US009233135B1

(12) **United States Patent**
Hayer et al.

(10) **Patent No.: US 9,233,135 B1**
(45) **Date of Patent: Jan. 12, 2016**

(54) **COMPOSITIONS AND METHODS TO INHIBIT KIDNEY STONE GROWTH**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **14/845,612**

(22) Filed: **Sep. 4, 2015**

(51) **Int. Cl.**

A61K 36/00	(2006.01)
A61K 36/88	(2006.01)
A61K 31/194	(2006.01)
A61K 31/6615	(2006.01)
A61K 31/4415	(2006.01)
A61K 9/00	(2006.01)

(52) **U.S. Cl.**
CPC ***A61K 36/88*** (2013.01); ***A61K 9/0053*** (2013.01); ***A61K 31/194*** (2013.01); ***A61K 31/4415*** (2013.01); ***A61K 31/6615*** (2013.01)

(58) **Field of Classification Search**
None
See application file for complete search history.

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(57) **ABSTRACT**

An oral dosage form or plurality of oral dosage forms comprising as active ingredients citric acid, magnesium citrate, phytin, pyridoxine, and musa is disclosed. The oral dosage form(s) is useful for inhibiting calcium oxalate crystal growth and for treating or inhibiting growth of kidney stones. Methods of inhibiting calcium oxalate crystal growth and of treating or preventing kidney stones are also disclosed.

7 Claims, 29 Drawing Sheets

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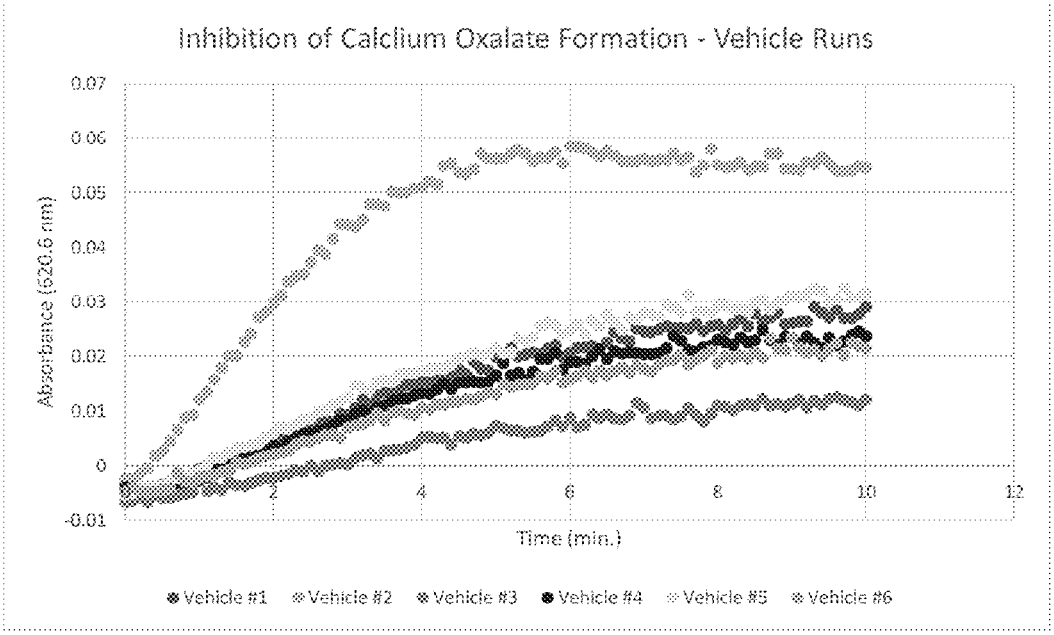
Fig. 1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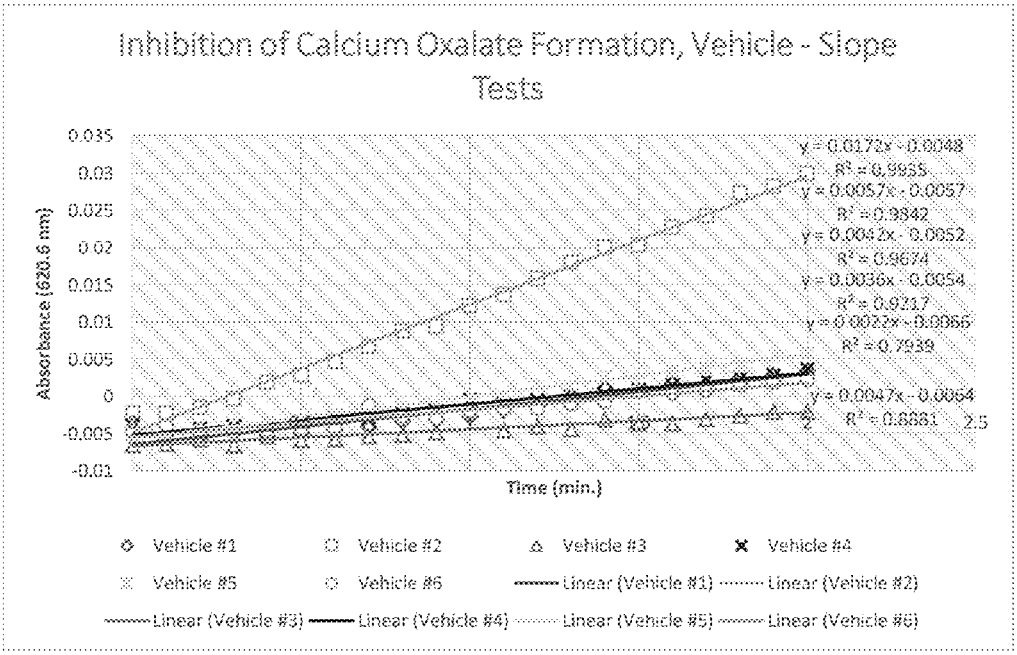
0.06
0.05
0.04
0.03
0.02
0.01
0
-0.01
2
4
6
8
10
12
Time (min.)
Vehicle #1
Vehicle #2
Vehicle #3
Vehicle #4
Vehicle #5
Vehicle #6

Fig. 2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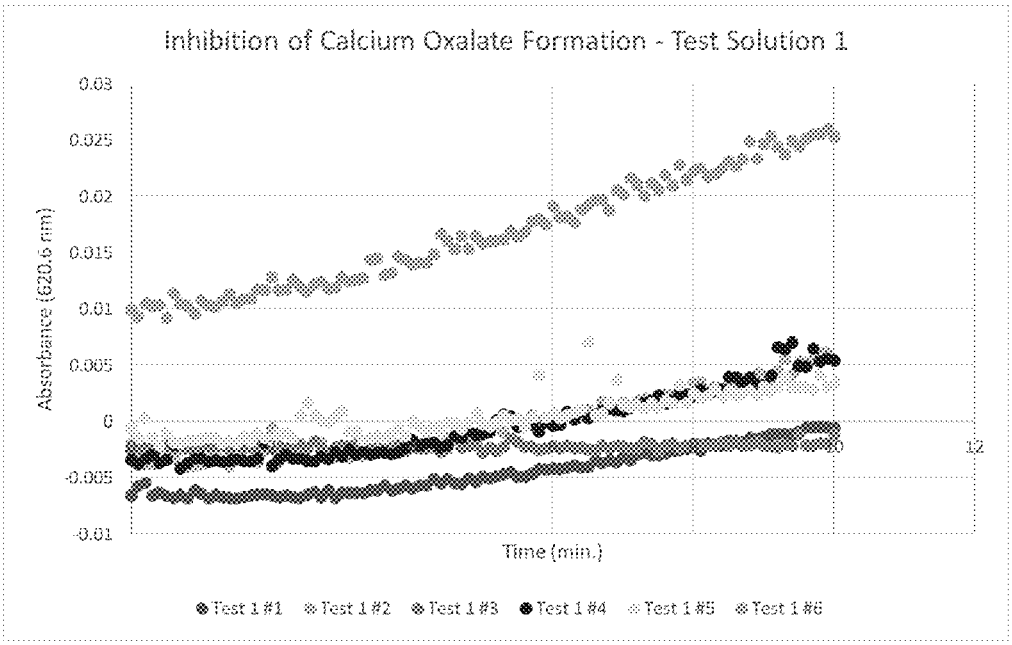
Absorbance (620.6 nm)
0.035
0.03
0.025
0.02
0.015
0.01
0.005
0
-0.005
-0.01
y = 0.0172x - 0.0048
R² = 0.9935
y = 0.0057x - 0.0057
R² = 0.9842
y = 0.0042x - 0.0052
R² = 0.9674
y = 0.0036x - 0.0054
R² = 0.9217
y = 0.0022x - 0.0066
R² = 0.7939
y = 0.0047x - 0.0064
R² = 0.8681
2.5
Time (min.)
Vehicle #1
Vehicle #2
Vehicle #3
Vehicle #4
Vehicle #5
Vehicle #6
Linear (Vehicle #1)
Linear (Vehicle #2)
Linear (Vehicle #3)
Linear (Vehicle #4)
Linear (Vehicle #5)
Linear (Vehicle #6)

Fig. 3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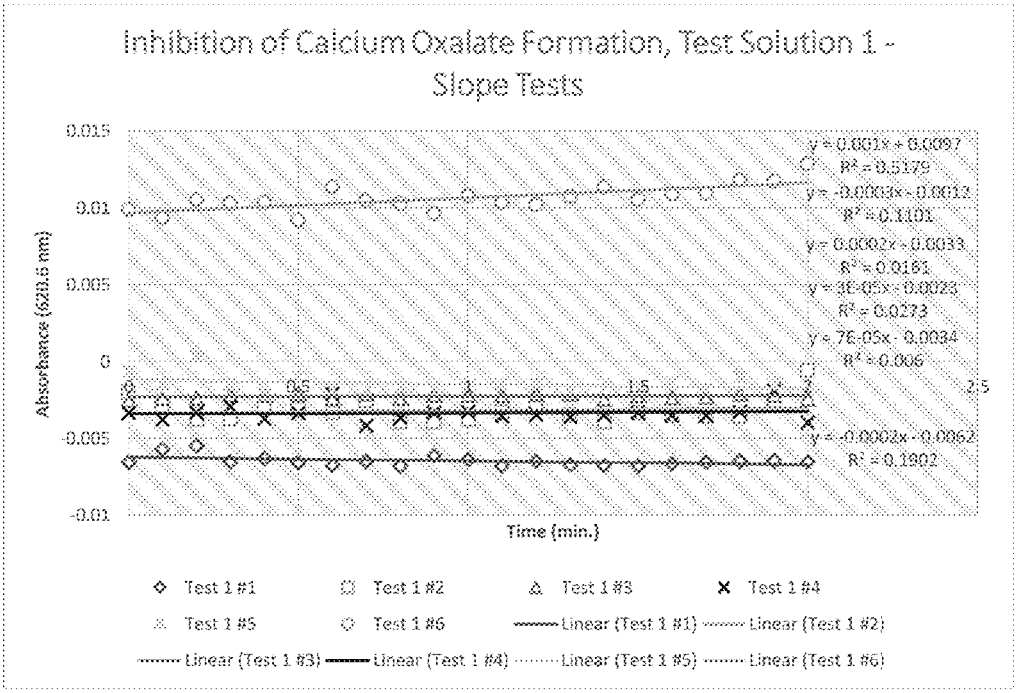
0.025
0.02
0.015
0.01
0.005
0
-0.005
-0.01
Time (min.)
12
Test 1 #1
Test 1 #2
Test 1 #3
Test 1 #4
Test 1 #5
Test 1 #6

Fig. 4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Time (min.)
0.015
0.01
0.005
0
-0.005
-0.01
0
0.5
1
1.5
2
2.5
y = 0.001x + 0.0097
R² = 0.5179
y = -0.0003x - 0.0012
R² = 0.1101
y = 0.0002x + 0.0033
R² = 0.0161
y = 3E-05x + 0.0023
R² = 0.0273
y = 7E-05x - 0.0034
R² = 0.006
y = -0.0002x - 0.0062
R² = 0.1902
Test 1 #1
Test 1 #2
Test 1 #3
Test 1 #4
Test 1 #5
Test 1 #6
Linear (Test 1 #1)
Linear (Test 1 #2)
Linear (Test 1 #3)
Linear (Test 1 #4)
Linear (Test 1 #5)
Linear (Test 1 #6)

Fig. 5

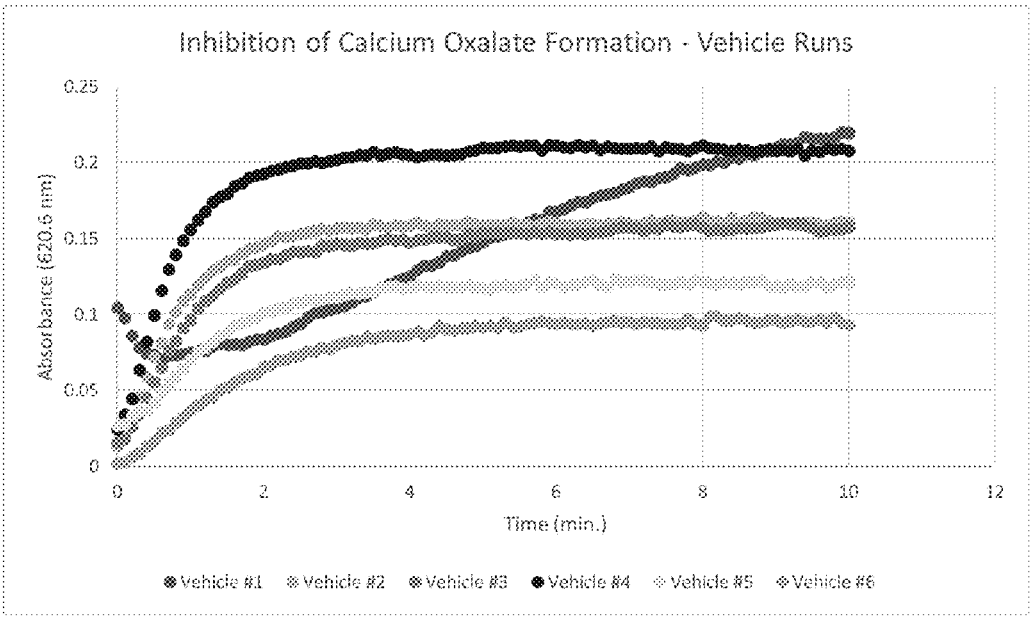

Inhibition of Calcium Oxalate Formation - Vehicle Runs
Absorbance (620.6 nm)
0.25
0.2
0.15
0.1
0.05
0
0
2
4
6
8
10
12
Time (min.)
Vehicle #1
Vehicle #2
Vehicle #3
Vehicle #4
Vehicle #5
Vehicle #6

Fig. 6

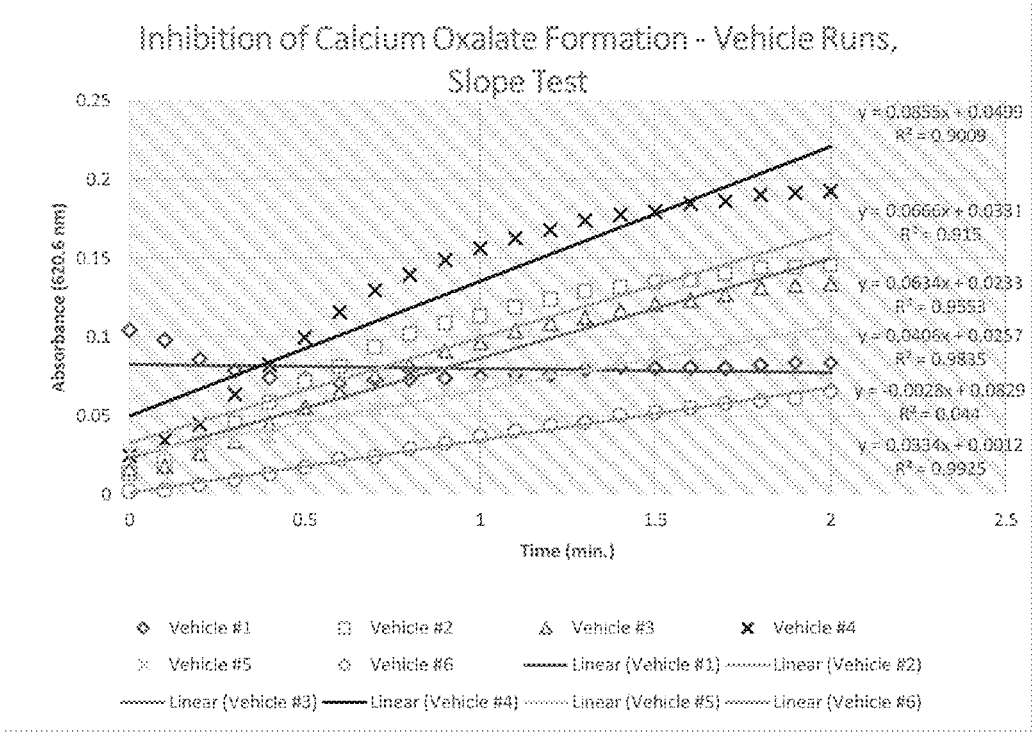
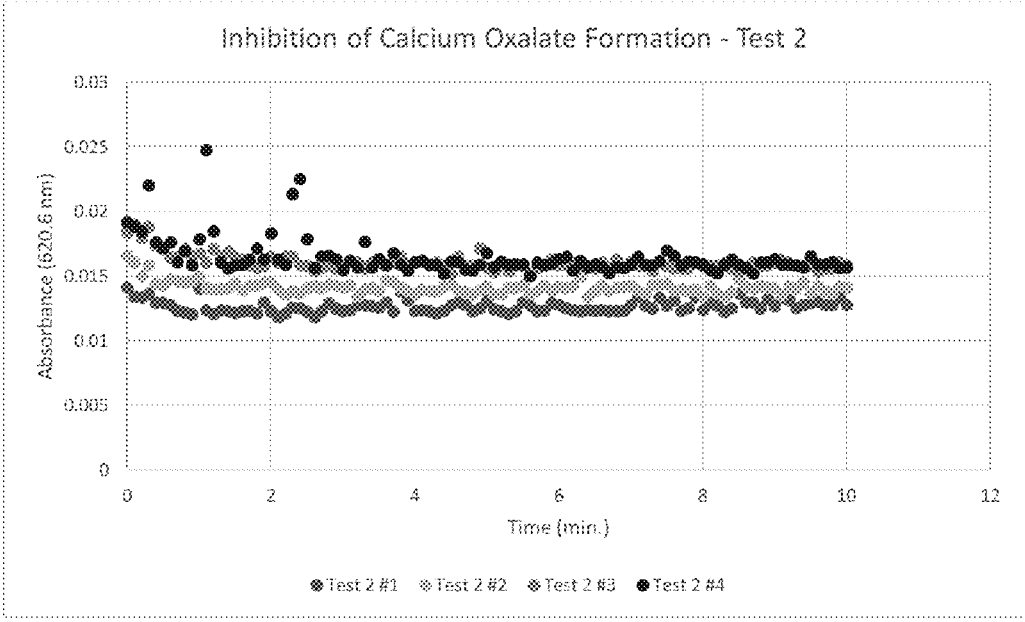

