容器的饮料向消耗者提供 3 至 3.5mmol 的柠檬酸钠，4.5 至 5.5mmol 的柠檬酸钾，18 至 22mmol 的柠檬酸，2 至 3mg 的吡哆醇，和 1.5 至 2.5mmol 的氢氧化镁。在一个实施方案中，该 1 升饮料不包含任何其他钠盐或钾盐或任何其他柠檬酸盐，且不包含任何会改变尿中草酸盐量的其他试剂。然而，可以向饮料中加入如颜料和香料的非活性试剂。饮料可以是无卡路里的、低卡路里的或者可以提供超过 40 卡路里。

[0066] 本发明还提供了一种用于预防或降低肾结石发生的方法。该方法包括向个体提供足以降低或预防肾结石形成的量的本发明的饮料。可以认为本发明的饮料通过提高尿柠檬酸盐和尿 pH 来改变尿组合物以使尿不适合肾结石形成。本发明的饮料还降低了尿草酸盐水平。在一个实施方案中，个体每天 (24 小时时间) 消耗 1 至 2 升的饮料。

[0067] 本发明组合物还可以用于改善骨矿物质密度并因此用于治疗、预防或降低骨质疏松症、骨质降低和转移性骨癌。在一个实施方案中，所述组合物可以用于治疗、预防或降低慢性肾功能不全。

[0068] 在一个实施方案中，所述饮料可以包含从 0.1％至 10％的甜味剂且其间的所有百

分数到小数点第十位。这类甜味剂可以是营养性的和非营养性的，天然的和人工的或合成的。这种甜味剂是本领域众所周知的。

[0069] 在一些方面和实施方案中，本发明提供了以下：

[0070] 一种基本上由增加的尿柠檬酸盐组分和降低的尿草酸盐组分组成的无卡路里、无钙饮料。

[0071] 一种基本上由1.0至4.0mmol/L的柠檬酸钠、3.5至7.5的柠檬酸钾、15至25mmol/L的柠檬酸、1至3mmol/L的氢氧化镁和1.5至3.5mg/L的吡哆醇组成的无卡路里、无钙饮料，其中该饮料的pH为3.3-7.0。

[0072] 一种用于通过向个体提供饮料来增加尿柠檬酸盐和降低尿草酸盐的方法，所述饮料基本上由1.0至4.0mmol/L的柠檬酸钠、3.5至7.5的柠檬酸钾、15至25mmol/L的柠檬酸、1至3mmol/L的氢氧化镁和1.5至3.5mg/L的吡哆醇组成，其中所述饮料的pH为从3.3至7.0。

[0073] 一种通过向个体提供饮料来预防或降低肾结石的发生的方法，所述饮料包括增加的尿柠檬酸盐组分和降低的尿草酸盐组分，其中1-2升体积的所述饮料在24小时的时间内被个体消耗掉。

[0074] 一种试剂盒，包括：包装在容器中的粉末状混合物、浓缩物或片剂；和一套指令。每升粉末状混合物、浓缩物或片剂包括柠檬酸钠、柠檬酸钾、柠檬酸、氢氧化镁和吡哆醇的量使得由它所制备的饮料会具有1.0至4.0mmol的柠檬酸钠、3.5至7.5mmol的柠檬酸钾、15至25mmol的柠檬酸、1至3mmol的氢氧化镁和1.5至3.5mg的吡哆醇。所述指令描述了如何利用粉末状混合物或片剂如何制备并储存饮料，还描述了饮料被个体消耗的频率和体积。

