Changes in Urinary Compositions among Children after Consuming Prepared Oral Doses of Aloe (Aloe vera Linn)

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Objectives: *1) To investigate the amount of citrate and tartrate in aloe gel, and in the urine of healthy normal children, before and after consuming fresh aloe gel. 2) To evaluate the changes in the chemical composition of urine among subjects after taking aloe gel. 3) To determine the value of consuming aloe gel for prevention of renal stone formation.*
Design: *Experimental study.*
Material and Method: *Thirteen healthy boys between 9 and 13 years of age were enrolled (with informed permission) in the clinical trial. Subjects ingested 100 g of fresh prepared aloe gel twice a day for seven consecutive days. The 24-hour urine was collected one day prior to taking the gel (Day 0), Days 2 and 5 of consumption, and Day 8 (one day after completion). The authors determined the urine volume, osmolality, potassium, sodium, phosphate, calcium, magnesium, uric acid, citrate, tartrate, oxalate, Permissible Increment in Calcium (PI Ca), Permissible Increment in Oxalate (PI Ox), Concentration Product Ratio of Calcium Phosphate (CPR $CaPO_4$) and the citrate per creatinine ratio.*
Results: *The citrate and tartrate concentration in 100 g of fresh aloe gel was 96.3 and 158.9 mg, respectively. The 24-hr urine volume and urinary citrate excretion were significantly increased ($p < 0.05$). The PI Ca and the PI Ox were also significantly increased ($p < 0.05$). The other measurements were unremarkable.*
Conclusion: *One hundred grams of fresh Aloe vera gel contains 96.3 milligrams of citrate and 158.9 milligrams of tartrate and were in the mid-range among Thai fruits. Changes in chemical compositions of urine after aloe gel consumption shows potential for preventing kidney stone formation among children.*

Keywords: *Aloe vera, Children, Citrate, PI, Renal stone prevention*

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Renal stone disease is a common health problem among people living in rural Northeastern Thailand[1,2]. Two predominant abnormalities among patients with renal stone disease are hypocitraturia and potassium deficiency[3,4]. Medicinal herbs have been used successfully to prevent renal stone formation, ostensibly because they contain tartrate and citrate[5-7]. Aloe vera contains several pharmacologically active ingredients useful for treatment of radiation burns, ulcers, contact burns, arthritis, diabetes, and preventative of atheromatous heart disease[8-10].

In vitro studies of the effects of aloe in medicinal use have been reported using both controlled and uncontrolled designs. The known and researched chemical composition of aloe includes anthraquinones, saccharides, enzymes, vitamins, essential amino acids, nonessential amino acids, and inorganic elements[11]. Research on the components of citrate and tartrate has not yet been published.

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Thus, the authors investigated the amount of citrate and tartrate in aloe gel, and in the urine of healthy normal children before and after consuming fresh (edible) aloe gel. The other objectives were: (1) to evaluate the changes in the chemical compositions of urine among subjects after taking aloe gel; and (2) to determine the value of their regular ingestion for prevention of stone formation.

Material and Method

The present research protocol was reviewed and approved by the Khon Kaen University Ethics Committee for Human Research. Following informed consent, thirteen healthy boys between 9-13 years of age (mean $\pm$ SD = 12.42 $\pm$ 0.34 years) were enrolled in the clinical trial.

The inclusion criteria were: (1) males between 9 to 15 years of age; (2) healthy physical condition as determined by a pediatrician (Sukachart Kirdpon MD); (3) able to complete the 24-hr urine collection during the study; (4) able to consume 100 grams of aloe gel twice daily at the prescribed time during the study; and (5) informed consent from both parents and assent by each youth.

The exclusion criteria were: (1) a serum creatinine level above 2.0 mg/dl; (2) any major illness, (3) a condition requiring medication; or (4) indication of a urinary tract infection.

Leaves of aloe plants grown for a year were collected for; (1) species identification; (2) determination of citrate and tartrate in the fresh aloe gel; and (3) preparation of fresh aloe gel for consumption. The aloe leaves were identified as Aloe vera Linn by a plant taxonomist.