Inhibition of Calcium Oxalate Formation - Vehicle Runs, Slope Test
Absorbance (620.6 nm)
Time (min.)
0.25
0.2
0.15
0.1
0.05
0
0
0.5
1
1.5
2
2.5
y = 0.0855x + 0.0409
R² = 0.9009
y = 0.0666x + 0.0331
R² = 0.915
y = 0.0634x + 0.0233
R² = 0.9553
y = 0.0406x + 0.0257
R² = 0.9835
y = 0.0028x + 0.0829
R² = 0.044
y = 0.0334x + 0.0012
R² = 0.9925
Vehicle #1
Vehicle #2
Vehicle #3
Vehicle #4
Vehicle #5
Vehicle #6
Linear (Vehicle #1)
Linear (Vehicle #2)
Linear (Vehicle #3)
Linear (Vehicle #4)
Linear (Vehicle #5)
Linear (Vehicle #6)

Fig. 7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Absorbance (620.6 nm)
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0.025
0.02
0.015
0.01
0.005
0
0
2
4
6
8
10
12
Time (min.)
Test 2 #1
Test 2 #2
Test 2 #3
Test 2 #4

Fig. 8

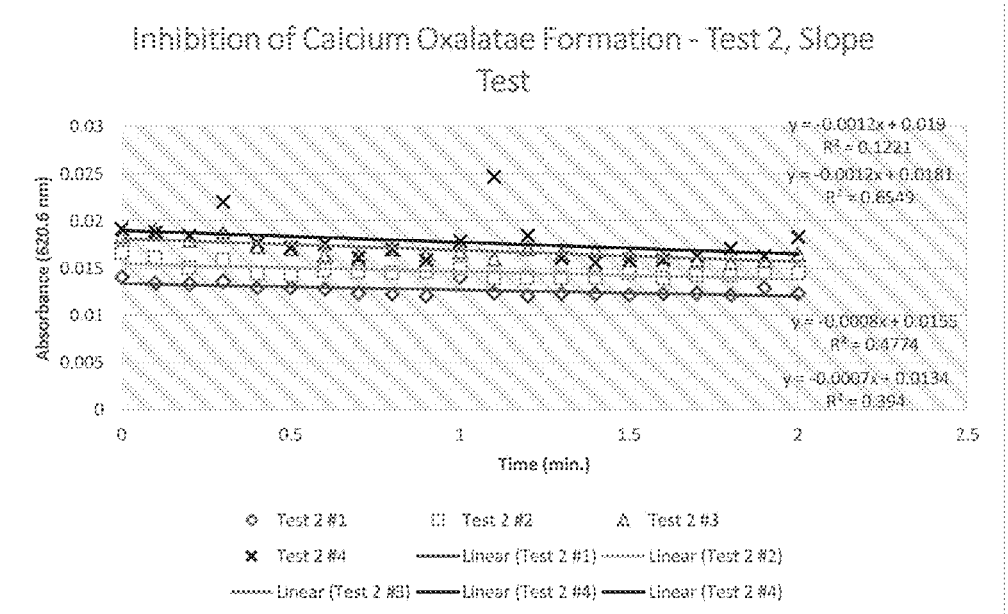

Inhibition of Calcium Oxalatae Formation - Test 2, Slope Test
Absorbance (620.6 nm)
Time (min.)
0.03
0.025
0.02
0.015
0.01
0.005
0
0
0.5
1
1.5
2
2.5
y = -0.0012x + 0.019
R² = 0.1221
y = -0.0012x + 0.0181
R² = 0.6549
y = -0.0008x + 0.0155
R² = 0.4774
y = -0.0007x + 0.0134
R² = 0.394
Test 2 #1
Test 2 #2
Test 2 #3
Test 2 #4
Linear (Test 2 #1)
Linear (Test 2 #2)
Linear (Test 2 #3)
Linear (Test 2 #4)
Linear (Test 2 #4)

Fig. 9

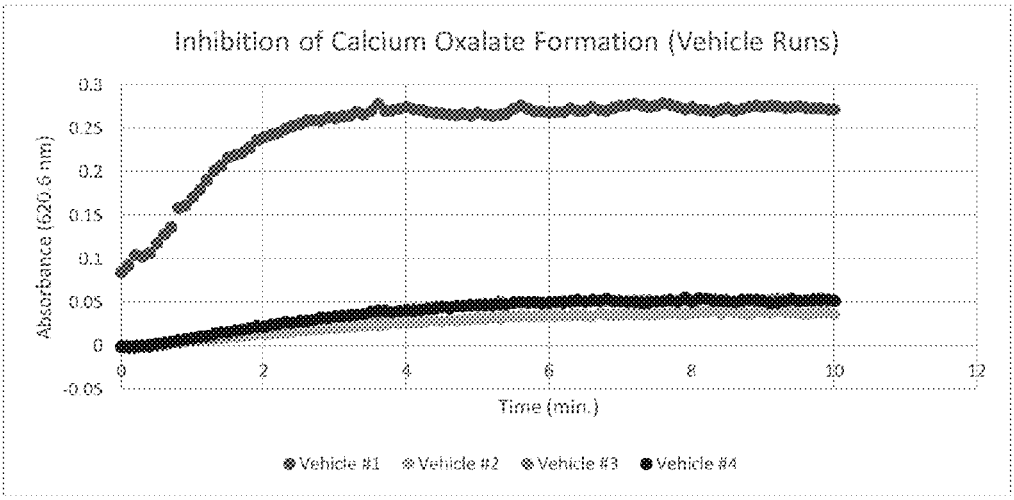

Inhibition of Calcium Oxalate Formation (Vehicle Runs)
Absorbance (620.6 nm)
0.3
0.25
0.2
0.15
0.1
0.05
0
-0.05
0
2
4
6
8
10
12
Time (min.)
Vehicle #1
Vehicle #2
Vehicle #3
Vehicle #4

Fig. 10

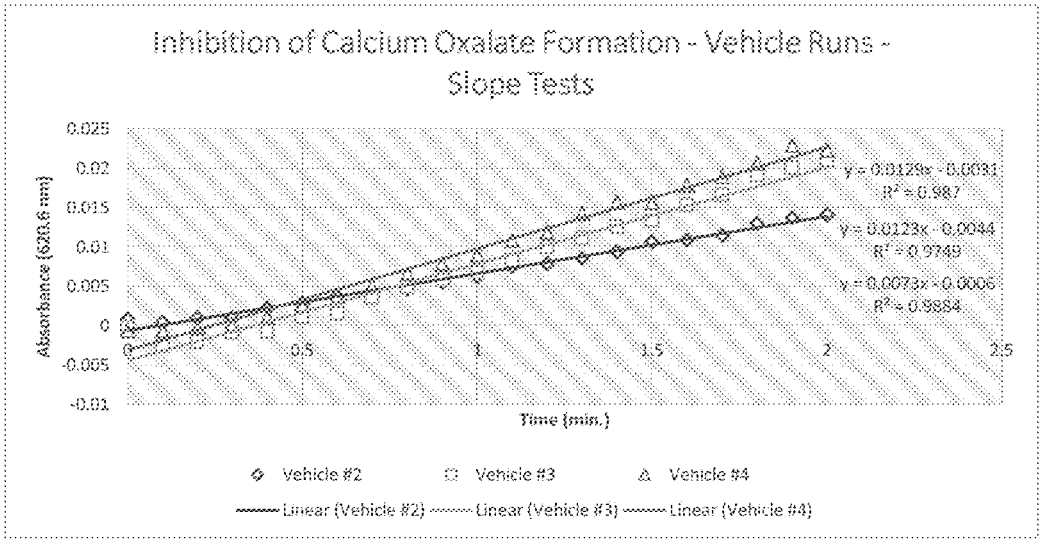

Inhibition of Calcium Oxalate Formation - Vehicle Runs - Slope Tests
Absorbance (620.6 nm)
0.025
0.02
0.015
0.01
0.005
0
-0.005
-0.01
0.5
1
1.5
2
2.5
Time (min.)
y = 0.0129x - 0.0031
R² = 0.987
y = 0.0123x - 0.0044
R² = 0.9749
y = 0.0073x - 0.0006
R² = 0.9884
Vehicle #2
Vehicle #3
Vehicle #4
Linear (Vehicle #2)
Linear (Vehicle #3)
Linear (Vehicle #4)

Fig. 11

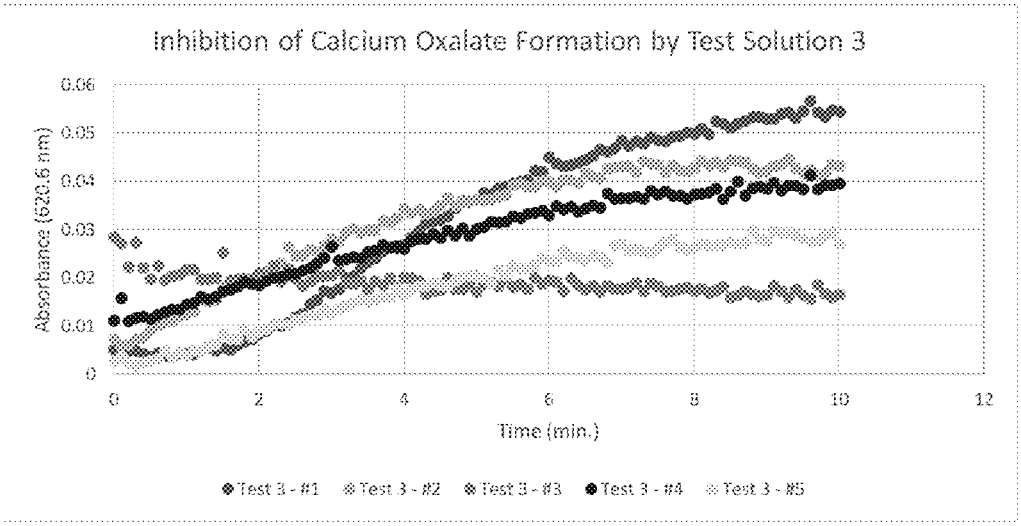

Inhibition of Calcium Oxalate Formation by Test Solution 3
Absorbance (620.6 nm)
0.06
0.05
0.04
0.03
0.02
0.01
0
0
2
4
6
8
10
12
Time (min.)
Test 3 - #1
Test 3 - #2
Test 3 - #3
Test 3 - #4
Test 3 - #5

Fig. 12

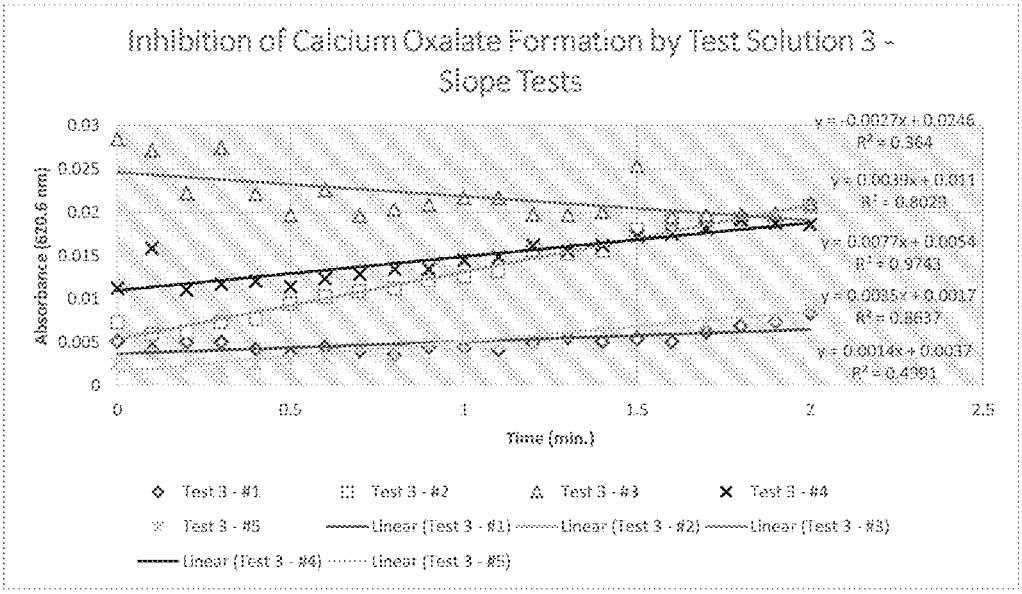

Inhibition of Calcium Oxalate Formation by Test Solution 3 - Slope Tests
Absorbance (620.6 nm)
Time (min.)
0.03
0.025
0.02
0.015
0.01
0.005
0
0
0.5
1
1.5
2
2.5
y = -0.0027x + 0.0246
R² = 0.364
y = 0.0039x + 0.011
R² = 0.8028
y = 0.0077x + 0.0054
R² = 0.9743
y = 0.0035x + 0.0017
R² = 0.8637
y = 0.0014x + 0.0037
R² = 0.4791
Test 3 - #1
Test 3 - #2
Test 3 - #3
Test 3 - #4
Test 3 - #5
Linear (Test 3 - #1)
Linear (Test 3 - #2)
Linear (Test 3 - #3)
Linear (Test 3 - #4)
Linear (Test 3 - #5)

Fig. 13

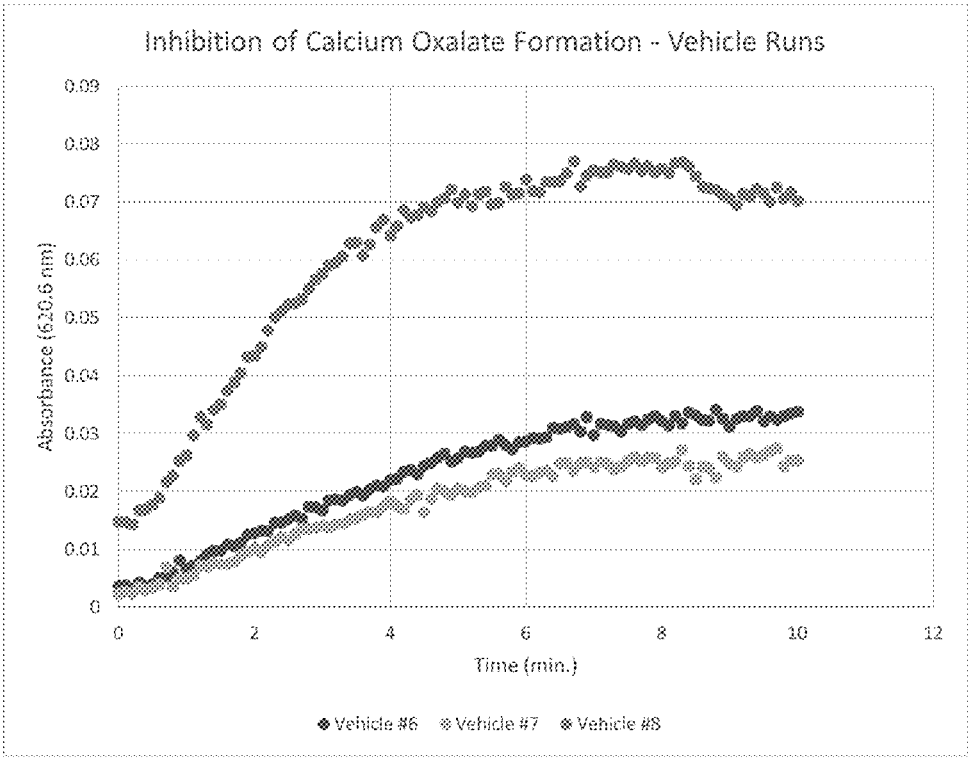

Inhibition of Calcium Oxalate Formation - Vehicle Runs
Absorbance (620.6 nm)
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
0
2
4
6
8
10
12
Time (min.)
Vehicle #6
Vehicle #7
Vehicle #8