[0075] 以下提供本发明的一些具体实施方案的示例：

[0076] 一种饮料，包括：增加的尿柠檬酸盐组分和降低的尿草酸盐组分。

[0077] 一种饮料，包括：增加的尿柠檬酸盐组分和降低的尿草酸盐组分，其中所述增加的尿柠檬酸盐组分包括柠檬酸钠。

[0078] 一种饮料，包括：增加的尿柠檬酸盐组分和降低的尿草酸盐组分，其中所述增加的尿柠檬酸盐组分包括柠檬酸钾。

[0079] 一种饮料，包括：增加的尿柠檬酸盐组分和降低的尿草酸盐组分，其中所述增加的尿柠檬酸盐组分包括柠檬酸镁。

[0080] 一种饮料，包括：增加的尿柠檬酸盐组分和降低的尿草酸盐组分，其中所述增加的尿柠檬酸盐组分选自由柠檬酸钠、柠檬酸钾、柠檬酸镁它们的组合组成的组。

[0081] 一种饮料，包括：柠檬酸钠、柠檬酸钾、柠檬酸镁、柠檬酸、吡哆醇和它们的组合。

[0082] 一种饮料，包括：增加的尿柠檬酸盐组分和降低的尿草酸盐组分，其中所述降低的尿草酸盐组分是镁盐。

[0083] 一种饮料，包括：增加的尿柠檬酸盐组分和降低的尿草酸盐组分，其中所述降低的尿草酸盐组分是镁盐并且其中所述镁盐是氢氧化镁。

[0084] 一种饮料，包括：增加的尿柠檬酸盐组分和降低的尿草酸盐组分，其中所述降低的尿草酸盐组分选自由镁、吡哆醇和它们的组合组合的组。

[0085] 一种饮料，包括：增加的尿柠檬酸盐组分和降低的尿草酸盐组分，还包括维生素、

矿物质、植酸盐、氨基酸和它们的组合。

[0086] 一种无卡路里饮料，包括：增加的尿柠檬酸盐组分和降低的尿草酸盐组分。

[0087] 一种无钙饮料，包括：增加的尿柠檬酸盐组分和降低的尿草酸盐组分。

[0088] 一种用于管理有需要的人类体内肾结石疾病的方法，包括：给药包括增加的尿柠檬酸盐组分和降低的尿草酸盐组分的饮料。

[0089] 一种用于管理有需要的人类体内骨疾病的方法，包括：给药包括增加的尿柠檬酸盐组分和降低的尿草酸盐组分的饮料。

[0090] 一种饮料，包括：柠檬酸盐、镁和吡哆醇。

[0091] 一种饮料，包括：柠檬酸盐、镁和吡哆醇，其中柠檬酸盐离子源选自由柠檬酸钠、柠檬酸钾、柠檬酸镁和它们的组合组成的组。

[0092] 一种饮料，包括：柠檬酸盐、镁和吡哆醇，其中镁源是氢氧化镁或柠檬酸镁。

[0093] 一种饮料，包括：

[0094] (1)1.0 至 4.0mmol/L 的柠檬酸钠；

[0095] (2)3.0 至 7.5mmol/L 的柠檬酸钾；

[0096] (3)15 至 25mmol/L 的柠檬酸；

[0097] (4)1 至 3mmol/L 的氢氧化镁；和

[0098] (5)1.5-3.5mg/L 的吡哆醇，

[0099] 其中所述饮料的 pH 为 3.3-7.0。

[0100] 一种饮料，包括：

[0101] (1)3.33mmol/L 的柠檬酸钠；

[0102] (2)5.0mmol/L 的柠檬酸钾；

[0103] (3)19.67mmol/L 的柠檬酸；

[0104] (4)2.0mmol/L 的氢氧化镁；和

[0105] (5)2.5mg/L 的吡哆醇，

[0106] 其中所述饮料的 pH 为 3.5。

[0107] 一种饮料，包括：1.0 至 4.0mmol/L 的柠檬酸钠；3.0 至 7.5mmol/L 的柠檬酸钾；15 至 25mmol/L 的柠檬酸；1 至 3mmol/L 的氢氧化镁；和 1.5-3.5mg/L 的吡哆醇，其中饮料的 pH 为 3.3-7.0 并且其中所述饮料是无钙的。

[0108] 一种饮料，包括：1.0 至 4.0mmol/L 的柠檬酸钠；3.0 至 7.5mmol/L 的柠檬酸钾；15 至 25mmol/L 的柠檬酸；1 至 3mmol/L 的氢氧化镁；和 1.5-3.5mg/L 的吡哆醇，其中所述饮料的 pH 为 3.3-7.0 并且其中所述饮料是无卡路里的。