The subjects ingested 100 grams of fresh aloe gel twice a day, in the morning and in the afternoon, for 7 consecutive days. The 24-hr urine was collected one day prior to taking the gel (Day 0), Day 2 and Day 5 (of consumption), and Day 8 (one day after finishing the course). The collected urine was stored cool at 4-8 C without any preservative. Urine specimens with a creatinine value of less than the formula guide were discarded[12].

An enzymatic method was used to determine the citrate content[13]. The amount of tartaric acid (tartrate) was determined using the method reported by Underhill et al[14]. Uric acid and oxalate were determined using an enzymatic method[15,16]. Urine-calcium was analyzed by a standard method using atomic absorption. Sodium, potassium, uric acid, creatinine, phosphorus, and magnesium were analyzed by a Synchron Clinical System CX7 (Beckman Instruments INC, Brea, CA. USA).

The Concentration Product Ratio (CPR) of brushite was determined by a method published elsewhere[17,18]. Briefly, a portion of urine, with a pH adjusted to 6.0, was centrifuged to remove cell debris and crystalline substances. A 10-ml aliquot was added to 100 mg of seed crystals of calcium phosphate and incubated with stirring at 37 C for 48 hours, then filtered through a 0.22 micromillipore membrane. The filtrate was analyzed for calcium and phosphate. The formula used for calculate CPR was:

$$\text{CPR of calcium phosphate} = \frac{CaPO_4 \text{ before incubation}}{CaPO_4 \text{ after incubation}}$$

The saturation of calcium phosphate is indexed by CPR values: above 1 indicates over-saturation, equal to 1 indicates saturation, and below 1 indicates under-saturation.

Potential of calcium or oxalate inhibition was assessed by Permissible Increments in Calcium (PI Ca) or Permissible Increments in Oxalate (PI Ox). An increasing value of PI indicates the inhibitory activity is increasing in the urine. The PI was measured as per Nicar et al[19]. In brief, sodium oxalate (for measurement of PI in oxalate) or calcium chloride (for measurement of PI in calcium) were added stepwise (in 1 mg increments with stirring) to each of the twelve 10-ml aliquots of centrifuged urine, and incubated at 37 C for 3 hours. The first precipitated tube was recorded for calculated PI.

Urine osmolality was determined by a 3DII osmometer, Advanced Instruments, INC. and urinalysis (including pH, glucose, and protein) was determined with a Labstix from Bayer Diagnostics Aust. Pty. Ltd.

The repeated measurement design and ANOVA with multiple comparison tests were used for the related groups between the parameters of Day 0, 2, 5, and 8. Statistical significance was accepted at $p < 0.05$.

Results

Citrate and tartrate concentration in 100 g of fresh aloe gel was 96.3 and 158.9 mg, respectively.

The 24-hr urine volume, citrate, PI Ox and PI Ca were significantly increased ($p < 0.05$, Fig. 1-4). The difference in excretion of sodium, potassium, phosphate, calcium, magnesium, tartrate, oxalate, and uric acid was not statistically significant. The urine osmolality showed no significant change. The CPR of calcium phosphate (brushite) was not significantly decreased.