Fig. 14

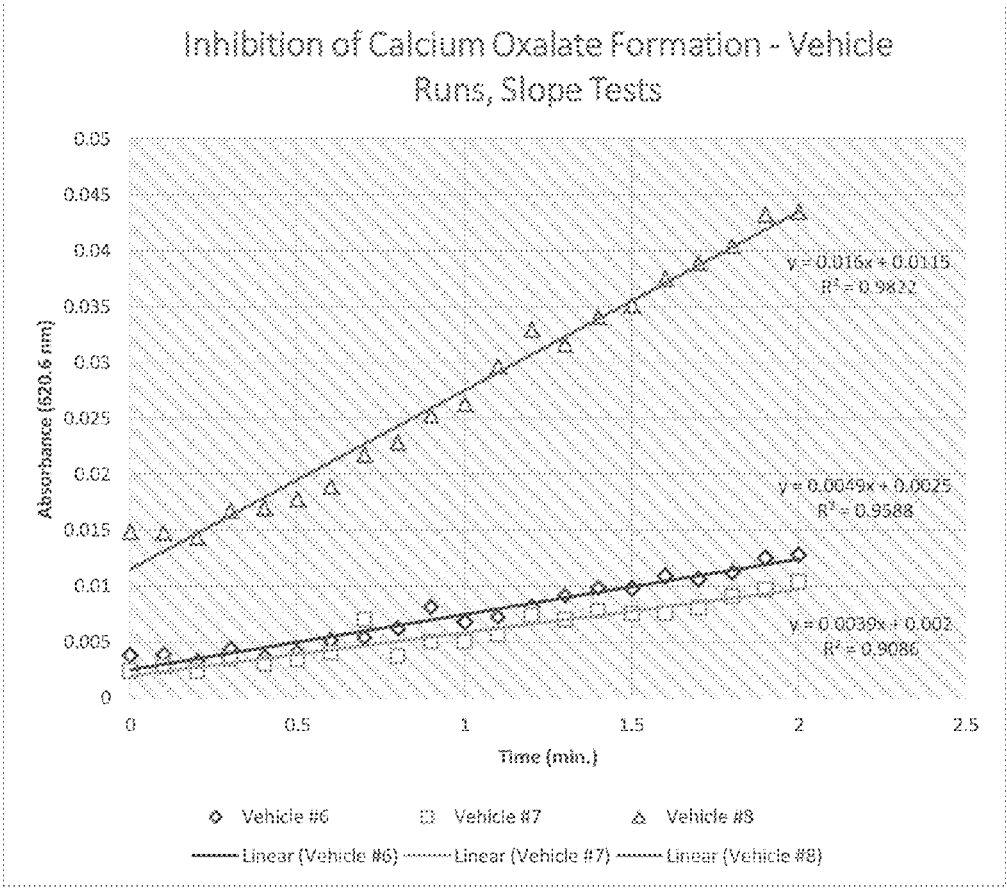

Inhibition of Calcium Oxalate Formation - Vehicle Runs, Slope Tests
Absorbance (620.6 nm)
Time (min.)
y = 0.016x + 0.0115
R² = 0.9822
y = 0.0049x + 0.0025
R² = 0.9588
y = 0.0039x + 0.002
R² = 0.9086
Vehicle #6
Vehicle #7
Vehicle #8
Linear (Vehicle #6)
Linear (Vehicle #7)
Linear (Vehicle #8)

Fig. 15

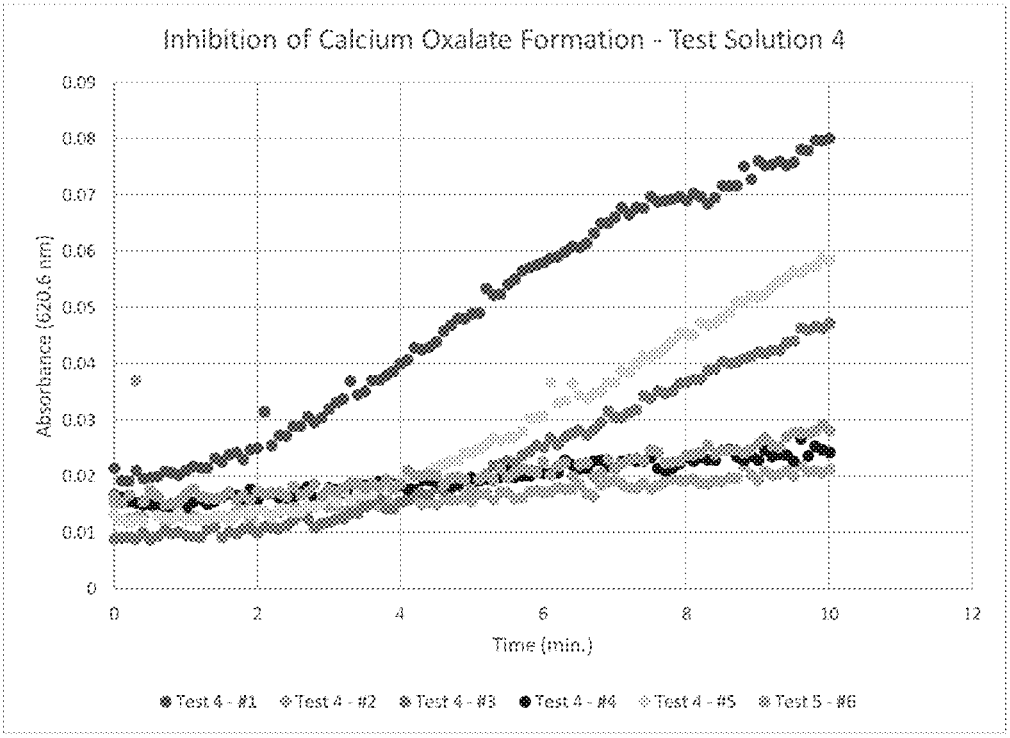

Inhibition of Calcium Oxalate Formation - Test Solution 4
Absorbance (620.6 nm)
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
0
2
4
6
8
10
12
Time (min.)
Test 4 - #1
Test 4 - #2
Test 4 - #3
Test 4 - #4
Test 4 - #5
Test 5 - #6

Fig.16

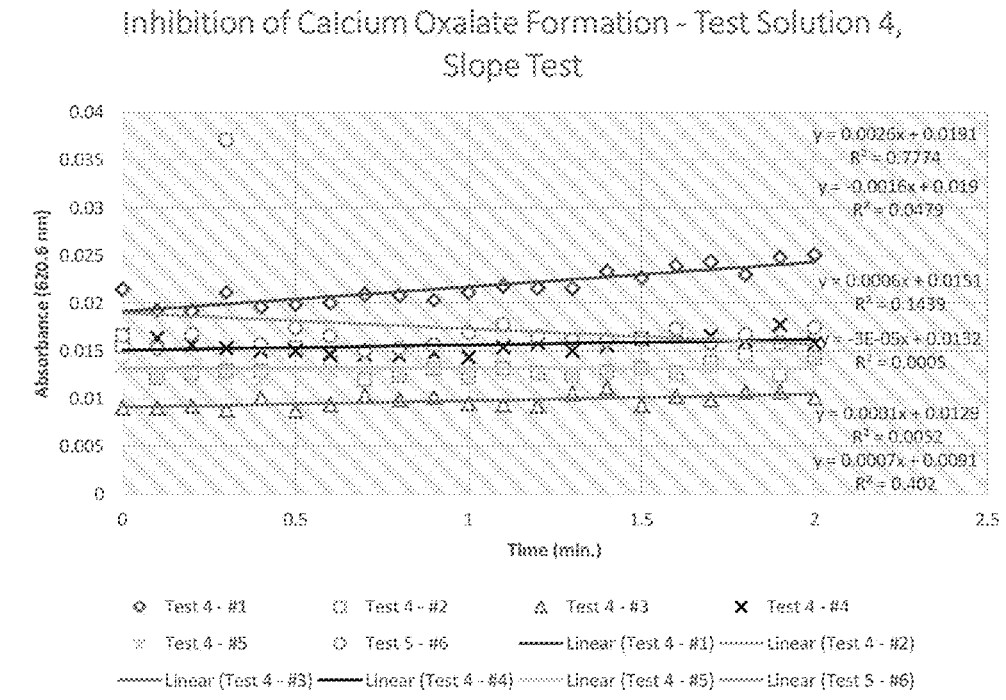

Inhibition of Calcium Oxalate Formation - Test Solution 4, Slope Test
Absorbance (620.6 nm)
Time (min.)
0.04
0.035
0.03
0.025
0.02
0.015
0.01
0.005
0
0
0.5
1
1.5
2
2.5
y = 0.0026x + 0.0181
R² = 0.7774
y = -0.0016x + 0.019
R² = 0.0479
y = 0.0006x + 0.0151
R² = 0.1439
y = -3E-05x + 0.0132
R² = 0.0005
y = 0.0031x + 0.0129
R² = 0.0052
y = 0.0007x - 0.0091
R² = 0.402
Test 4 - #1
Test 4 - #2
Test 4 - #3
Test 4 - #4
Test 4 - #5
Test 5 - #6
Linear (Test 4 - #1)
Linear (Test 4 - #2)
Linear (Test 4 - #3)
Linear (Test 4 - #4)
Linear (Test 4 - #5)
Linear (Test 5 - #6)

Fig. 17

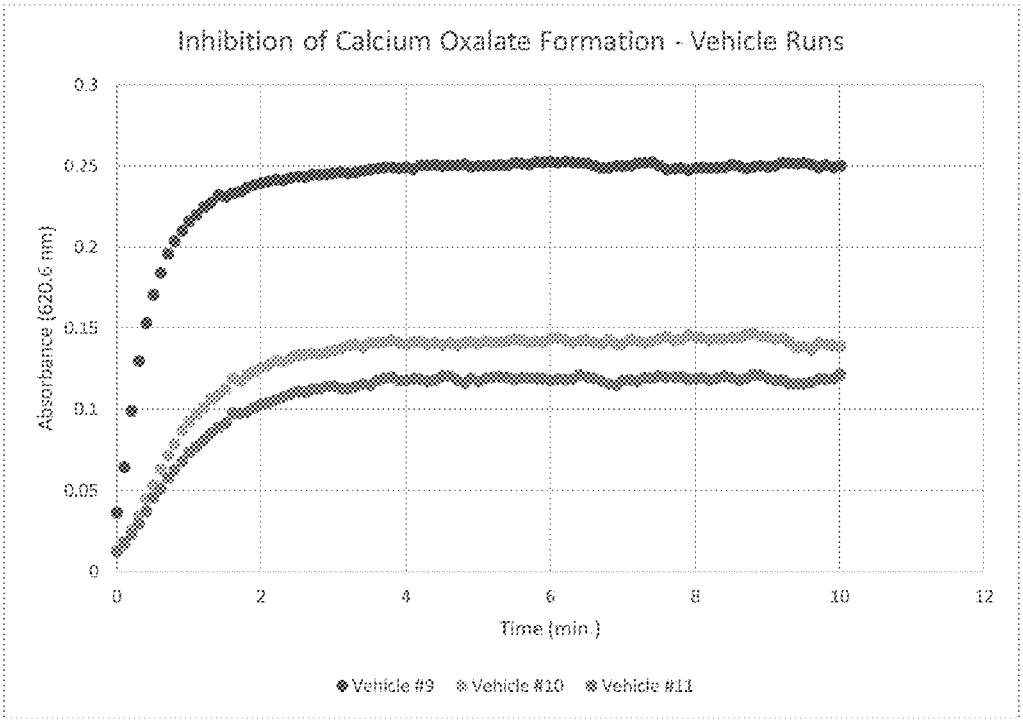

Inhibition of Calcium Oxalate Formation - Vehicle Runs
Absorbance (620.6 nm)
0.3
0.25
0.2
0.15
0.1
0.05
0
0
2
4
6
8
10
12
Time (min.)
Vehicle #9
Vehicle #10
Vehicle #11

Fig. 18

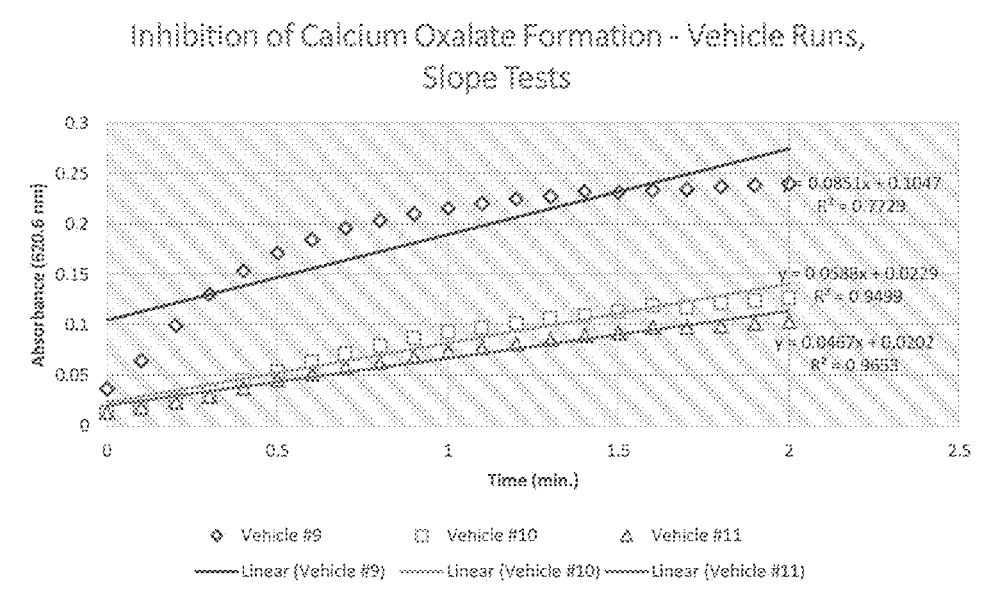

Inhibition of Calcium Oxalate Formation - Vehicle Runs, Slope Tests
Absorbance (620.6 nm)
Time (min.)
y = 0.0851x + 0.3047
R² = 0.7729
y = 0.0588x + 0.0229
R² = 0.9498
y = 0.0467x + 0.0202
R² = 0.9653
Vehicle #9
Vehicle #10
Vehicle #11
Linear (Vehicle #9)
Linear (Vehicle #10)
Linear (Vehicle #11)

Fig. 19

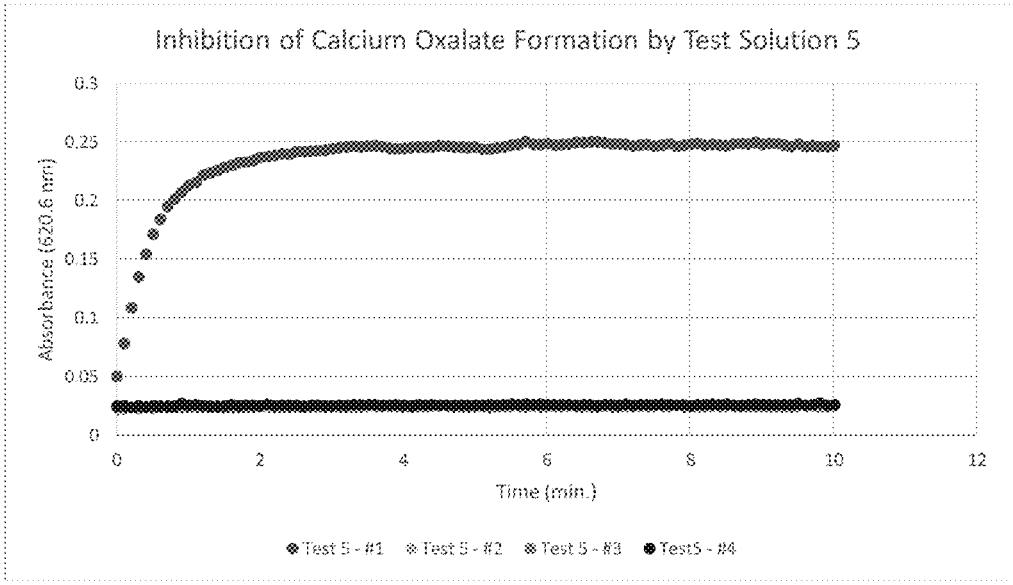

Inhibition of Calcium Oxalate Formation by Test Solution 5
Absorbance (620.6 nm)
0.3
0.25
0.2
0.15
0.1
0.05
0
0
2
4
6
8
10
12
Time (min.)
Test 5 - #1
Test 5 - #2
Test 5 - #3
Test5 - #4