[0109] 一种饮料，包括：3.33mmol/L 的柠檬酸钠；5.0mmol/L 的柠檬酸钾；19.67mmol/L 的柠檬酸；2.0mmol/L 的氢氧化镁；和 2.5mg/L 的吡哆醇，其中所述饮料的 pH 为 3.5 并且其中饮料是无钙的。

[0110] 一种饮料，包括：3.33mmol/L 的柠檬酸钠；5.0mmol/L 的柠檬酸钾；19.67mmol/L 的柠檬酸；2.0mmol/L 的氢氧化镁；和 2.5mg/L 的吡哆醇，其中所述饮料的 pH 为 3.5 并且其中饮料是无卡路里的。

[0111] 一种用于通过向个体提供饮料以增加尿柠檬酸盐和降低尿草酸盐的方法，所述饮料包括 1 至 4.0mmol/L 的柠檬酸钠；3.0 至 7.5mmol/L 的柠檬酸钾；15 至 25mmol/L 的柠檬

酸；1 至 3mmol/L 的氢氧化镁；和 1.5-3.5mg/L 的吡哆醇，其中所述饮料的 pH 为 3.3-7.0。

[0112] 一种用于通过向个体提供饮料以增加尿柠檬酸盐和降低尿草酸盐的方法，所述饮料包括 3.33mmol/L 的柠檬酸钠；5.0mmol/L 的柠檬酸钾；19.67mmol/L 的柠檬酸；2.0mmol/L 的氢氧化镁；和 2.5mg/L 的吡哆醇，其中所述饮料的 pH 为 3.5。

[0113] 一种用于管理有需要的人类体内肾结石的方法，包括将饮料给药至所述人类，所述饮料包括 1 至 4.0mmol/L 的柠檬酸钠；3.0 至 7.5mmol/L 的柠檬酸钾；15 至 25mmol/L 的柠檬酸；1 至 3mmol/L 的氢氧化镁；和 1.5-3.5mg/L 的吡哆醇，其中所述饮料的 pH 为 3.3-7.0。

[0114] 一种用于管理有需要的人类体内肾结石的方法，包括将饮料给药至所述人类，所述饮料包括 3.33mmol/L 的柠檬酸钠；5.0mmol/L 的柠檬酸钾；19.67mmol/L 的柠檬酸；2.0mmol/L 的氢氧化镁；和 2.5mg/L 的吡哆醇，其中所述饮料的 pH 为 3.5。

[0115] 一种用于管理有需要人类体内骨疾病的方法，包括将饮料给药至所述人类，所述饮料包括 1 至 4.0mmol/L 的柠檬酸钠；3.0 至 7.5mmol/L 的柠檬酸钾；15 至 25mmol/L 的柠檬酸；1 至 3mmol/L 的氢氧化镁；和 1.5-3.5mg/L 的吡哆醇，其中所述饮料的 pH 为 3.3-7.0。

[0116] 一种用于管理有需要的人类体内骨疾病的方法，包括将饮料给药至所述人类，所述饮料包括 3.33mmol/L 的柠檬酸钠；5.0mmol/L 的柠檬酸钾；19.67mmol/L 的柠檬酸；2.0mmol/L 的氢氧化镁；和 2.5mg/L 的吡哆醇，其中所述饮料的 pH 为 3.5。

[0117] 一种包括粉末状混合物、浓缩物或片剂的试剂盒，包括：

[0118] (a) 每升柠檬酸钠、柠檬酸钾、柠檬酸、氢氧化镁和吡哆醇的量使得由它所制备的饮料会具有 1.0 至 4.0mmol 的柠檬酸钠、3.5 至 7.5mmol 的柠檬酸钾、15 至 25mmol 的柠檬酸、1 至 3mmol 的氢氧化镁和 1.5 至 3.5mg 的吡哆醇；