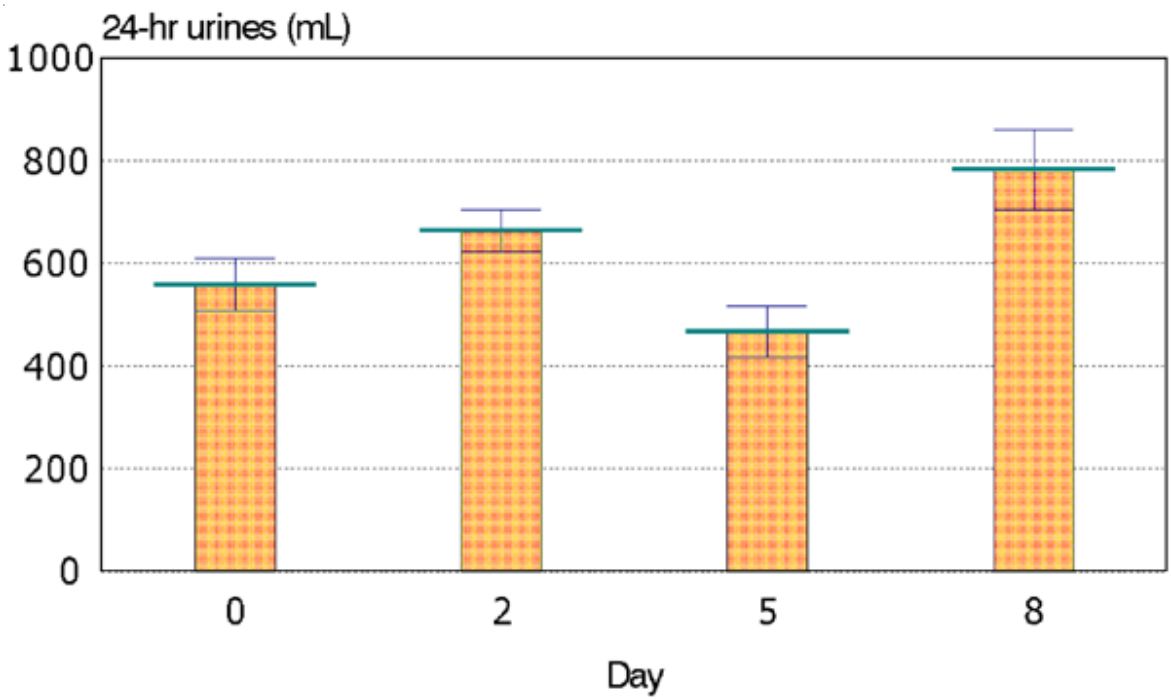

Fig. 1 Increased 24-hr urine volume after aloe gel consumption. A significant increase in urine volume occurred between Day 0 and 8 at $p < 0.05$

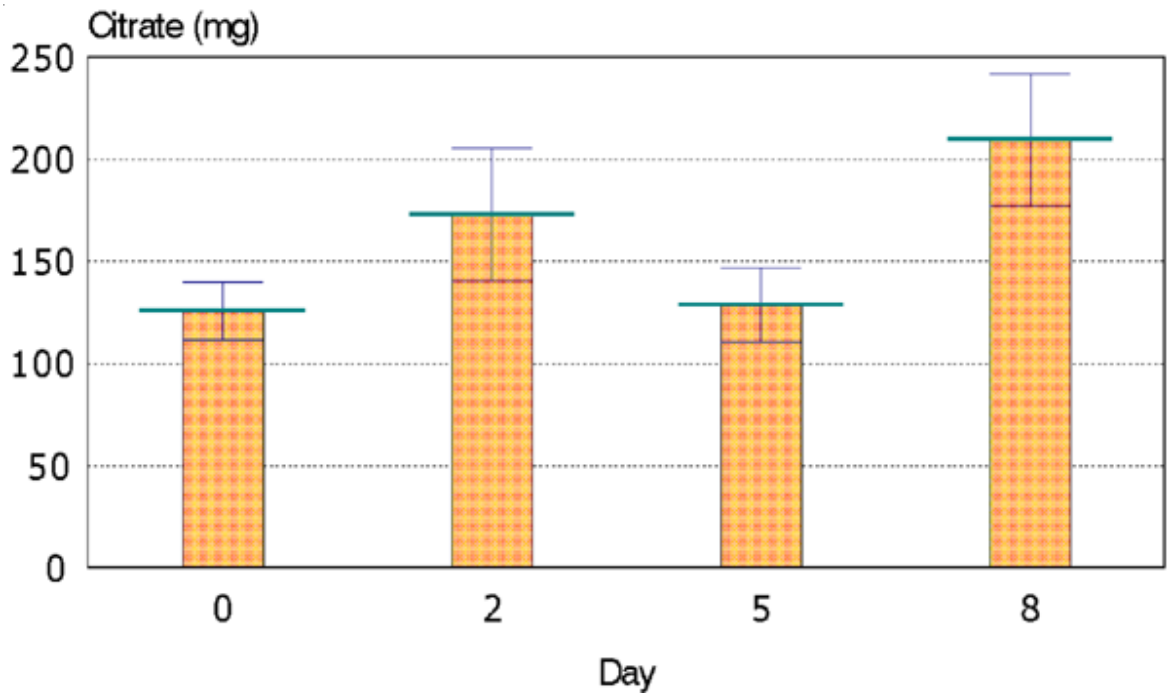

Fig. 2 Increased citrate excretion after aloe consumption. A significant increase occurred between Day 0 and 8 at $p < 0.05$

