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(71) Applicants: **NEW YORK UNIVERSITY** [US/US]; 70 Washington Square S., New York, NY 10012 (US). **GENERAL HOSPITAL CORPORATION** [US/US]; 55 Fruit Street, Boston, MA 02114 (US). **THE REGENTS OF THE UNIVERSITY OF CALIFORNIA** [US/US]; 1111 Franklin Street, Twelfth Floor, Oakland, CA 94607-5200 (US).

(72) Inventors: **GOLDFARB, David, S.**; 11 Ravine Drive, Hastings-on-hudson, NY 10706 (US). **EISNER, Brian**; 60 Parker Road, Needham, MA 02494 (US). **ASPLIN, John**; 2014 N. Honore Street, Chicago, IL 60614 (US). **STOLLER, Marshall, L.**; 50 Lopez Avenue, San Francisco, CA 94116 (US).

(74) Agents: **WATT, Rachel, S.** et al.; Hodgson Russ LLP, The Guaranty Building, 140 Pearl Street, Suite 100, Buffalo, NY 14202-4040 (US).

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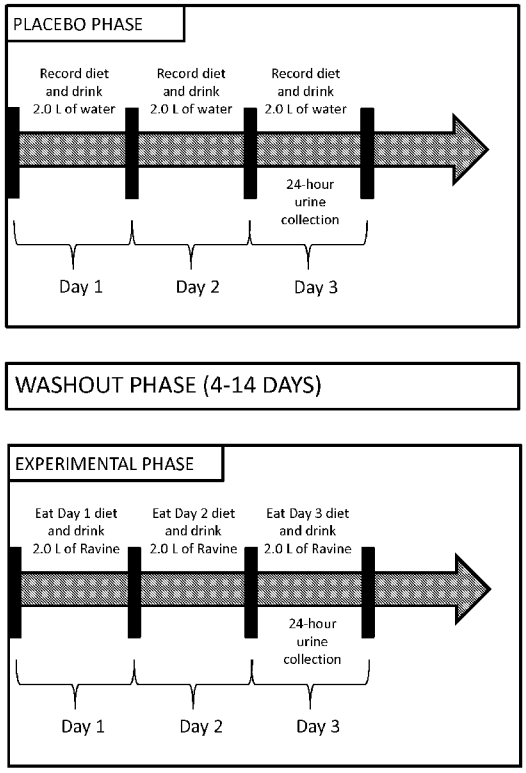

FIGURE 1

(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.

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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.

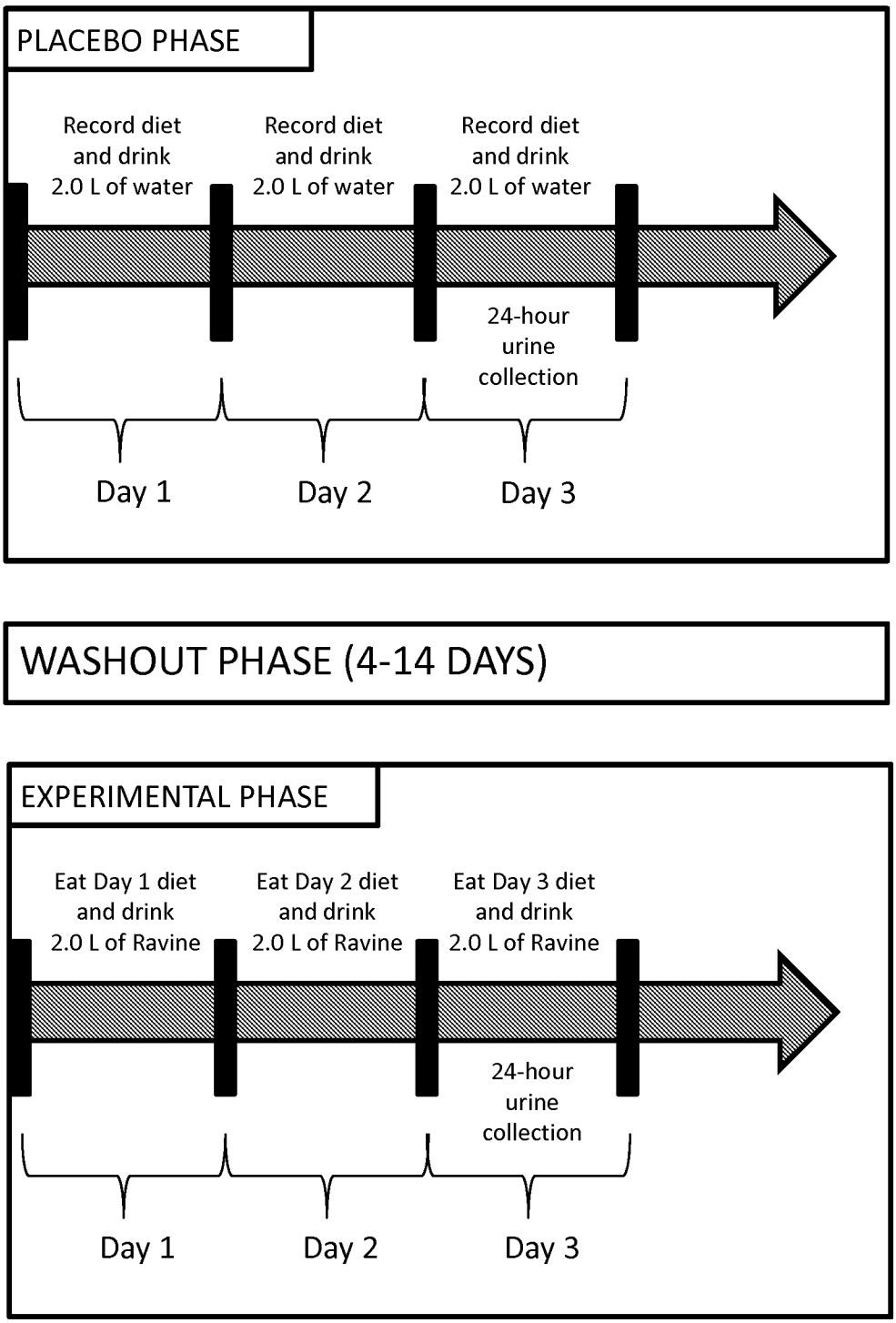
PLACEBO PHASE
Record diet and drink 2.0 L of water
Record diet and drink 2.0 L of water
Record diet and drink 2.0 L of water
24-hour urine collection
Day 1
Day 2
Day 3
WASHOUT PHASE (4-14 DAYS)
EXPERIMENTAL PHASE
Eat Day 1 diet and drink 2.0 L of Ravine
Eat Day 2 diet and drink 2.0 L of Ravine
Eat Day 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
12 June 2014 (12.06.2014)

Date of mailing of the international search report
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