[0119] (b) 用于容器的包装；

[0120] (c) 容器；和

[0121] (d) 一套指令，所述指令描述了如何利用粉末状混合物或片剂制备并储存饮料，并描述了所述饮料被个体消耗的频率和体积。

[0122] 一种包括粉末状混合物、浓缩物或片剂的试剂盒，包括：

[0123] (a) 每升柠檬酸钠、柠檬酸钾、柠檬酸、氢氧化镁和吡哆醇的量使得由它所制备的饮料会具有 3.33mmol 的柠檬酸钠；5.0mmol 的柠檬酸钾；19.67mmol 的柠檬酸；2.0mmol 的氢氧化镁；和 2.5mg 的吡哆醇；

[0124] (b) 用于容器的包装；

[0125] (c) 容器；和

[0126] (d) 一套指令，所述指令描述了如何利用粉末状混合物或片剂制备并储存饮料，并描述了饮料被个体消耗的频率和体积。

[0127] 一种饮料浓缩物，包括：增加的尿柠檬酸盐组分和降低的尿草酸盐组分。

[0128] 一种饮料浓缩物，包括：增加的尿柠檬酸盐组分和降低的尿草酸盐组分，其中所述增加的尿柠檬酸盐组分选自由柠檬酸钠、柠檬酸钾、柠檬酸镁和它们的组合组成的组。

[0129] 提供下列示例作为示例性的例子，且在任何情况下是不是限制性的。

[0130] 示例 1

[0131] 这个示例提供了从饮料的摄入得到的有关尿组合物的结果。进行了安慰剂对照试验，在该安慰剂对照试验中，饮用 2 升的水（安慰剂）时的同时收集 24 小时的尿样，然后饮

用 2 升的本发明的饮料，随后收集 24 小时尿样。图 1 中显示了遵循该试验的方案。洗出阶段在安慰剂阶段和实验阶段之间。在洗出阶段的过程，进行无限制饮食（意味着个体消耗他们想要的。）。所述饮料具有下列成分。

[0132]

柠檬酸钠	3.33 mmol/L
柠檬酸钾	5.0 mmol/L
柠檬酸	19.67 mmol/L
$Mg(OH)_2$	2.0 mmol/L
吡哆醇	2.5 mg/ L

[0133] 所述组合物的 pH 为 3.5。已经对十名参与者完成了试验，且对于每个参与者，观察到 pH 值、柠檬酸盐和钾显著增加，钙和尿酸过饱和 (SSUA) 显著下降。下表中提供了数据（平均值）。

[0134]

尿参数	安慰剂	本配方	统计学意义
钙	206.1 毫克/天	158.6 毫克/天	0.04
柠檬酸盐	616.4 毫克/天	945.1 毫克/天	<0.0001
pH	6.33	6.97	0.0003
尿酸过饱和 (SSUA)	0.37	0.12	0.02
钾	74.7 毫克当量/天	96.7 毫克当量/天	0.001

[0135] 可以认为，如果给定钙结石样板 (former)，柠檬酸盐的增加和钙的降低均表明所述饮料降低了产生草酸钙结石的可能性。如果给定尿酸结石样板，pH 的增加和 SSUA 的降低表明所述饮料降低了形成尿酸结石的可能性。如果给定胱氨酸结石样板，pH 的增加表明所述饮料降低了形成胱氨酸结石的可能性。钾的增加表明参与者的确“吸收”所述饮料中钾，并且这些参与者在试验过程中是顺从的（如果他们没有按正确量饮用饮料，钾不会改变）。