Fig. 20

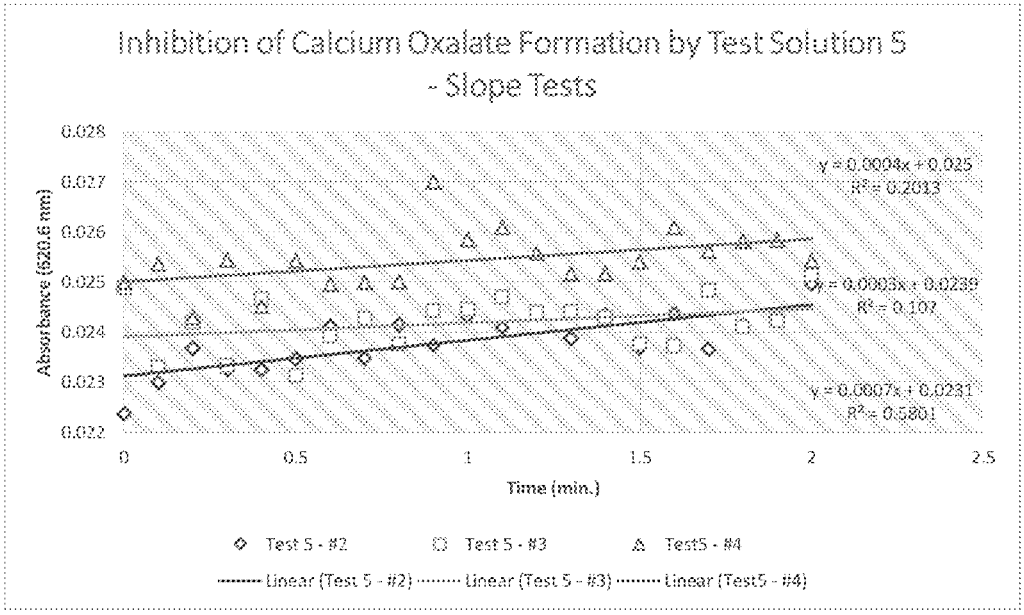

Inhibition of Calcium Oxalate Formation by Test Solution 5
- Slope Tests
Absorbance (620.6 nm)
0.028
0.027
0.026
0.025
0.024
0.023
0.022
0
0.5
1
1.5
2
2.5
Time (min.)
y = 0.0004x + 0.025
R² = 0.2013
y = 0.0003x + 0.0239
R² = 0.107
y = 0.0007x + 0.0231
R² = 0.5801
Test 5 - #2
Test 5 - #3
Test5 - #4
Linear (Test 5 - #2)
Linear (Test 5 - #3)
Linear (Test5 - #4)

Fig. 21

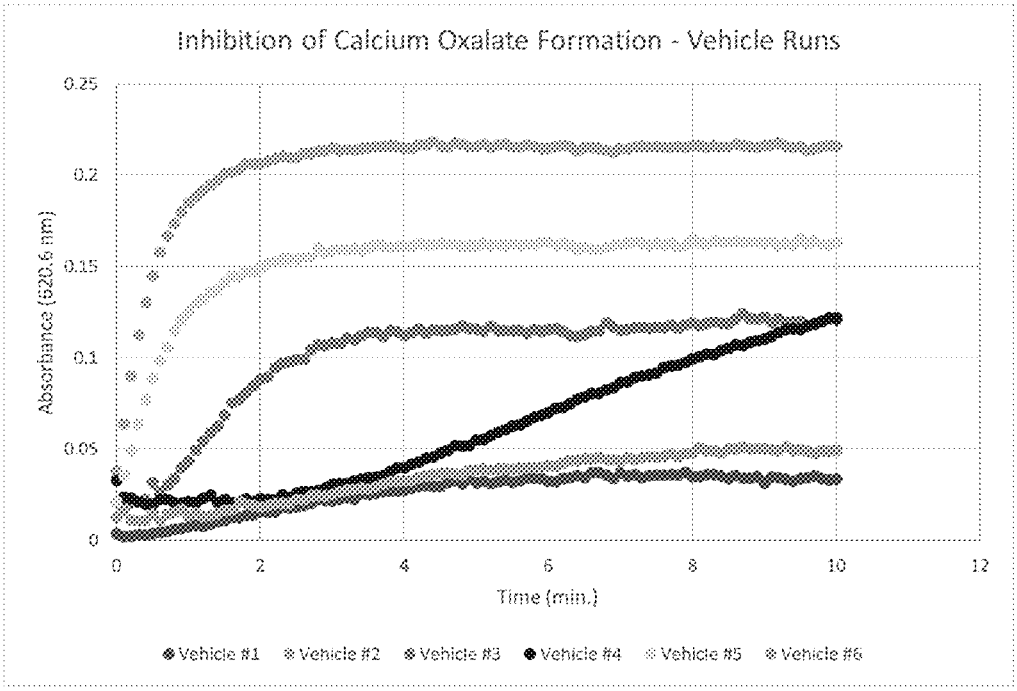

Inhibition of Calcium Oxalate Formation - Vehicle Runs
Absorbance (620.6 nm)
0.25
0.2
0.15
0.1
0.05
0
0
2
4
6
8
10
12
Time (min.)
Vehicle #1
Vehicle #2
Vehicle #3
Vehicle #4
Vehicle #5
Vehicle #6

Fig. 22

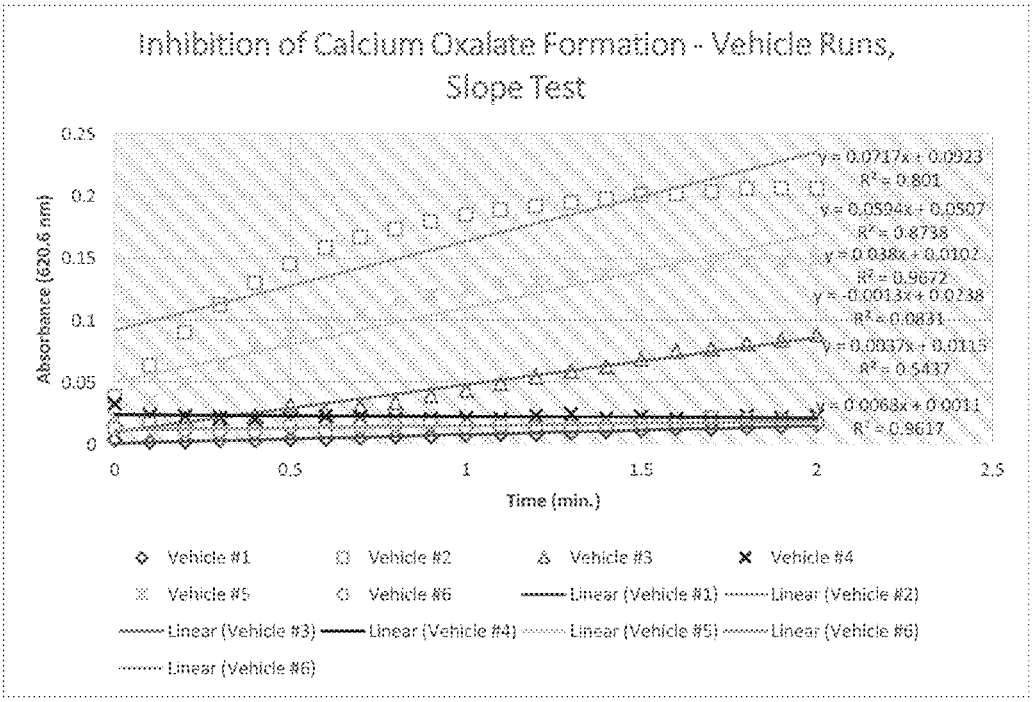

Inhibition of Calcium Oxalate Formation - Vehicle Runs, Slope Test
Absorbance (620.6 nm)
Time (min.)
0.25
0.2
0.15
0.1
0.05
0
0
0.5
1
1.5
2
2.5
y = 0.0717x + 0.0923
R² = 0.801
y = 0.0594x + 0.0507
R² = 0.8738
y = 0.038x + 0.0102
R² = 0.9672
y = -0.0013x + 0.0238
R² = 0.0831
y = 0.0037x + 0.0115
R² = 0.5437
y = 0.0068x + 0.0011
R² = 0.9617
Vehicle #1
Vehicle #2
Vehicle #3
Vehicle #4
Vehicle #5
Vehicle #6
Linear (Vehicle #1)
Linear (Vehicle #2)
Linear (Vehicle #3)
Linear (Vehicle #4)
Linear (Vehicle #5)
Linear (Vehicle #6)
Linear (Vehicle #6)

Fig. 23

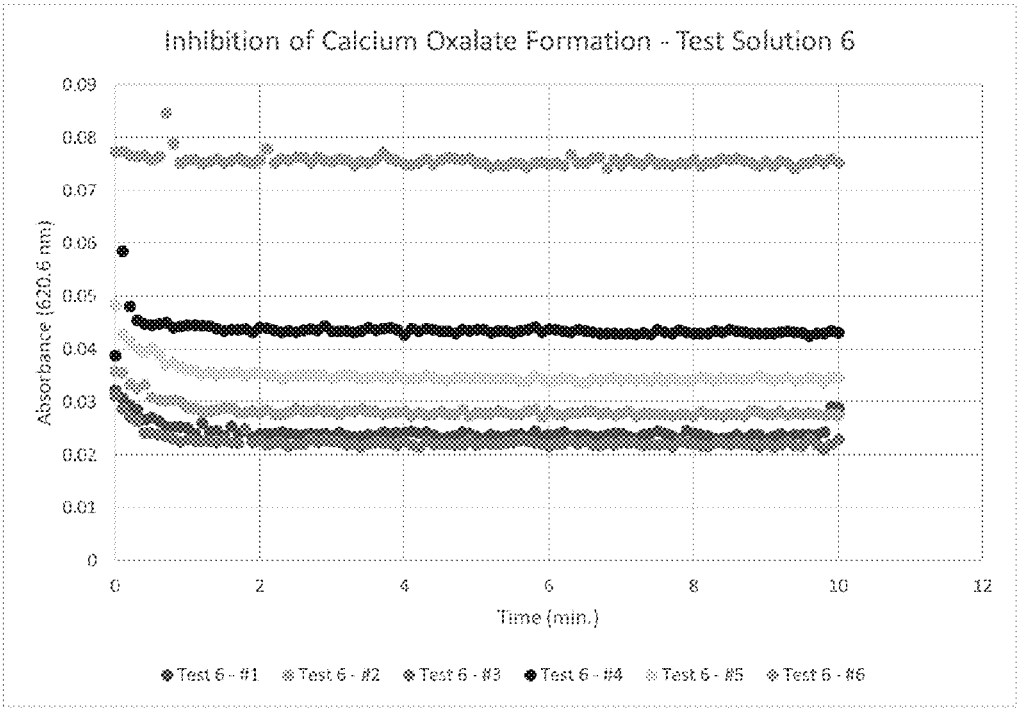

Inhibition of Calcium Oxalate Formation - Test Solution 6
Absorbance (620.6 nm)
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
0
2
4
6
8
10
12
Time (min.)
Test 6 - #1
Test 6 - #2
Test 6 - #3
Test 6 - #4
Test 6 - #5
Test 6 - #6

Fig. 24

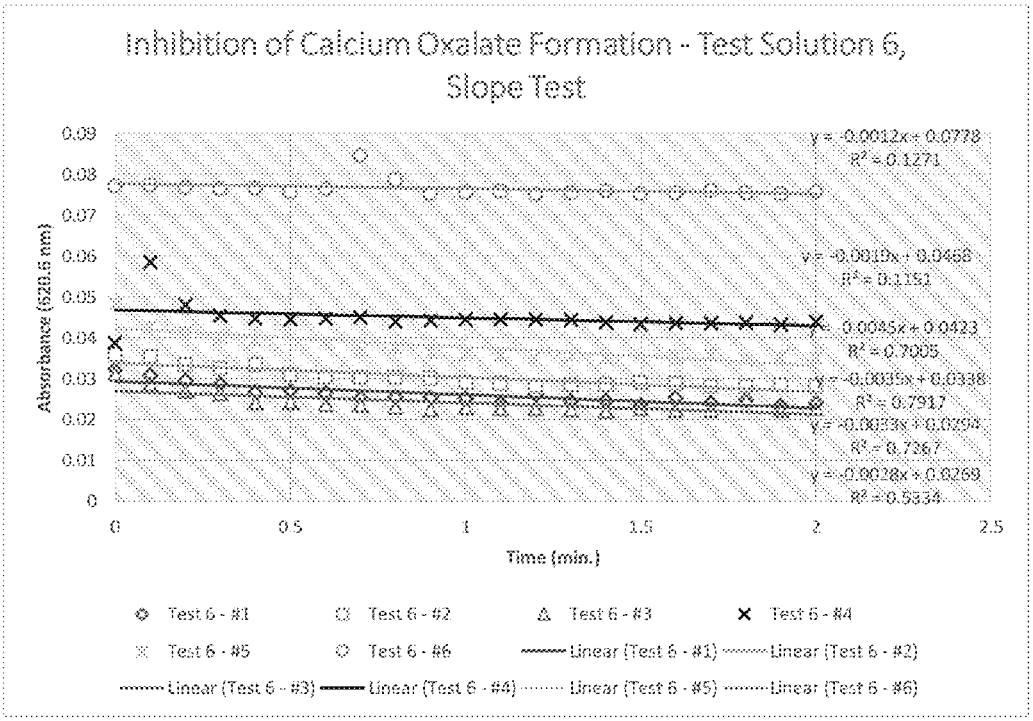

Inhibition of Calcium Oxalate Formation - Test Solution 6, Slope Test
Absorbance (620.6 nm)
Time (min.)
0
0.5
1
1.5
2
2.5
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
y = -0.0012x + 0.0778
R² = 0.1271
y = -0.0819x + 0.0468
R² = 0.1151
0.0045x + 0.0423
R² = 0.7005
y = -0.0035x + 0.0338
R² = 0.7917
y = -0.0033x + 0.0254
R² = 0.7267
y = -0.0028x + 0.0269
R² = 0.5834
Test 6 - #1
Test 6 - #2
Test 6 - #3
Test 6 - #4
Test 6 - #5
Test 6 - #6
Linear (Test 6 - #1)
Linear (Test 6 - #2)
Linear (Test 6 - #3)
Linear (Test 6 - #4)
Linear (Test 6 - #5)
Linear (Test 6 - #6)

Fig. 25

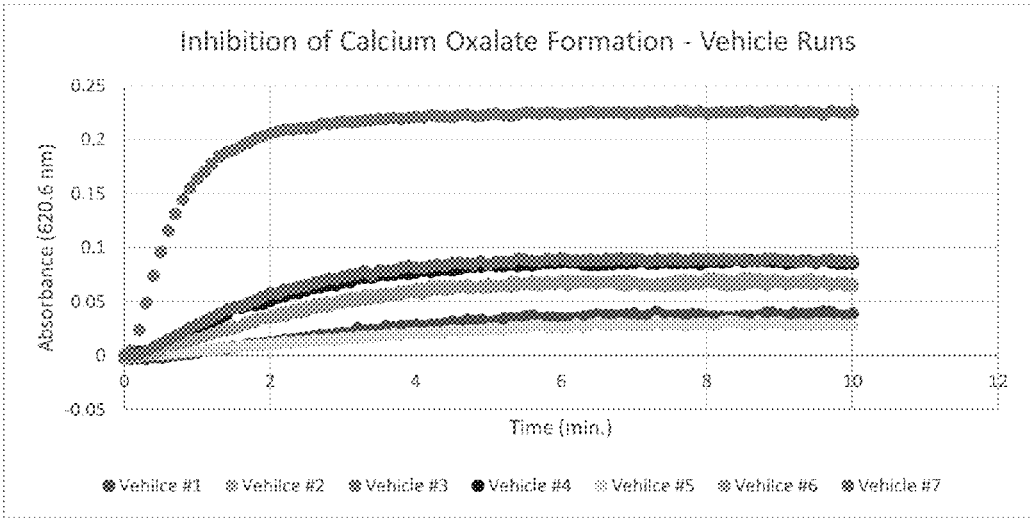

Inhibition of Calcium Oxalate Formation - Vehicle Runs
Absorbance (620.6 nm)
0.25
0.2
0.15
0.1
0.05
0
-0.05
0
2
4
6
8
10
12
Time (min.)
Vehicle #1
Vehicle #2
Vehicle #3
Vehicle #4
Vehicle #5
Vehicle #6
Vehicle #7