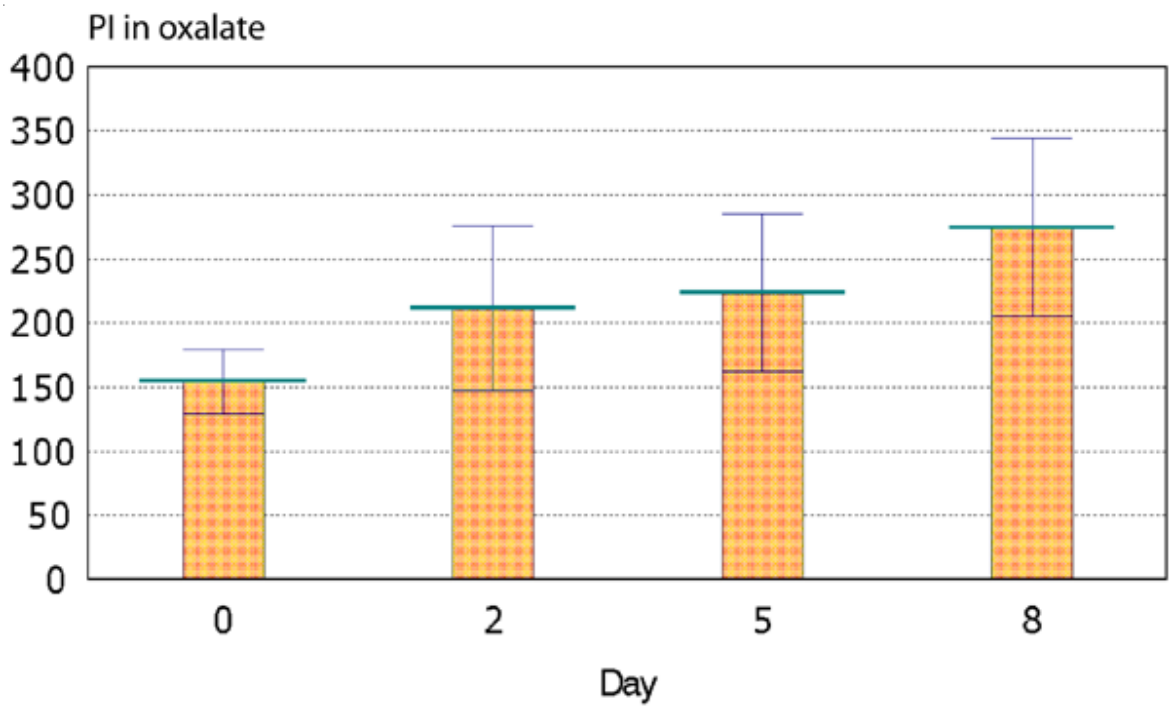

Fig. 3 Increased PI in oxalate after aloe gel consumption. A significant increase occurred between Day 0 and 5 and Day 0 and 8 at $p < 0.05$