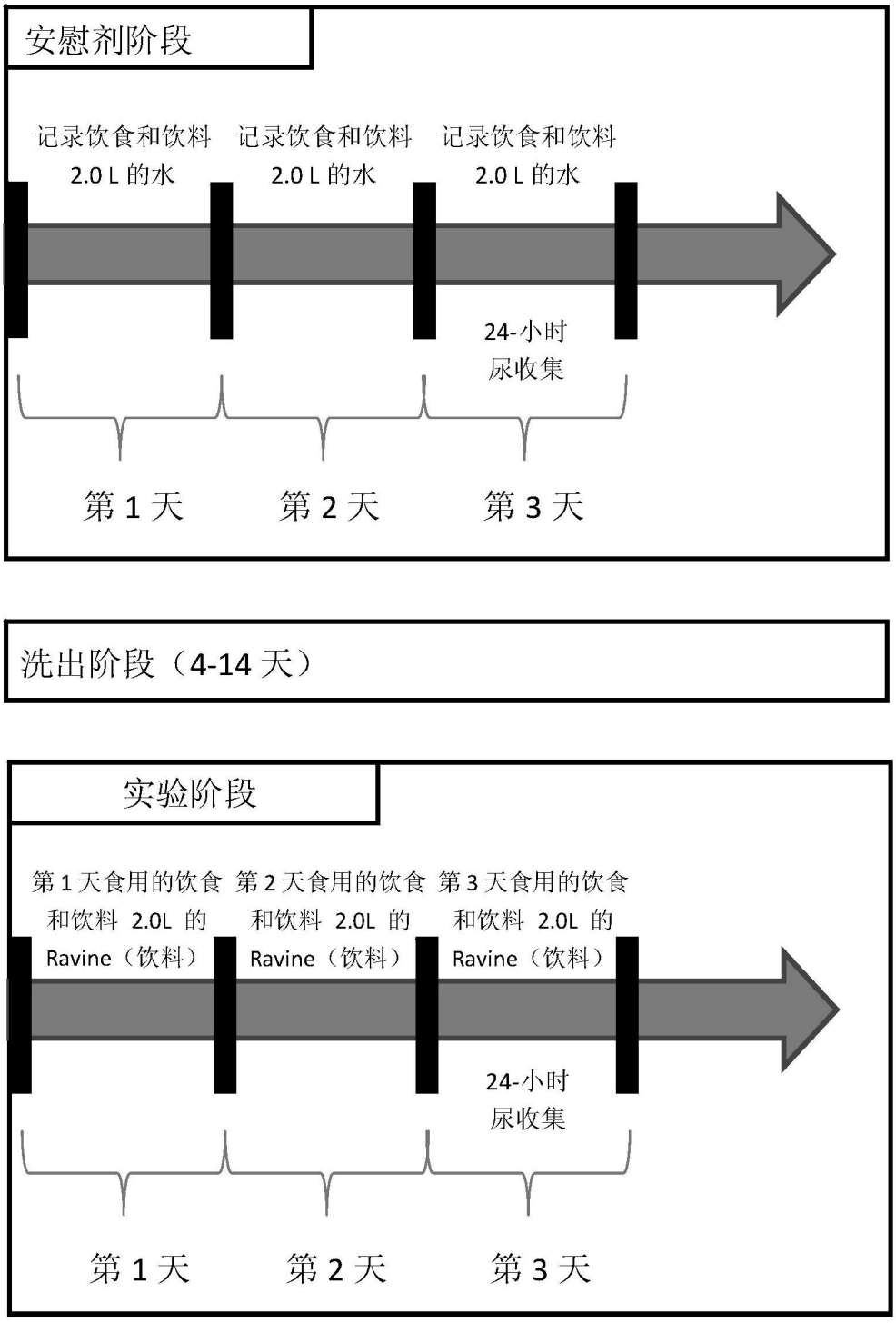

安慰剂阶段
记录饮食和饮料
2.0 L 的水
记录饮食和饮料
2.0 L 的水
记录饮食和饮料
2.0 L 的水
24-小时
尿收集
第 1 天
第 2 天
第 3 天
洗出阶段（4-14 天）
实验阶段
第 1 天食用的饮食
和饮料 2.0L 的
Ravine（饮料）
第 2 天食用的饮食
和饮料 2.0L 的
Ravine（饮料）
第 3 天食用的饮食
和饮料 2.0L 的
Ravine（饮料）
24-小时
尿收集
第 1 天
第 2 天
第 3 天

图 1

Abstract

Provided are beverage compositions comprising an increased urine citrate component and a reduced urine oxalate component. The beverage compositions may be provided in a ready-to-drink form or may be provided in a concentrate form. Also provided are kits comprising the beverage compositions and methods for treating various conditions by using the beverage compositions.