Fig. 26

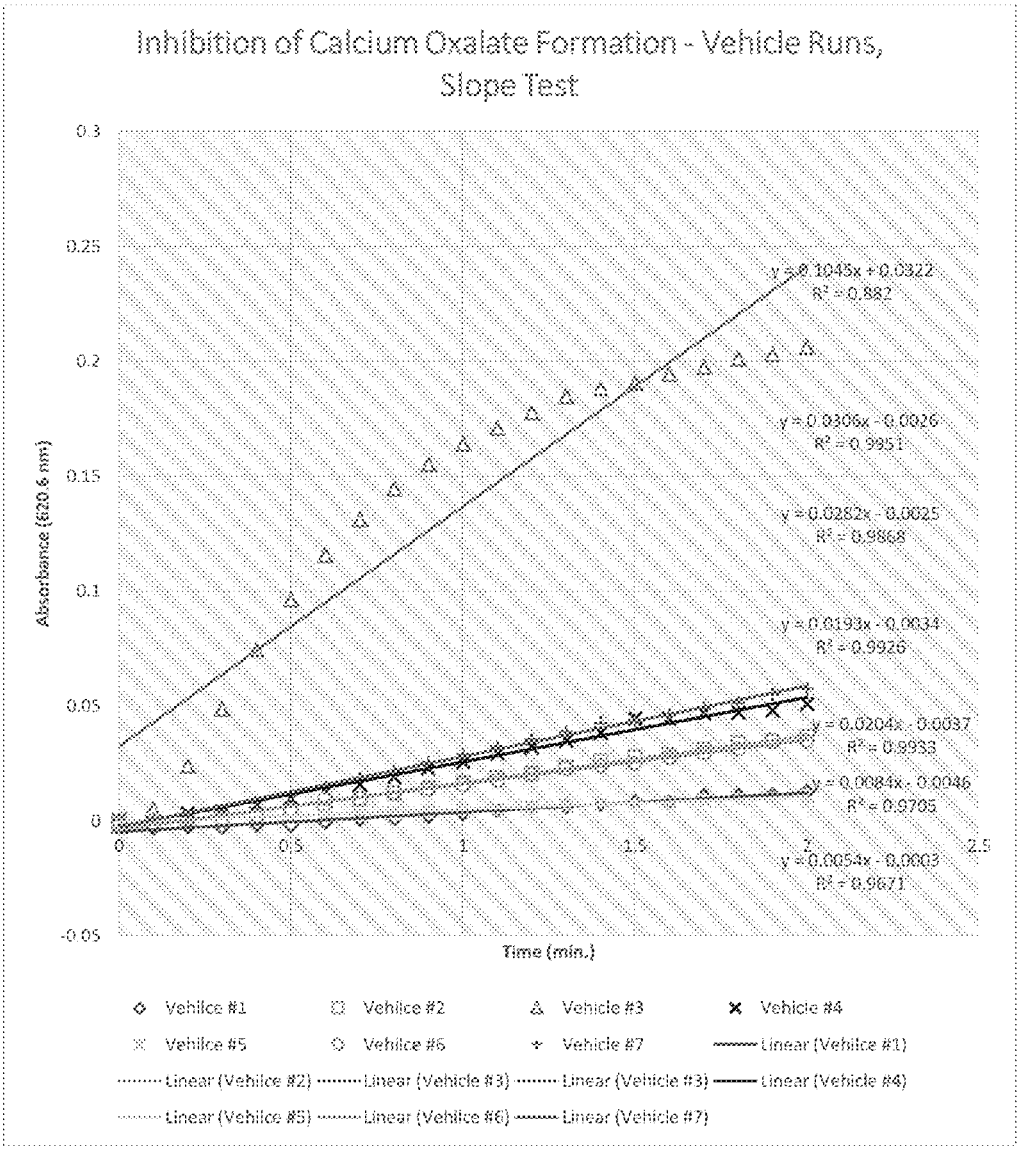

Inhibition of Calcium Oxalate Formation - Vehicle Runs, Slope Test
Absorbance (620.6 nm)
Time (min.)
0.3
0.25
0.2
0.15
0.1
0.05
0
-0.05
0
0.5
1
1.5
2
2.5
y = 0.1045x + 0.0322
R² = 0.882
y = 0.0306x - 0.0026
R² = 0.9951
y = 0.0282x - 0.0025
R² = 0.9868
y = 0.0193x - 0.0034
R² = 0.9926
y = 0.0204x - 0.0037
R² = 0.9933
y = 0.0084x - 0.0046
R² = 0.9705
y = 0.0054x - 0.0003
R² = 0.9671
Vehilce #1
Vehilce #2
Vehicle #3
Vehicle #4
Vehilce #5
Vehilce #6
Vehicle #7
Linear (Vehilce #1)
Linear (Vehilce #2)
Linear (Vehicle #3)
Linear (Vehicle #3)
Linear (Vehicle #4)
Linear (Vehilce #5)
Linear (Vehilce #6)
Linear (Vehicle #7)

Fig. 27

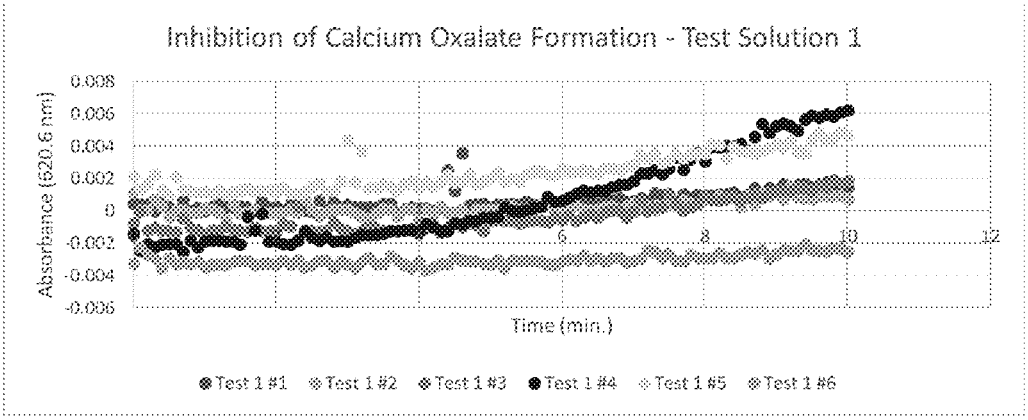

Inhibition of Calcium Oxalate Formation - Test Solution 1
Absorbance (620.6 nm)
0.008
0.006
0.004
0.002
0
-0.002
-0.004
-0.006
6
8
10
12
Time (min.)
Test 1 #1
Test 1 #2
Test 1 #3
Test 1 #4
Test 1 #5
Test 1 #6

Fig. 28

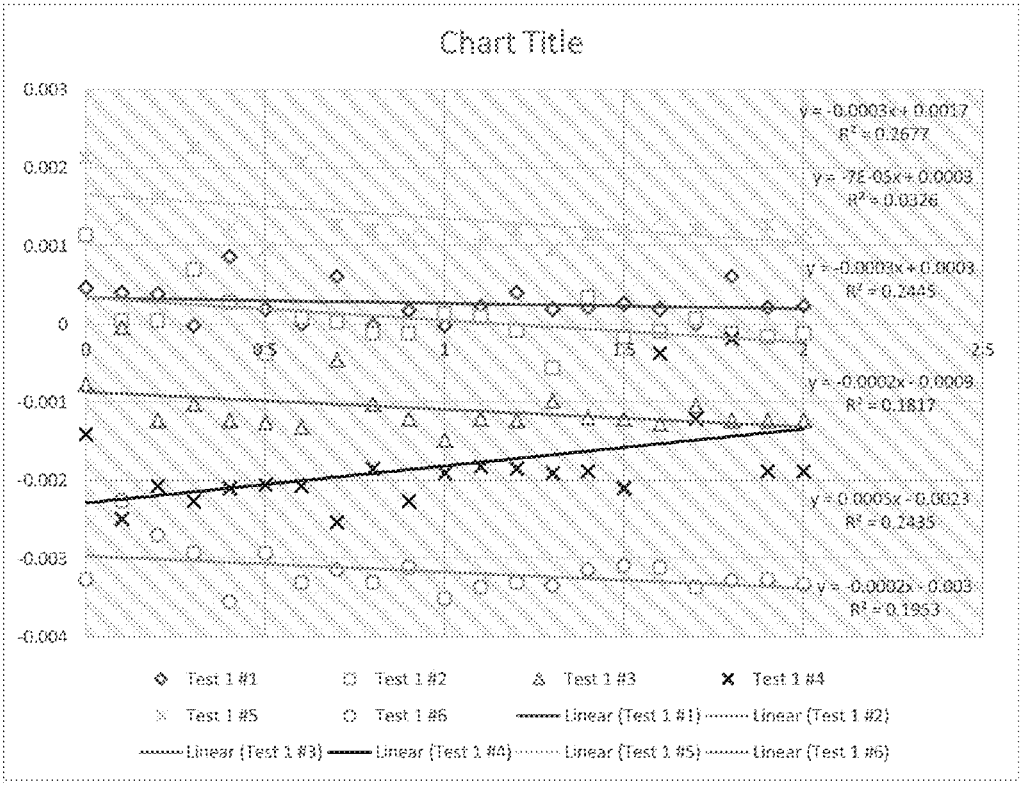
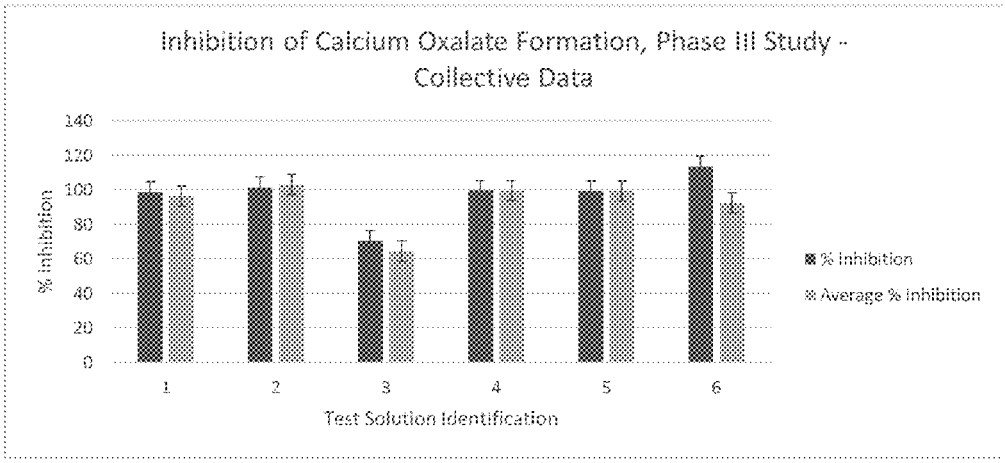


Chart Title
0.003
0.002
0.001
0
-0.001
-0.002
-0.003
-0.004
0
0.5
1
1.5
2
2.5
y = -0.0003x + 0.0017
R² = 0.3677
y = -7E-05x + 0.0003
R² = 0.0326
y = -0.0003x + 0.0003
R² = 0.2445
y = -0.0002x - 0.0009
R² = 0.1817
y = 0.0005x - 0.0023
R² = 0.2435
y = -0.0002x - 0.003
R² = 0.1953
Test 1 #1
Test 1 #2
Test 1 #3
Test 1 #4
Test 1 #5
Test 1 #6
Linear (Test 1 #1)
Linear (Test 1 #2)
Linear (Test 1 #3)
Linear (Test 1 #4)
Linear (Test 1 #5)
Linear (Test 1 #6)

Fig. 29


Inhibition of Calcium Oxalate Formation, Phase III Study - Collective Data
140
120
100
80
60
40
20
0
% Inhibition
1
2
3
4
5
6
Test Solution Identification
% Inhibition
Average % Inhibition

COMPOSITIONS AND METHODS TO INHIBIT KIDNEY STONE GROWTH

FIELD OF INVENTION

The disclosure relates to novel compositions comprised of active agents including vitamins, minerals, and food additives ingredients to prevent and treat kidney stone formation and promote overall improved kidney health for patients that may be susceptible to forming stones in the kidney, renal pelvis, ureter, bladder, or all other renal genitourinary areas.

BACKGROUND

Kidney stones, also called renal calculi, are solid crystal aggregations of dissolved minerals in urine. Depending on their location in the urinary tract these calculi are called by various names, e.g., kidney stones, ureteric stones, bladder stones, or urethral stones. Most kidney stones are caused by the precipitation of calcium in the form of calcium oxalate. A minority of stones may also be caused by or include precipitated calcium hydroxyl phosphate (apatite), magnesium ammonium phosphate (struvite), uric acid, or cysteine. In addition to excruciating pain, symptoms of kidney stones may also include blood in the urine due to minor damage to inside lining of kidney, ureter and urethra; reduced urine volume caused by obstruction of the bladder or urethra by the stones; kidney infection as a result of stone blockage; abdominal distention; nausea or vomiting; and fever and chills.

Kidney stone disease is an ailment afflicting human kind for many centuries. It can affect up to a quarter of the population in certain geographic areas and hence poses a significant health problem. Approximately 85% of the stones in human are calcium stones comprising oxalate and phosphate, either alone or combined. The pathogenesis of calcium oxalate stone formation is a multi-step process and in essence includes—nucleation, crystal growth, crystal aggregation and crystal retention. Various substances in the body have an effect on one or more of the above stone forming processes, thereby influencing a person's ability to promote or prevent stone formation. Low urine volume, low urine pH, calcium, sodium, oxalate, and urate are known to promote stone formation. Many inorganic (e.g., magnesium) and organic (e.g., urinary prothrombin fragment 1, glycosaminoglycans, osteopontin, citrate) substances are known to inhibit stone formation.

The initiation of growth of a calcium oxalate stone is thought to occur at sites of inflammation or damage within the kidney. The stones form by an initial deposition of calcium crystals at the sites of inflammation or damage and are known in the literature as Randall's plaques. These Randall's plaques then serve as nuclei for formation of calcium oxalate on top of the calcium hydroxyapatite mini-stones. Once of a certain size, stones often fragment or a break off from the Randall plaque region and can either pass out of the body or get stuck along the urinary tract, resulting in clinical symptoms such as reduced urine flow, pain or bleeding.

Prevalence of kidney stones in the United States has been estimated at 8.8% (roughly 1 in 11 people). Among men, the prevalence of stones was 10.6%, compared with 7.1% among women. Kidney stones were more common among obese than normal-weight individuals. (Eur Urol. 2012 July; 62(1): 160-5.)

Reoccurrence of stones in patients has been estimated to be as high as 50 percent within 5 years of the initial event. Rates

of emergency department visits for kidney stone disease have increased 20 percent between 2005 and 2009.

In 2014, one study suggested that kidney stone interventions cost an estimated $10 billion annually in the United States and patients who have an unplanned hospital visit for kidney stones incur average costs of nearly $30,000, depending on the type of procedure and the subsequent care. (Duke University Medical Center. "Complications from kidney stone treatments are common, costly." Science Daily. 28 Apr. 2014)

Medical treatment options depend on severity of pain, size of stone, and location of stone. Smaller stones will often pass on their own. For larger stones, some form of intervention is usually required and include: ureteroscopy and laser stone lithotripsy (the stone is located with a small camera inserted into the urethra and removed with a small basket or broken up with a laser); extracorporeal shockwave lithotripsy (ESWL; breaks up stone from the outside of the body with shockwaves that travel through a gel-like medium); Percutaneous Nephrolithotomy (PCNL; inpatient procedure for very large stones, which typically requires an overnight hospital stay). If patient has more than one kidney stone or stone occurrence, physician often recommends getting a special urine study done. A 24-hour urine study will show the composition of urine in relation to kidney stone formation. Diet can be altered or improved based on these results to help in preventing reoccurrence of a stone. Rarely patients are placed on a prescription medication as the options are very limited and can have serious side effects or risks for the patient. Sometimes pain medications are utilized as the stone is passing through the person's system. One goal in diet alteration is to try to prevent crystal formation. Common recommendations include: drink more water, often at least 6-8 glasses per day; decrease caffeine intake; eliminate colas due to phosphoric acid content; drink lemon water; decrease sodium, sugar, and red meat and oxalate-rich foods (e.g., Spinach, strawberries, nuts, tea); and increase fiber intake.

Various active agents are known to have an effect on kidney stones, including citric acid, magnesium citrate, phytin, pyridoxine, and musa, however, these active agents have not been combined in one composition, nor have they been combined in amounts that maximize the percent inhibition of crystal formation.

Thus, there remains a need for a simple and effective method and composition for preventing and treating kidney stones that optimizes the inhibition of crystal formation.

SUMMARY

Disclosed is a novel oral dosage form or a plurality of oral dosage forms.

In an embodiment, the oral dosage form or plurality of oral dosage forms comprises as active ingredients citric acid, magnesium citrate, phytin, pyridoxine, and musa.

Also disclosed is a method of treating and/or inhibiting growth of kidney stones.

In an embodiment, the method comprises administering to a patient in need thereof the oral dosage form or plurality of dosage forms disclosed herein.

In an embodiment, the method comprises administering to a patient in need thereof about 101 mg to about 700 mg citric acid; about 76 mg to about 226 mg magnesium citrate; about 3 mg to about 600 mg phytin; about 0.1 mg to about 15 mg pyridoxine; and about 1 mg to about 251 mg musa.

Also disclosed is a method of inhibiting growth of calcium oxalate crystals.

In an embodiment, the method comprises contacting an aqueous solution comprising calcium oxalate with the oral dosage form or plurality of dosage forms disclosed herein.

In an embodiment, the method comprises contacting an aqueous solution comprising calcium oxalate with a composition comprising as active ingredients citric acid, magnesium citrate, phytin, pyridoxine, and musa.

These and other advantages, as well as additional inventive features, will be apparent from the following Drawings, Detailed Description, Examples, and Claims.

BRIEF DESCRIPTION OF THE DRAWINGS

The following is a brief description of the drawings which are presented for the purposes of illustrating the exemplary embodiments disclosed herein and not for the purposes of limiting the same.

FIG. **1** is a graph showing absorbance at 620.6 nm as a function of time for Control Vehicle Runs Associated with Test Solution 1.

FIG. **2** is a graph showing absorbance at 620.6 nm as a function of time to determine the Slope for Control Vehicle Runs Associated with Test Solution 1.

FIG. **3** is a graph showing absorbance at 620.6 nm as a function of time for Test Solution 1.

FIG. **4** is a graph showing absorbance at 620.6 nm as a function of time to determine the Slope for Test Solution 1.

FIG. **5** is a graph showing absorbance at 620.6 nm as a function of time for Control Vehicle Runs Associated with Test Solution 2.

FIG. **6** is a graph showing absorbance at 620.6 nm as a function of time to determine the Slope for Control Vehicle Runs Associated with Test Solution 2.

FIG. **7** is a graph showing absorbance at 620.6 nm as a function of time for Test Solution 2.

FIG. **8** is a graph showing absorbance at 620.6 nm as a function of time to determine the Slope for Test Solution 2.

FIG. **9** is a graph showing absorbance at 620.6 nm as a function of time for Control Vehicle Runs Associated with Test Solution 3.

FIG. **10** is a graph showing absorbance at 620.6 nm as a function of time to determine the Slope for Control Vehicle Runs Associated with Test Solution 3.

FIG. **11** is a graph showing absorbance at 620.6 nm as a function of time for Test Solution 3.