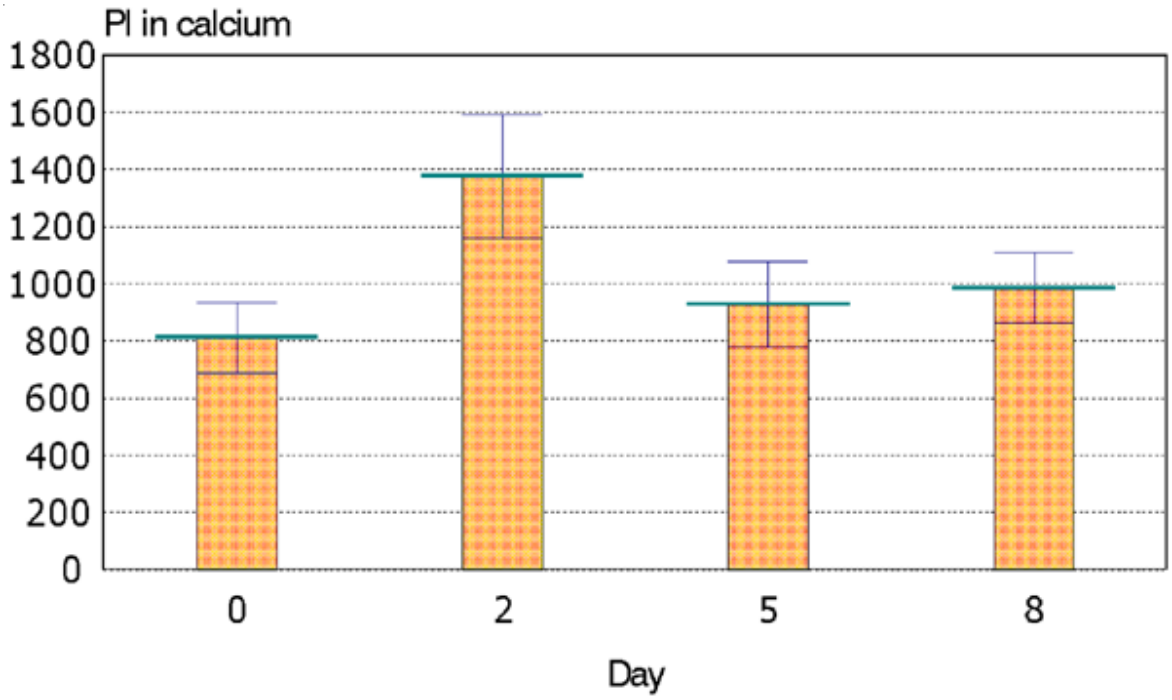

Fig. 4 Increased PI in calcium after aloe gel consumption. A significant increase occurred between Day 0 and 2 at $p < 0.05$

Table 1. 24-hr urine volume and urinary compositions before and after aloe gel consumption (n = 13)

Urine parameters	Day 0	Day 2	Day 5	Day 8	p-value
Volume (ml)	557.69±182.54	663.85±149.08	466.92±178.25	782.31±279.35*	<0.05
Osmolality	817.08±188.43	777.46±177.15	919.08±112.95	905.38±664.51	>0.05
Potassium (mmol/l)	32.45±14.05	33.52±15.67	45.00±16.59	32.28±13.55	>0.05
Sodium (mmol/l)	153.54±53.23	152.54±46.34	152.08±35.42	152.00±46.41	>0.05
Phosphate (mmol/l)	29.71±17.03	38.04±30.32	50.28±31.16	24.27±11.58	>0.05
Calcium (mmol/l)	1.49±0.64	1.38±0.75	1.98±1.55	1.48±1.21	>0.05
Magnesium (mmol/l)	4.45±1.90	3.41±1.51	4.60±1.58	3.00±2.09	>0.05
Uric acid (mmol/l)	4.32±1.64	3.68±1.67	5.36±1.65	3.71±1.67	>0.05
Citrate (mg/d)	125.83±51.14	172.85±117.94	128.75±66.16	209.65±116.23*	<0.05
Tartrate (mmol/l)	3.31±1.33	2.85±1.27	2.86±0.62	3.22±1.86	>0.05
Oxalate (mmol/l)	0.13±0.09	0.12±0.06	0.16±0.14	0.14±0.11	>0.05
PI Calcium	811.54±443.54	1,376.92±778.25*	926.92±540.30	984.62±443.18	<0.05
PI Oxalate	154.62±91.07	211.54±231.87	223.85±221.64*	274.62±249.92*	<0.05
CPR of brushite	2.01±2.15	2.11±2.03	1.56±1.28	4.00±7.64	>0.05
Citrate per creatinine	0.21±0.11	0.23±0.13	0.18±0.11	0.26±0.13	>0.05

*statistical significance of that day was with respect to Day 0

Discussion

The amount of citrate and tartrate in fresh aloe gel in the present study were mid-range compared with tamarind and other Thai fruits[20]. Increased urine volume decreases crystallization of salt in urine and alone this may be the effect of aloe consumption.

Approximately 50 per cent of the urinary inhibitory activity to calcium phosphate precipitation is due to urinary citrate[21]. Citrate also has an inhibiting effect on calcium oxalate crystal growth[22] and increased solubility of calcium oxalate[23]. Several reports claim that idiopathic stone-formers excrete significantly less citrate than do normal subjects[24,25]. The amount of citrate excretion in urine varies with the different kinds of herb ingested[26,27]. By the high citrate excretion in the urine, the present study shows that the moderately high citrate content of aloe may have benefit in preventing kidney stone prevention.