FIG. **12** is a graph showing absorbance at 620.6 nm as a function of time to determine the Slope for Test Solution 3.

FIG. **13** is a graph showing absorbance at 620.6 nm as a function of time for Control Vehicle Runs Associated with Test Solution 4.

FIG. **14** is a graph showing absorbance at 620.6 nm as a function of time to determine the Slope for Control Vehicle Runs Associated with Test Solution 4.

FIG. **15** is a graph showing absorbance at 620.6 nm as a function of time for Test Solution 4.

FIG. **16** is a graph showing absorbance at 620.6 nm as a function of time to determine the Slope for Test Solution 4.

FIG. **17** is a graph showing absorbance at 620.6 nm as a function of times for Control Vehicle Runs Associated with Test Solution 5.

FIG. **18** is a graph showing absorbance at 620.6 nm as a function of time to determine the Slope for Vehicle Runs Associated with Test Solution 5.

FIG. **19** is a graph showing absorbance at 620.6 nm as a function of time for Test Solution 5.

FIG. **20** is a graph showing absorbance at 620.6 nm as a function of time to determine the Slope for Test Solution 5.

FIG. **21** is a graph showing absorbance at 620.6 nm as a function of time for Control Vehicle Runs Associated with Test Solution 6.

FIG. **22** is a graph showing absorbance at 620.6 nm as a function of time to determine the Slope for Control Vehicle Runs Associated with Test Solution 6.

FIG. **23** is a graph showing absorbance at 620.6 nm as a function of time for Test Solution 6.

FIG. **24** is a graph showing absorbance at 620.6 nm as a function of time to determine the Slope for Test Solution 6.

FIG. **25** is a graph showing absorbance at 620.6 nm as a function of time for Control Vehicle Runs Associated with Test Solution 7 (Repeat of Test Solution 1).

FIG. **26** is a graph showing absorbance at 620.6 nm as a function of time to determine the Slope for Control Vehicle Runs Associated with Test Solution 7 (Repeat of Test Solution 1).

FIG. **27** is a graph showing absorbance at 620.6 nm as a function of time for Test Solution 7 (Repeat of Test Solution 1).

FIG. **28** is a graph showing absorbance at 620.6 nm as a function of time to determine the Slope for Test Solution 7 (Repeat of Test Solution 1).

FIG. **29** is a histogram showing median and mean inhibition of calcium oxalate crystal formation by Test Solutions 1-6.

DETAILED DESCRIPTION

A novel oral dosage form or a plurality of oral dosage forms comprising the ingredients citric acid, magnesium citrate, phytin, pyridoxine, and musa is disclosed herein. The disclosed oral dosage form or plurality of dosage forms is useful for treating and/or inhibiting growth of kidney stones. Methods of using the oral dosage form or plurality of dosage forms to treat or inhibit growth of kidney stones are also disclosed.

Although there is some clinical evidence that each of these ingredients individually plays a role in preventing or treating kidney stones, all five ingredients have never previously been combined in one formulation or dosing regimen for treating or inhibiting formation of kidney stones.

Surprisingly, not all concentration ranges of the active ingredients in the combination provide effective inhibition of kidney stones or calcium oxalate growth. In particular, we have discovered preferred ranges in the combination of the five active ingredients that maximize the percent inhibition of kidney stones and more particularly calcium oxalate crystal growth, resulting in mean percent inhibition of the calcium oxalate crystal growth of at least about 92%. Compositions of the five active ingredients having concentrations outside the preferred ranges are unexpectedly much less effective in inhibiting calcium oxalate crystal growth.

A preferred range for citric acid is about 101 mg to about 700 mg; and more preferably about 101 mg to about 352 mg, about 101 mg to about 176 mg, about 176 mg to about 700 mg, or about 352 mg to about 700 mg. A preferred range for magnesium citrate is about 76 mg to about 226 mg; and more preferably about 76 mg to about 201 mg, about 76 mg to about 150 mg, about 150 to about 226 mg, or about 201 mg to about 226 mg. A preferred range for phytin is about 3 mg to about 600 mg; more preferably about 3 mg to about 400 mg, about 3 mg to about 202 mg, about 3 mg to about 100 mg, about 100 mg to about 600 mg, about 201 mg to about 600 mg, or about 400 mg to about 600 mg. A preferred range for pyridoxine is about 0.2 mg to about 15 mg; more preferably about 0.2 mg to about 10.1 mg, about 0.2 mg to about 6 mg, about 0.2 mg to about 2.7 mg, about 2.7 mg to about 15 mg, about 6.0 mg to

about 15 mg, or about 10 mg to about 15 mg. A preferred range for musa is about 1 mg to about 251 mg; more preferably about 1 mg to about 167 mg, about 1 mg to about 85 mg, about 1 mg to about 41 mg, about 41 mg to about 251 mg, about 85 mg to about 251 mg, or about 167 mg to about 251 mg.

Most preferred is an oral dosage form or a plurality of dosage forms comprising citric acid, magnesium citrate, phytin, pyridoxine, and musa where citric acid is present in an amount of about 350 mg, magnesium citrate is present in an amount of about 150 mg, phytin is present in an amount of about 200 mg, pyridoxine is present in an amount of about 5 mg, and musa is present in amount of about 250 mg.

Also disclosed is an oral dosage form or plurality of dosage forms comprising as active ingredients citric acid, magnesium citrate, phytin, pyridoxine, and musa wherein the percent inhibition of the formation of calcium oxalate crystals caused by this combination of active ingredients is greater than about 92%, more preferably greater than about 96%, and most preferably greater than about 99%.

Also disclosed herein are methods for treating and/or inhibiting formation of kidney stones.

In an embodiment, the method comprises administering the oral dosage form or plurality of dosage forms disclosed herein to a patient in need thereof. The dosage form(s) can be administered to the patient one time or multiple times per day, preferably one to four times per day and more preferably twice per day. Multiple oral dosage forms can be taken per dosing, preferably one to four dosage forms, preferably one to two dosage forms, and more preferably 1 dosage form.

In an embodiment, the method comprises administering to a patient in need thereof about 101 mg to about 700 mg citric acid; about 76 mg to about 226 mg magnesium citrate; about 3 mg to about 600 mg phytin; about 0.1 mg to about 15 mg pyridoxine; and about 1 mg to about 251 mg musa. In an embodiment, the method comprises administering to the patient about 350 mg citric acid, about 150 magnesium citrate, about 200 mg phytin, about 5 mg pyridoxine, and about 250 mg musa. The administering can occur one time or multiple times per day, preferably 1 to 4 times per day, and more preferably twice per day. The combination of the citric acid, magnesium citrate, phytin, pyridoxine, and musa can be administered to the patient in form of an oral dosage form, e.g. a tablet or a capsule, preferably a capsule.

Also disclosed is a method of inhibiting growth of calcium oxalate crystals.

In an embodiment, the method comprises contacting an aqueous solution comprising calcium oxalate with the oral dosage form or plurality of dosage forms disclosed herein.

In an embodiment, the method comprises contacting an aqueous solution comprising calcium oxalate with a composition comprising as active ingredients citric acid, magnesium citrate, phytin, pyridoxine, and musa. A preferred range for citric acid is about 101 mg to about 700 mg; and more preferably about 101 mg to about 352 mg, about 101 mg to about 176 mg, about 176 mg to about 700 mg, or about 352 mg to about 700 mg. A preferred range for magnesium citrate is about 76 mg to about 226 mg; and more preferably about 76 mg to about 201 mg, about 76 mg to about 150 mg, about 150 to about 226 mg, or about 201 mg to about 226 mg. A preferred range for phytin is about 3 mg to about 600 mg; more preferably about 3 mg to about 400 mg, about 3 mg to about 202 mg, about 3 mg to about 100 mg, about 100 mg to about 600 mg, about 201 mg to about 600 mg, or about 400 mg to about 600 mg. A preferred range for pyridoxine is about 0.2 mg to about 15 mg; more preferably about 0.2 mg to about 10.1 mg, about 0.2 mg to about 6 mg, about 0.2 mg to about 2.7 mg, about 2.7 mg to about 15 mg, about 6.0 mg to about 15 mg, or about 10 mg to about 15 mg. A preferred range for musa is about 1 mg to about 251 mg; more preferably about 1 mg to about 167 mg, about 1 mg to about 85 mg, about 1 mg to about 41 mg, about 41 mg to about 251 mg, about 85 mg to about 251 mg, or about 167 mg to about 251 mg. In an embodiment, the composition comprises about 101 mg to about 700 mg citric acid; about 76 mg to about 226 mg magnesium citrate; about 3 mg to about 600 mg phytin; about 0.1 mg to about 15 mg pyridoxine; and about 1 mg to about 251 mg musa; specifically, the composition comprises citric acid in an amount of about 350 mg, magnesium citrate in an amount of about 150 mg, phytin in an amount of about 200 mg, pyridoxinet in an amount of about 5 mg, and musa in amount of about 250 mg.

DEFINITIONS

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of ordinary skill in the art to which this invention belongs. In the event that there is a plurality of definitions for a term used herein, those definitions in this section shall prevail.

The terms "a" and "an" do not denote a limitation of quantity, but rather denote the presence of at least one of the referenced item.

The term "about" as used herein is inclusive of the stated value and means within the routine experimental error associated with measurement of the particular quantity (i.e., the limitations of the measurement system) or in the case of a weight, within ±10% of the stated value.

The term "active agent" or "active ingredient" as used herein includes all pharmaceutically acceptable molecules, plant extracts, vitamins, salt forms, crystalline forms, amorphous form, polymorphic forms, solvates, and hydrates that are useful for treating a medical condition.

"Administering an oral dosage form or plurality of dosage forms comprising as active ingredients citric acid, magnesium citrate, phytin, pyridoxine, and musa" or "co-administering a plurality of dosage forms comprising as active ingredients citric acid, magnesium citrate, phytin, pyridoxine, and musa" means that each active ingredient is administered simultaneously in a single dosage form, administered concomitantly in separate dosage forms, or administered in separate dosage forms separated by some amount of time that is within the time in which all of the active ingredients are within the blood stream of a patient.

The terms "comprising", "having", "including", and "containing" are to be construed as open-ended terms (i.e., meaning "including, but not limited to").

A "dosage form" means a unit of administration of an active agent. An "oral dosage form" means a unit dosage form for oral administration.

As used herein "food" means a solid food with sufficient bulk and fat content that it is not rapidly dissolved and absorbed in the stomach. More specifically, the food is a meal, such as breakfast, lunch, or dinner. An oral dosage form administered to a patient "with food" is administered to the patient between about 30 minutes prior to eating a meal to about 2 hours after eating a meal; more specifically, the dosage is administered within 15 minutes of eating a meal. The term "without food" is defined to mean the condition of the patient not having consumed solid food for about one hour prior to administration of the oral dosage form until about 2 hours after administration of the oral dosage form.

The term "kidney stone" includes a stone, crystal, calculus, or nephrolith that is formed and affects any part of the urinary tract including the kidney, bladder, and ureter.

The term "medical condition" includes disease, illness, ailment, syndrome, and/or disorder.

The term "patient" means a human or non-human animal in need of medical treatment.

The terms "treating" and "treatment" mean implementation of therapy with the intention of reducing in severity or frequency symptoms, elimination of symptoms or underlying cause, prevention of the occurrence of symptoms or their underlying cause, and improvement or remediation of damage.

By an "effective amount" or a "therapeutically effective amount" of an active agent is meant a sufficient amount of the active agent to produce a therapeutic effect in the patient. The amount that is "effective" will vary from subject to subject, depending on the age and general condition of the individual, the particular active agent, and the like. Thus, it is not always possible to specify an exact "effective amount." However, an appropriate "effective" amount in any individual case may be determined by one of ordinary skill in the art using routine experimentation.

The suffix "(s)" as used herein is intended to include both the singular and the plural of the term that it modifies, thereby including one or more of that term (e.g., the dosage form(s) includes one or more dosage forms).

Ingredients

Citric acid is a GRAS food additive that is well absorbed and is excreted into the renal tubule where it forms soluble complexes with calcium, reducing the concentration of free calcium in the urine. Citric acid can be in the form of citric acid or a citrate salt such as magnesium citrate, calcium citrate or other physiologically acceptable salts. Low urinary citrate excretion is a risk factor for the development of kidney stones. Citrate inhibits stone formation by complexing with calcium in the urine, inhibiting spontaneous nucleation, and preventing growth and agglomeration of crystals. Citric acid has been shown to inhibit the initial crystallization of calcium hydroxyapatite at Randall's plaques as well as the aggregation of calcium oxalate crystals and their attachment to urinary epithelium. For citric acid, this term is defined to include other compounds that provide the equivalent amount of citrate ion in solution as the amount available from citric acid used in the invention.

Ingestion of alkali salts (i.e. potassium and magnesium salts) reduces urine calcium excretion and increases the reabsorption of calcium in the proximal tubule reabsorption. Oral administration of potassium citrate is known to prevent the recurrence of kidney stones. Potassium citrate attaches to calcium in the urine, preventing the formation of mineral crystals that can develop into kidney stones. Potassium citrate also prevents the urine from becoming too acidic. This helps prevent uric acid or cysteine kidney stones from forming. Magnesium inhibits calcium oxalate crystallization in human urine and model systems by forming a soluble chelate with oxalate in the urine allowing for excretion. Magnesium also inhibits absorption of dietary oxalate from the gut lumen. Magnesium has been shown to inhibit crystal formation thus reducing the risk for forming kidney stones. Various forms of alkali salt can be used in the compositions of this invention. For magnesium citrate, this term is defined to include other magnesium compounds that provide the equivalent amount of free magnesium ion in solution as the amount of magnesium citrate used in the invention.

Phytin is a calcium-magnesium salt of phytic acid that occurs in plants. Phytic acid (known as inositol hexakisphosphate (IP6), inositol polyphosphate, or phytate when in salt form) has a strong binding affinity for calcium. Phytin acts by preventing crystallization of calcium salts. For phytin, this term is defined to include other compounds that provide the equivalent amount of phytate ion in solution as the amount available from phytin used in the invention.

Pyridoxine (4,5-Bis(hydroxymethyl)-2-methylpyridin-3-ol, or vitamin B6) reduces oxalate levels. It is believed that pyridoxine enhances the activity of an enzyme (alanine:glyoxylate aminotransferase) which diverts metabolites to other uses in the body rather than having them form oxalate. For pyridoxine, this term is defined to include vitamers of vitamin B_6, including pyridoxine (PN), pyridoxine 5'-phosphate (PNP), pyridoxal (PL), pyridoxal 5'-phosphate (PLP also known as P-5-P vitamin supplement), pyridoxamine (PM), pyridoxamine 5'-phosphate (PMP) and 4-Pyridoxic acid (PA).

Musa (extracts from the banana plant or stem) been used in traditional medicine to prevent stone growth and to aid stone passage. From a mechanistic standpoint, extracts from Musa normalize multiple abnormal urinary parameters which are known to induce stone growth, including calcium, phosphate, and oxalate. In this manner, high levels of the precipitating species that initiate stone growth are no longer excreted into the urine at high levels. Furthermore, Musa decreases the expression of liver glycolate oxidase and lactate dehydrogenase, enzymes associated with the production of oxalate in the body. In addition to these activities, Musa extracts have significant diuretic effect that aids the passage of any stones as they are generated (Devi, V. K. et al., Ancient Science of Life, 1993, 12(3&4):451-461; Pillai, R. G. Ancient Science of Life, 1995, 15(1):2-6; Patankar, S. et al., 2008, The Journal of Alternative and Complementary Medicine 14(10):1287-90; Prasobh, G. R., International Journal of Research in Pharmaceutical and Biomedical Sciences, 2012, 3(4):1251-1255). For musa, this term is defined to include all musa varieties listed in *World Checklist of Selected Plant Families*. Royal Botanic Gardens, Kew.

Formulation

Active agents used in this invention can be formulated into any oral dosage form including, solid, semi-solid, liquid, powder, sachet and the like. Solid oral dosage forms can include, for example, a tablet, a capsule (hard or soft), or subunits, and the like. "Subunit" includes a minitablet, a bead, a spheroid, a microsphere, a seed, a pellet, a caplet, a microcapsule, a granule, a particle, and the like that can provide an oral dosage form alone or when combined with other subunits. Exemplary semi-solid or liquid dosage forms include a suspension, a solution, an emulsion, and the like.

The oral dosage form can be formulated for a specific type of release including immediate-release, controlled-release, sustained-release, or extended-release.

Exemplary solid oral dosage forms can be prepared by combining active agents with one or more pharmaceutically acceptable excipients and then forming into the dosage form. As used herein, "pharmaceutically acceptable excipient" means any other component added to the pharmaceutical formulation other than the active agent. Excipients may be added to facilitate manufacture, enhance stability, enhance product characteristics, enhance bioavailability, enhance patient acceptability, etc. Pharmaceutical excipients include carriers, fillers, binders, disintegrants, lubricants, glidants, granulating agent, compression aids, colors, sweeteners, preservatives, suspending agents, dispersing agents, film formers, flavors, printing inks, buffer agents, pH adjusters, preservatives etc. In some instances, a single material will meet two or more of the foregoing general classifications.

Exemplary pharmaceutically acceptable excipients include fillers, such as water-insoluble filler, water soluble filler, or a combination thereof. The filler may be a water-insoluble filler, such as carnauba wax, stearic acid, silicon dioxide, titanium dioxide, talc, alumina, starch, kaolin, polacrilin potassium, powdered cellulose, microcrystalline cellulose, sodium citrate, dicalcium phosphate, or a combination thereof. Exemplary water-soluble fillers include water soluble sugars and sugar alcohols, specifically lactose, glucose, fructose, sucrose, mannose, dextrose, galactose, the corresponding sugar alcohols and other sugar alcohols, such as mannitol, sorbitol, xylitol, or a combination thereof.

Exemplary binders include alginic acid, a carbomer, carboxymethylcellulose calcium, carboxymethylcellulose sodium, carrageenan, cellulose acetate phthalate, chitosan, ethyl cellulose, guar gum, hydroxyethyl cellulose, hydroxyethylmethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, methyl cellulose, microcrystalline cellulose, poloxamer, polyethylene oxide, polymethacrylates, povidone, a saccharide, starch, partially pregelatinized starch, and the like, or a combination thereof.

Exemplary disintegrants include alginic acid, carboxymethylcellulose calcium, carboxymethylcellulose sodium, cross-linked sodium carboxymethylcellulose (sodium croscarmellose), powdered cellulose, chitosan, croscarmellose sodium, crospovidone, guar gum, low substituted hydroxypropyl cellulose, methyl cellulose, microcrystalline cellulose, sodium alginate, sodium starch glycolate, partially pregelatinized starch, pregelatinized starch, starch, sodium carboxymethyl starch, and the like, or a combination thereof.

Exemplary lubricants include calcium stearate, magnesium stearate, glyceryl behenate, glyceryl palmitostearate, hydrogenated castor oil, light mineral oil, sodium lauryl sulfate, magnesium lauryl sulfate, sodium stearyl fumarate, stearic acid, zinc stearate, or a combination thereof.

Exemplary glidants include colloidal silica, amorphous silica, precipitated silica, talc, calcium phosphate tribasic, calcium silicate, magnesium silicate, magnesium trisilicate, or a combination thereof, and the like.

Active agents can be formulated into dosage forms using known techniques in the pharmaceutical art including dry blending and compression, wet granulation, encapsulation, dry granulation or wet granulation followed by compression or compaction, melt extrusion and spheronization, layering (e.g., spray layering suspension or solution), and the like. Examples of such techniques include direct compression, using appropriate punches and dies, the punches and dies are fitted to a suitable rotary tableting press; injection or compression molding using suitable molds fitted to a compression unit, granulation followed by compression; and extrusion in the form of a paste, into a mold or to an extrudate to be cut into lengths.

Tablets can be prepared by compression into a compressed form using conventional tableting equipment using standard techniques. Techniques and compositions for making tablets (compressed and molded) are described in Remington's Pharmaceutical Sciences, (Aurther Osol., editor), pp. 1553-1593 (1980).

Layering techniques suitable to prepare subunits include coating inert cores with a layering solution or dispersion of the active agent and a pharmaceutically acceptable excipient. Repeated layering can be used to build the subunit size and increase active agent amount.

The controlled-release dosage form can be prepared using controlled-release matrix materials, controlled-release coating materials, or a combination thereof.

The dosage forms may include functional or nonfunctional coatings. By "functional coating" is meant to include a coating that modifies the release properties of the total composition, for example, a controlled-release coating including a sustained-release or delayed-release coating. By "non-functional coating" is meant to include a coating that is not a functional coating, for example, a cosmetic coating. A non-functional coating can have some impact on the release of the active agent due to the initial dissolution, hydration, perforation of the coating, etc., but would not be considered to be a significant deviation from the non-coated composition.

Exemplary non-functional coatings include film forming polymers such as a water soluble hydroxyl cellulose (e.g. hydroxylpropyl methylcellulose, etc.), polyvinyl alcohol, and the like; optionally further including an additional pharmaceutically acceptable coating excipient such as a plasticizer, a stabilizer, an anti-tacking agent (e.g., talc), a surfactant, and the like, or a combination thereof.

Exemplary functional coatings include polymers such as cellulose esters (e.g. ethylcellulose); a polymethacrylate (e.g. copolymers of acrylic and methacrylic acid esters), and the like; optionally further including an additional pharmaceutically acceptable coating excipient such as a plasticizer, a stabilizer, a water-soluble component (e.g. pore formers), an anti-tacking agent (e.g., talc), a surfactant, and the like, or a combination thereof.

Suitable methods known in the pharmaceutical art can be used to apply the coating material. Processes such as simple or complex coacervation, interfacial polymerization, liquid drying, thermal and ionic gelation, spray drying, spray chilling, fluidized bed coating, pan coating, or electrostatic deposition may be used.

Dosing and Administration

Oral dosage forms containing active agents can be administered to prevent or treat formation of kidney stones anywhere from once to multiple times per day, preferably one to four times per day and most preferably twice per day. Multiple dosage forms can be taken per dosing, preferably one to four dosage forms and most preferably one to two dosage forms and ideally, 1 dosage form. The dosage form can be taken with or without regard to food.

EXAMPLES

Example 1

A series of tests was run to evaluate the impact that various formulations of ingredients had on the rate of calcium oxalate crystal. Formulations were evaluated for their ability to achieve 100% inhibition of the in vitro growth rate of calcium oxalate crystals. Initially, the growth of calcium oxalate crystals in aqueous solution was determined by UV-Visible spectroscopy and is referred to as a "Control Vehicle". Then, various formulations were evaluated for their ability to inhibit the growth rate of calcium oxalate crystals compared to the Control Vehicle.

All reagents were chemical grade or plant extracts as listed in the Reagent Table below. Other grades and sources of reagents may be used.

Reagent Table

Reagent	Chemical Grade	Commercial Source	Lot #
Calcium chloride, dihydrate	ACS analytical grade	Mallinkrodt	G23H14
Sodium oxalate	ACS Reagent ≥99.5%	Sigma-Aldrich	MKBP6508V

-continued

Reagent Table

Reagent	Chemical Grade	Commercial Source	Lot #
Sodium acetate	AR analytical reagent	Fisher Scientific	7372KVND
Sodium Chloride	USP food grade	Mallinkrodt	7532KVPG
Banana stem extract - Musa		Acetar Biotech	TY140603
Phytin		TCI America	FFEKL-FA
Magnesium citrate		BulkSupplements.com	20141019
Pyridoxine HCl	≥98% HPLC	Sigma Aldrich	SLBK1634V
Citric acid		TCI America	SVJKMIT

Experimental Spectrophotometric Method:

The spectrophotometric method employed was based on the work of Chow (Chow, 2004b, Citrate inhibits growth of residual fragments in an in vitro model of calcium oxalate renal stones. Kidney International, 665:1724-1730) and is briefly described below. The study was conducted using a sodium acetate/sodium chloride buffer at pH 5.7 as recommended by Khan (Khan 2012, Antiurolithic activity of *Origanum vulgare* is mediated through multiple pathways BMC Complementary and Alternative Medicine 11: 96-112.).

The kinetics of calcium oxalate crystal formation in a control vehicle were characterized by the slope method of Hess (Hess, B. et al., Nephrol. Dial. Transplant, 2000, 15(3): 366-374). Briefly, 1.6 milliliters of an 8.5 mM solution of calcium chloride was added to a plastic cuvette and 1.6 milliliters of a 1.5 mM sodium oxalate solution was then added. Both of the solutions were prepared in a buffer composed of 50 mM sodium acetate and 100 mM sodium chloride at pH 5.7. Immediately upon combining the solutions, the cuvette was mixed by inversion and the kinetics of calcium oxalate crystal formation were monitored at 620 nm using a spectrophotometer. A Vernier SpectroVis spectrophotometer was used. Measurements were made in the Absorbance versus Time mode, using ten (10) minutes for a full run with an acquisition of 10 samples per minute. Other spectrophotometers, wavelengths, and methods may also be used to determine calcium oxalate crystal formation over time.

The inhibition of the kinetics of calcium oxalate crystal formation by the various Test Solutions set forth below were determined using the method described above with the following change. Before the sodium oxalate solution was added, 200 μL of the Test Solution is added to the cuvette. The remainder of the procedure was the same as described above. The inhibition of crystal growth was determined by comparison of the effect of the Test Solution on the slope of the initial velocity (compared to vehicle control, during the first two minutes), as described by Hess (Hess, 2000). Individual replicates identified as outliers by the Grubb's test were not included in the calculation (Grubbs, Frank E., 1950, Sample criteria for testing outlying observations, The Annals of Mathematical Statistics 21(1), p. 27-58.). Other methods of determining percent inhibition of calcium oxalate crystal formation, such as by individual runs or other statistical methods are also possible.

The Test Solutions were prepared by adding the following ingredients in the amounts given in Table 1 in the order listed to a 100 mL volumetric flask:

- Citric acid—added as a dry powder to a 100 mL volumetric flask;
- Magnesium citrate—added as a dry powder to above volumetric flask and 50 mL distilled H_2O added and vortexed until clear
- Phytin—added to above volumetric flask and vortexed until clear
- Pyridoxine—added to above volumetric flask and vortexed until clear
- Musa—50 ml, of the prepared solution (see below) added to the above volumetric flask and made up to final volume of 100 mL with water.

The Musa samples were prepared by placing the indicated amount of Musa, as a dry powder, (see Table 1) in a 100 mL volumetric flask and making up to volume with water. The flask was vortexed intermittently for 5 minutes. At this time the sample was transferred to a centrifuge tube and centrifuged at 3000 rpm for 30 minutes. 50 mL of the supernatant was carefully transferred to a 50 mL volumetric flask and vortexed to assure complete solubility. This 50 mL homogeneous solution was transferred to the original 100 mL volumetric flask and vortexed to assure complete solubility.

TABLE 1

Amounts of Active Ingredients in Test Solutions.

Active Ingredient	Test Solution 1	Test Solution 2	Test Solution 3	Test Solution 4	Test Solution 5	Test Solution 6	Test Solution 7
Citric Acid	352 mg	101 mg	1050 mg	700 mg	352 mg	176 mg	351 mg
Mg Citrate	151 mg	76 mg	2.02 mg	226 mg	201 mg	150 mg	152 mg
Phytin	202 mg	201 mg	100 mg	3.03	600 mg	400 mg	200 mg
Pyridoxine	5.4 mg	10.1 mg	5.99 mg	2.67	0.2 mg	15.1 mg	5.3 mg
Musa	251 mg	251 mg	167 mg	85 mg	41 mg	1.4 mg	251 mg

FIG. **1** shows the absorbance as function of time for the first 10 minutes and measures the formation of calcium oxalate over time for the Control Vehicle runs used for Test Solution 1. From the figure it can be seen that calcium oxalate crystals are indeed forming during the ten minutes of the run. FIG. **2** shows the slopes of the curves for the initial two minutes of the runs for the Control Vehicle used for Test Solution 1. Since the data was linear (R^2>0.95) for the first two (2) minutes, this data was plotted for slope determination by linear regression analysis. FIG. **3** shows the absorbance as function of time for the first 10 minutes and measures the formation of calcium oxalate over time for the Control Vehicle runs used for Test Solution 1. FIG. **4** shows the slopes of the curves for the initial two minutes of the runs for Test Solution 1. Since the data was linear (R^2>0.95) for the first two (2) minutes, this data was plotted for slope determination by linear regression analysis.

Table 2 shows the analysis of the slopes FIGS. **2** and **4**. Each run is designated as a Replicate. Outlier data identified using the Grubbs' Test (Grubbs, 1950) were not included in % inhibition calculations. The median % Inhibition was calculated according to the method of Hess (Hess, 2000) using the following equation:

%Inhibition=100%*(1−(Slope of Test Solution/Slope of Control Vehicle)).

TABLE 2

Data Analysis for Slope Test, Control Vehicle & Test Solution 1

	Replicate #1	Replicate #2	Replicate #3	Replicate #4	Replicate #5	Replicate #6	Median	Median % Inhibition
Control Vehicle	0.0047	0.0172	0.0022	0.0042	0.0057	0.0036	0.00445	
Test Solution 1	−0.0002	0.0002	0.00003	0.00007	−0.0003	0.001	0.00005	98.8764

FIG. **5** shows the absorbance as function of time for the first 10 minutes and measures the formation of calcium oxalate over time for the Control Vehicle runs used for Test Solution 2. From the figure it can be seen that calcium oxalate crystals are indeed forming during the ten minutes of the run. FIG. **6** shows the slopes of the curves for the initial two minutes of the runs for the Control Vehicle used for Test Solution 2. Since the data was linear (R2>0.95) for the first two (2) minutes, this data was plotted for slope determination by linear regression analysis. FIG. **7** shows the absorbance as function of time for the first 10 minutes and measures the formation of calcium oxalate over time for the Control Vehicle runs used for Test Solution 1. FIG. **8** shows the slopes of the curves for the initial two minutes of the runs for Test Solution 2. Since the data was linear (R2>0.95) for the first two (2) minutes, this data was plotted for slope determination by linear regression analysis. Table 3 shows the analysis of the slopes FIGS. **6** and **8**. Each run is designated as a Replicate.

TABLE 3

Data Analysis for Slope Test, Control Vehicle & Test Solution 2

	Replicate #1	Replicate #2	Replicate #3	Replicate #4	Replicate #5	Replicate #6	Median	Median % Inhibition
Control Vehicle	−0.028	0.0666	0.0634	0.0855	0.0406	0.0334	0.0634	
Test Solution 2	−0.0007	−0.0008	−0.0012	−0.0012	—	—	−0.001	101.5773

FIG. **9** shows the absorbance as function of time for the first 10 minutes and measures the formation of calcium oxalate over time for the Control Vehicle runs used for Test Solution 3. From the figure it can be seen that calcium oxalate crystals are indeed forming during the ten minutes of the run. FIG. **10** shows the slopes of the curves for the initial two minutes of the runs for the Control Vehicle used for Test Solution 3. Since the data was linear (R^2>0.95) for the first two (2) minutes, this data was plotted for slope determination by linear regression analysis. FIG. **11** shows the absorbance as function of time for the first 10 minutes and measures the formation of calcium oxalate over time for the Control Vehicle runs used for Test Solution 3. FIG. **12** shows the slopes of the curves for the initial two minutes of the runs for Test Solution 3. Since the data was linear (R^2>0.95) for the first two (2) minutes, this data was plotted for slope determination by linear regression analysis. Table 4 shows the analysis of the slopes FIGS. **10** and **12**. Each run is designated as a Replicate.

TABLE 4

Data Analysis for Slope Test, Control Vehicle & Test Solution 3

	Replicate #1	Replicate #2	Replicate #3	Replicate #4	Median	Median % Inhibition
Control Vehicle	0.0073	0.0123	0.0129	0.0115	0.0119	
Test Solution 3	0.0014	0.0077	0.0039	0.0035	0.0035	70.5882

FIG. **13** shows the absorbance as function of time for the first 10 minutes and measures the formation of calcium oxalate over time for the Control Vehicle runs used for Test Solution 4. From the figure it can be seen that calcium oxalate crystals are indeed forming during the ten minutes of the run. FIG. **14** shows the slopes of the curves for the initial two minutes of the runs for the Control Vehicle used for Test Solution 4. Since the data was linear (R2>0.95) for the first two (2) minutes, this data was plotted for slope determination by linear regression analysis. FIG. **15** shows the absorbance as function of time for the first 10 minutes and measures the formation of calcium oxalate over time for the Control Vehicle runs used for Test Solution 4. FIG. **16** shows the slopes of the curves for the initial two minutes of the runs for Test Solution 4. Since the data was linear (R2>0.95) for the first two (2) minutes, this data was plotted for slope determination by linear regression analysis. Table 5 shows the analysis of the slopes FIGS. **14** and **16**. Each run is designated as a Replicate.

TABLE 5

Data Analysis for Slope Test, Control Vehicle & Test Solution 4

	Replicate #1	Replicate #2	Replicate #3	Median	Median % Inhibition
Control Vehicle	0.0772	0.107	0.081	0.081	
Test Solution 4	0.0026	0.0007	0.0006	0.0004	99.5679

FIG. **17** shows the absorbance as function of time for the first 10 minutes and measures the formation of calcium

oxalate over time for the Control Vehicle runs used for Test Solution 5. From the figure it can be seen that calcium oxalate crystals are indeed forming during the ten minutes of the run. FIG. **18** shows the slopes of the curves for the initial two minutes of the runs for the Control Vehicle used for Test Solution 5. Since the data was linear (R2>0.95) for the first two (2) minutes, this data was plotted for slope determination by linear regression analysis. FIG. **19** shows the absorbance as function of time for the first 10 minutes and measures the formation of calcium oxalate over time for the Control Vehicle runs used for Test Solution 5. FIG. **20** shows the slopes of the curves for the initial two minutes of the runs for Test Solution 5. Since the data was linear (R2>0.95) for the first two (2) minutes, this data was plotted for slope determination by linear regression analysis. Table 6 shows the analysis of the slopes FIGS. **18** and **20**. Each run is designated as a Replicate.