Increasing of PI Ox and PI Ca indicates that oxalate and calcium salts are more easily soluble in the urine. The PI Ox showed a statistically significant difference from Day 5 through Day 8 of aloe consumption, whereas the PI Ca showed a statistically significant difference between Day 0 and Day 2 although the values of Day 5 and Day 8 were higher than Day 0. A larger sample size would be needed to confirm this trend.

Even though many parameters of the urine show no significant changes, the PI Ox and PI Ca shows the overall outcome of the condition of the urine not available for precipitation to oxalate and calcium salts. The authors, therefore, conclude that aloe consumption has a beneficial effect for the prevention of both oxalate and calcium stone in children; however, a small sample size was a limitation in this study.

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การเปลี่ยนแปลงขององค์ประกอบปัสสาวะในเด็กหลังจากรับประทานว่านหางจระเข้

สุขชาติ เกิดผล, วิจิตร เกิดผล, วันชัย ไอรารัตน์, แก้วใจ เทพสุธรรมรัตน์, สมทรง ณ นคร

วัตถุประสงค์: *1) เพื่อหาปริมาณสารซิเตรตและทาร์เตรตในว่านหางจระเข้และในปัสสาวะของเด็กปรกติก่อนและหลังรับประทานว่านหางจระเข้ 2) เพื่อประเมินการเปลี่ยนแปลงทางเคมีขององค์ประกอบในปัสสาวะหลังจากรับประทานว่านหางจระเข้ 3) เพื่อดูคุณค่าของการรับประทานว่านหางจระเข้ต่อการป้องกันการเกิดนิ่วไตในเด็ก*

วัสดุและวิธีการ: *ได้ศึกษาในเด็กผู้ชายจำนวน 13 คนมีอายุระหว่าง 9-13 ปี โดยให้รับประทานว่านหางจระเข้สดครั้งละ 100 กรัม วันละ 2 ครั้งติดต่อกันเป็นเวลา 7 วัน เก็บปัสสาวะ 24 ชั่งโมงที่ 1 วัน ก่อนรับประทานว่านหางจระเข้ (วันที่ 0) และเมื่อรับประทานแล้ว 2 วัน (วันที่ 2), 5 วัน (วันที่ 5), และ 1 วัน หลังรับประทานครบ (วันที่ 8) ได้ตรวจปัสสาวะเพื่อหาค่าต่างๆดังต่อไปนี้ได้แก่ ปริมาตร,ออสโมแลลลิตี, โพแทสเซียม, โซเดียม, ฟอสเฟต, แคลเซียม, แมกนีเซียม, กรดยูริก, ซิเตรต, ทาร์เตรต, ออกซาเลต, ค่าพีไอของแคลเซียม, ค่าพีไอของออกซาเลต, ค่าซีพีอาร์ของแคลเซียมฟอสเฟตและค่าอัตราส่วนของซิเตรตต่อครีอาตินีน*

ผลการศึกษา: *ในว่านหางจระเข้สด 100 กรัมมีปริมาณของซิเตรตและทาร์เตรตเท่ากับ 96.3 และ 158.9 มิลลิกรัมตามลำดับ จากการศึกษาพบว่าหลังจากรับประทานว่านหางจระเข้สดแล้ว จะมีปริมาตรปัสสาวะและการขับออกของซิเตรตในปัสสาวะเพิ่มขึ้นอย่างมีนัยสำคัญ ($p < 0.05$) ค่าพีไอ (ศักยภาพในการละลาย) ของออกซาเลตและของแคลเซียมเพิ่มขึ้นอย่างมีนัยสำคัญ ($p < 0.05$) ส่วนการวัดหาค่าอื่น ๆ นอกจากนี้ไม่พบการเปลี่ยนแปลงที่มีนัยสำคัญ*

สรุป: *ว่านหางจระเข้สดมีปริมาณของซิเตรตและทาร์เตรตในระดับปานกลางเมื่อเทียบกับผลไม้ไทยอื่น ๆ การเปลี่ยนแปลงทางเคมีขององค์ประกอบในปัสสาวะหลังจากรับประทานว่านหางจระเข้บอกได้ว่าว่านหางจระเข้มีศักยภาพเพียงพอที่จะป้องกันการเกิดนิ่วไตในเด็กได้*