TABLE 6

Data Analysis for Slope Test, Control Vehicle & Test Solution 5

	Replicate #1	Replicate #2	Replicate #3	Median	Median % Inhibition
Control Vehicle	0.0851	0.0508	0.0467	0.0588	

TABLE 6-continued

Data Analysis for Slope Test, Control Vehicle & Test Solution 5

	Replicate #1	Replicate #2	Replicate #3	Median	Median % Inhibition
Test Solution 5	0.0007	0.0003	0.0004	0.0004	99.3197

FIG. **21** shows the absorbance as function of time for the first 10 minutes and measures the formation of calcium oxalate over time for the Control Vehicle runs used for Test Solution 6. From the figure it can be seen that calcium oxalate crystals are indeed forming during the ten minutes of the run. FIG. **22** shows the slopes of the curves for the initial two minutes of the runs for the Control Vehicle used for Test Solution 6. Since the data was linear (R2>0.95) for the first two (2) minutes, this data was plotted for slope determination by linear regression analysis. FIG. **23** shows the absorbance as function of time for the first 10 minutes and measures the formation of calcium oxalate over time for the Control Vehicle runs used for Test Solution 6. FIG. **24** shows the slopes of the curves for the initial two minutes of the runs for Test Solution 6. Since the data was linear (R2>0.95) for the first two (2) minutes, this data was plotted for slope determination by linear regression analysis. Table 7 shows the analysis of the slopes FIGS. **22** and **24**. Each run is designated as a Replicate.

TABLE 7

Data Analysis for Slope Test, Control Vehicle & Test Solution 6

	Replicate #1	Replicate #2	Replicate #3	Replicate #4	Replicate #5	Median	Median % Inhibition
Control Vehicle	0.0068	0.0717	0.038	0.0594	0.0037	0.0224	
Test Solution 6	−0.0033	−0.0035	−0.0028	−0.0045	−0.0012	−0.0031	113.6161

Table 8 shows the analysis of the slopes of solution 7, a duplicate of test solution 1, which was calculated similarly to Test Solution 1. Each run is designated as a Replicate. The data from these experiments are shown FIGS. **25-28**.

TABLE 8

Data Analysis for Slope Test, Control Vehicle & Test Solution 7

	Replicate #1	Replicate #2	Replicate #3	Replicate #4	Replicate #5	Replicate #6	Median	% Inhibition
Vehicle	0.0084	0.0204	0.0282	0.0054	0.0193	0.0306	0.01985	
Test Solution 1	−0.0000005	−0.0003	−0.0002	0.0005	−0.0003	−0.0002	−0.0002	101.0076

Table 9 shows the percent inhibition results (calculated as median and average) and the ingredient weights for Test Solutions 1 through Test Solution 7.

TABLE 9

Median and Mean Inhibition of Calcium Oxalate Crystal Growth by Test Solutions

	Test Solution 1	Test Solution 2	Test Solution 3	Test Solution 4	Test Solution 5	Test Solution 6	Test Solution 7
Median % Inhibition	98.88	101.58	70.59	99.57	99.32	113.62	101.00

TABLE 9-continued

Median and Mean Inhibition of Calcium Oxalate Crystal Growth by Test Solutions

	Test Solution 1	Test Solution 2	Test Solution 3	Test Solution 4	Test Solution 5	Test Solution 6	Test Solution 7
Average % Inhibition	96.26	103.11	64.39	99.48	99.27	92.44	99.19
Citric Acid	352 mg	101 mg	1050 mg	700 mg	352 mg	176 mg	351 mg
Mg Citrate	151 mg	75 mg	2.02 mg	226 mg	201 mg	150 mg	152 mg
Phytin	202 mg	201 mg	100 mg	3.03 mg	600 mg	400 mg	200 mg
Pyridoxine	5.4 mg	10.2 mg	5.99 mg	2.67 mg	0.2 mg	15.1 mg	5.3 mg
Musa	251 mg	251 mg	167 mg	85 mg	41 mg	1.4 mg	251 mg

The results in Table 9 show that compositions having about 101 mg to about 700 mg citric acid; about 76 mg to about 226 mg magnesium citrate; about 3 mg to about 600 mg phytin; about 0.1 mg to about 15 mg pyridoxine; and about 1 mg to about 251 mg musa. result in a mean percent inhibition of calcium oxalate crystal growth of at least about 92%, while compositions having citric acid, magnesium citrate, phytin, pyridoxine, and musa concentrations outside these ranges are unexpectedly much less effective, resulting in mean percent inhibition of calcium oxalate crystal growth of only about 64%.

Example 2

Oral Dosage Form

TABLE 10

Oral Capsule

Ingredient	Amount
Citric Acid	about 101 mg to about 700 mg
Mg Citrate	about 76 mg to about 226 mg
Phytin	about 3 mg to about 600 mg
Pyridoxine	about 0.1 mg to about 15 mg
Musa	about 1 mg to about 251 mg

The five active ingredients are blended in the above amounts and deposited into a hard shell capsule, e.g., a hydroxypropyl methylcellulose (HPMC) capsule, such as a DRcap™ (Capsugel®, Morristown, N.J.).

Set forth below are some embodiments of the oral dosage forms and methods for disclosed herein.

Embodiment 1

An oral dosage form or a plurality of dosage forms comprising as active ingredients citric acid, magnesium citrate, phytin, pyridoxine, and musa.

Embodiment 2

The oral dosage form or plurality of dosage forms of embodiment 1, wherein citric acid is present in an amount of about 101 mg to about 700 mg.

Embodiment 3

The oral dosage form or plurality of dosage forms according to embodiment 2 wherein citric acid is present in an amount selected from: about 101 mg to about 352 mg, about 101 mg to about 176 mg, about 176 mg to about 700 mg, and about 352 mg to about 700 mg.

Embodiment 4

The oral dosage form or plurality of dosage forms of embodiment 1, wherein magnesium citrate is present in an amount of about 76 mg to about 226 mg.

Embodiment 5

The oral dosage form or plurality of dosage forms according to embodiment 4 wherein magnesium citrate is present in an amount selected from: about 76 mg to about 201 mg, about 76 mg to about 150 mg, about 150 to about 226 mg, and about 201 mg to about 225 mg.

Embodiment 6

The oral dosage form or plurality of dosage forms of embodiment 1, wherein phytin is present in an amount of about 3 mg to about 600 mg.

Embodiment 7

The oral dosage form or plurality of dosage forms according to embodiment 6 wherein phytin is present in an amount selected from: about 3 mg to about 400 mg, about 3 mg to about 202 mg, about 3 mg to about 100 mg, about 100 mg to about 600 mg, about 200 mg to about 600 mg, and about 400 mg to about 600 mg.

Embodiment 8

The oral dosage form or plurality of dosage forms of embodiment 1, wherein pyridoxine is present in an amount of about 0.2 mg to about 15 mg.

Embodiment 9

The oral dosage form or plurality of dosage forms according to embodiment 8 wherein pyridoxine is present in an amount selected from: about 0.2 mg to about 10 mg, about 0.2 mg to about 6 mg, about 0.2 mg to about 2.7 mg, about 2.7 mg to about 15 mg, about 6.0 mg to about 15 mg, and about 10 mg to about 15 mg.

Embodiment 10

The oral dosage form or plurality of dosage forms of embodiment 1, wherein musa is present in amount of about 1 mg to about 251 mg.

Embodiment 11

The oral dosage form or plurality of dosage forms according to embodiment 10 wherein musa is present in an amount selected from: about 1 mg to about 167 mg, about 1 mg to about 85 mg, about 1 mg to about 41 mg, about 41 mg to about 251 mg, about 85 mg to about 251 mg, and about 167 mg to about 251 mg.

Embodiment 12

The oral dosage form or plurality of dosage forms of embodiment 1 wherein citric acid is present in an amount of about 101 mg to about 700 mg; magnesium citrate is present in an amount of about 76 mg to about 226 mg; phytin is present in an amount of about 3 mg to about 600 mg; pyridoxine is present in an amount of about 0.1 mg to about 15 mg; and musa is present in amount of about 1 mg to about 251 mg.

Embodiment 13

The oral dosage form or plurality of dosage forms according to embodiment 12 wherein citric acid is present in an amount selected from: about 51 mg to about 352 mg, about 101 mg to about 176 mg, about 176 mg to about 700 mg, and about 352 mg to about 700 mg; magnesium citrate is present in an amount selected from: about 76 mg to about 201 mg, about 76 mg to about 150 mg, about 150 to about 226 mg, and about 201 mg to about 225 mg; phytin is present in an amount selected from: about 3 mg to about 400 mg, about 3 mg to about 202 mg, about 3 mg to about 100 mg, about 100 mg to about 600 mg, about 200 mg to about 600 mg, and about 400 mg to about 600 mg; pyridoxine is present in an amount selected from: about 0.2 mg to about 10 mg, about 0.2 mg to about 6 mg, about 0.2 mg to about 2.7 mg, about 2.7 mg to about 15 mg, about 6.0 mg to about 15 mg, and about 10 mg to about 15 mg; and musa is present in an amount selected from: about 1 mg to about 167 mg, about 1 mg to about 85 mg, about 1 mg to about 41 mg, about 41 mg to about 251 mg, about 85 mg to about 251 mg, and about 167 mg to about 251 mg.

Embodiment 14

The oral dosage form or plurality of dosage forms of embodiment 1, wherein the amount of one of the active ingredients is selected from: citric acid is present in an amount of about 101 mg to about 700 mg; magnesium citrate is present in an amount of about 76 mg to about 226 mg; phytin is present in an amount of about 3 mg to about 600 mg; pyridoxine is present in an amount of about 0.1 mg to about 15 mg; and musa is present in amount of about 1 mg to about 251 mg.

Embodiment 15

The oral dosage form or plurality of dosage forms of embodiment 1, wherein the amounts of two of the active ingredients are selected from: citric acid is present in an amount of about 101 mg to about 700 mg; magnesium citrate is present in an amount of about 76 mg to about 226 mg; phytin is present in an amount of about 3 mg to about 600 mg; pyridoxine is present in an amount of about 0.1 mg to about 15 mg; and musa is present in amount of about 1 mg to about 251 mg.

Embodiment 16

The oral dosage form or plurality of dosage forms of embodiment 1, wherein the amounts of 3 of the ingredients are selected from: citric acid is present in an amount of about 101 mg to about 700 mg; magnesium citrate is present in an amount of about 76 mg to about 226 mg; phytin is present in an amount of about 3 mg to about 600 mg; pyridoxine is present in an amount of about 0.1 mg to about 15 mg; and musa is present in amount of about 1 mg to about 251 mg.

Embodiment 17

The oral dosage form or plurality of dosage forms of embodiment 1, wherein the amounts of 4 of the ingredients are selected from: citric acid is present in an amount of about 101 mg to about 700 mg; magnesium citrate is present in an amount of about 76 mg to about 226 mg; phytin is present in an amount of about 3 mg to about 600 mg; pyridoxine is present in an amount of about 0.1 mg to about 15 mg; and musa is present in amount of about 1 mg to about 251 mg.

Embodiment 18

The oral dosage form or plurality of dosage forms of embodiment 1, wherein citric acid is present in an amount of about 350 mg; magnesium citrate is present in an amount of about 150 mg; phytin is present in an amount of about 200 mg; pyridoxine is present in an amount of about 5 mg; and musa is present in amount of about 250 mg.

Embodiment 19

The oral dosage form or a plurality of dosage forms according to any one of embodiments 1-18, wherein the percent inhibition of calcium oxalate crystal formation by the combination of active ingredients is greater than about 92%.

Embodiment 20

The oral dosage form or plurality of dosage forms according to embodiment 19, where the percent inhibition is greater than about 96%.

Embodiment 21

The oral dosage form or plurality of dosage forms according to embodiment 20 where the percent inhibition is greater than about 99%.

Embodiment 22

The oral dosage form or plurality of dosage forms according to any one of embodiments 1-21, comprising an oral dosage form in the form of a capsule.

Embodiment 23

The oral dosage form or plurality of dosage forms of embodiment 22, wherein the capsule is a hard capsule.

Embodiment 24

A method of treating or inhibiting formation of kidney stones comprising administering to a patient in need thereof

the oral dosage form or plurality of dosage forms according to any one of embodiments 1-23.

Embodiment 25

The method of embodiment 24, wherein the oral dosage form or plurality of dosage forms is administered once daily.

Embodiment 26

The method of embodiment 24, wherein the oral dosage form or plurality of dosage forms is administered twice daily.

Embodiment 27

The method of any one of embodiments 24 to 26, wherein the oral dosage form or plurality of dosage forms comprises about 101 mg to about 700 mg citric acid; about 76 mg to about 226 mg magnesium citrate; about 3 mg to about 600 mg phytin; about 0.1 mg to about 15 mg pyridoxine; and about 1 mg to about 251 mg musa.

Embodiment 28

The method of embodiment 27, wherein the oral dosage form or plurality of dosage forms comprises about 350 mg citric acid, about 150 magnesium citrate, about 200 mg phytin, about 5 mg pyridoxine, and about 250 mg musa.

Embodiment 29

The method of any one of embodiments 24 to 26, wherein the oral dosage form or plurality of dosage forms is an oral capsule or a plurality of oral capsules comprising the citric acid, magnesium citrate, phytin, pyridoxine, and musa.

Embodiment 30

The method of any one of embodiments 24-29, wherein the administering is without regard to food.

Embodiment 31

The method of any one of embodiments 24-29, wherein the administering is with food.

Embodiment 32

The method of any one of embodiments 24-29, wherein the administering is without food.

Embodiment 33

A method of inhibiting growth of calcium oxalate crystals comprising contacting an aqueous solution comprising calcium oxalate with the oral dosage form or plurality of dosage forms according to any one of embodiments 1-23.

Embodiment 34

The method of embodiment 33, wherein the oral dosage form or plurality of dosage forms comprises about 101 mg to about 700 mg citric acid; about 76 mg to about 226 mg magnesium citrate; about 3 mg to about 600 mg phytin; about 0.1 mg to about 15 mg pyridoxine; and about 1 mg to about 251 mg musa.

In general, the invention may alternatively comprise, consist of, or consist essentially of, any appropriate components herein disclosed. The invention may additionally, or alternatively, be formulated so as to be devoid, or substantially free, of any components, materials, ingredients, adjuvants or species used in the prior art compositions or that are otherwise not necessary to the achievement of the function and/or objectives of the present invention. The endpoints of all ranges directed to the same component or property are inclusive and independently combinable (e.g., ranges of "less than or equal to 25 wt %, or 5 wt % to 20 wt %," is inclusive of the endpoints and all intermediate values of the ranges of "5 wt % to 25 wt %," etc.). Disclosure of a narrower range or more specific group in addition to a broader range is not a disclaimer of the broader range or larger group.

Reference throughout the specification to "some embodiments", "another embodiment", "an embodiment", and so forth, means that a particular element (e.g., feature, structure, and/or characteristic) described in connection with the embodiment is included in at least one embodiment described herein, and may or may not be present in other embodiments. In addition, it is to be understood that the described elements may be combined in any suitable manner in the various embodiments.

All cited patents, patent applications, and other references are incorporated herein by reference in their entirety. However, if a term in the present application contradicts or conflicts with a term in the incorporated reference, the term from the present application takes precedence over the conflicting term from the incorporated reference

While particular embodiments have been described, alternatives, modifications, variations, improvements, and substantial equivalents that are or may be presently unforeseen may arise to applicants or others skilled in the art. Accordingly, the appended claims as filed and as they may be amended are intended to embrace all such alternatives, modifications variations, improvements, and substantial equivalents.

The invention claimed is:

1. An oral dosage form or plurality of dosage forms comprising as active ingredients citric acid, magnesium citrate, phytin, pyridoxine, and musa, wherein

citric acid is present in an amount of about 101 mg to about 700 mg;

magnesium citrate is present in an amount of about 76 mg to about 226 mg;

phytin is present in an amount of about 3 mg to about 600 mg;

pyridoxine is present in an amount of about 0.1 mg to about 15 mg; and

musa is present in amount of about 1 mg to about 251 mg.

2. The oral dosage form or plurality of dosage forms according to claim **1** wherein

citric acid is present in an amount selected from: about 101 mg to about 352 mg, about 101 mg to about 176 mg, about 176 mg to about 700 mg, and about 352 mg to about 700 mg;

magnesium citrate is present in an amount selected from: about 76 mg to about 201 mg, about 76 mg to about 150 mg, about 150 to about 226 mg, and about 201 mg to about 225 mg;

phytin is present in an amount selected from: about 3 mg to about 400 mg, about 3 mg to about 202 mg, about 3 mg to about 100 mg, about 100 mg to about 600 mg, about 200 mg to about 600 mg, and about 400 mg to about 600 mg;

pyridoxine is present in an amount selected from: about 0.2 mg to about 10 mg, about 0.2 mg to about 6 mg, about

0.2 mg to about 2.7 mg, about 2.7 mg to about 15 mg, about 6.0 mg to about 15 mg, and about 10 mg to about 15 mg; and

musa is present in an amount selected from: about 1 mg to about 167 mg, about 1 mg to about 85 mg, about 1 mg to about 41 mg, about 41 mg to about 251 mg, about 85 mg to about 251 mg, and about 167 mg to about 251 mg.

3. The oral dosage form or plurality of dosage forms of claim **1**, wherein

citric acid is present in an amount of about 350 mg;

magnesium citrate is present in an amount of about 150 mg;

phytin is present in an amount of about 200 mg;

pyridoxine is present in an amount of about 5 mg; and

musa is present in amount of about 250 mg.

4. The oral dosage form or a plurality of dosage forms according to claim **3**, wherein the percent inhibition of calcium oxalate crystal formation by the combination of active ingredients is greater than about 96%.

5. The oral dosage form or a plurality of dosage forms according to claim **1**, wherein the percent inhibition of calcium oxalate crystal formation by the combination of active ingredients is greater than about 92%.

6. The oral dosage form or plurality of dosage forms according to claim **5**, where the percent inhibition is greater than about 96%.

7. The oral dosage form or plurality of dosage forms according to claim **5** where the percent inhibition is greater than about 99%.

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