Effect of Aloe (*Aloe vera* Linn.) on Healthy Adult Volunteers: Changes in Urinary Composition

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Objective: *1. To investigate the amount of citrate and tartrate in aloe gel, and in the urine of healthy normal volunteers, 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.*
Designs: *Experimental study; before and after experiment with no control group*
Material and Method: *Thirty one healthy male medical students between 18 and 23 years of age were enrolled (with informed consent) in the clinical trial. Subjects ingested 100 g of fresh aloe gel twice a day for seven consecutive days. The 24-hr 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 in calcium), Permissible Increment in oxalate (PI in oxalate), Concentration product ratio of calcium phosphate (CPR of $CaPO_4$) 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 urinary excretion of oxalate was significantly decreased ($p < 0.05$). The PI in calcium was significantly increased ($p < 0.05$), while the citrate excretion and PI in oxalate were consistently, albeit non-significantly, increased. The mean CPR values of $CaPO_4$ were decreased non-significantly. The other measurements were unremarkable.*
Conclusion: *Fresh Aloe vera gel (100 g) contains 96.3 mg of citrate and 158.9 mg of tartrate. This is mid-range for Thai fruits. Changes in chemical compositions of urine after aloe consumption shows its potential for preventing kidney stone formation among adults.1*

Keywords : *Aloe vera , Adults, Oxalate, PI, Renal stone prevention*

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Renal stone disease is a world-wide health problem and common in rural Northeast Thailand[1,2]. Renal stones are caused by multiple factors and there is no single theory that completely explains their formation. Among the available theories, an inhibitory theory and a hypersaturation theory are well accepted. Citrate and tartrate, as medicinal herbs, play a role in inhibiting stone formation[3-5]. Aloe vera is a medicinal herb containing several pharmacologically-active ingredients useful for treatment of radiation burns, ulcers, contact burns, arthritis, diabetes, and the prevention of atheromatous heart disease[6-8].

Several in vitro studies of the effects of medicinal herbs using aloe have been reported. The known chemical composition of aloe gel includes anthraquino-

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nes, saccharides, enzymes, vitamins, essential amino acids, non-essential amino acids and other inorganic elements[9]. Research on the putative renal stone prevention effects of aloe has yet to be published.

The authors, therefore, conducted a clinical trial on healthy adult volunteers for determination of citrate and tartrate concentration in fresh aloe gel. The main objectives were: 1) to evaluate the changes in the urinary chemical composition after aloe gel consumption; and, 2) to determine the value of aloe gel consumption for renal stone prevention.

Material and Method

The presented research protocol was reviewed and approved by the Khon Kaen University Ethics Committee for Human Research. Following informed consent, 31 healthy male medical students between 18 and 23 years of age (mean SD = 20.85 1.26 years) were enrolled in the clinical trial.

The inclusion criteria were: 1) males between 18 and 25 years of age; 2) healthy physical condition as determined by a physician (SK); 3) able to complete the 24-hr urine collection during the study; 4) able to consume 100 g of aloe gel twice daily at a set time during the study; and, 5) willing to give informed consent.

The exclusion criteria were: 1) a serum creatinine level > 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 by a plant taxonomist.

The subjects ingested 100 g of fresh aloe gel mixed with 15 ml syrup (contained 1.95 g of sucrose) 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 at 4 to 8 C without any preservative. Urine specimens with a creatinine value of less than the formula guide were discarded[10].

The extraction of aloe gel was performed by adding 1 M perchloric acid, which was vigorously mixed in a centrifuge. The supernatant was then used to determine 1) the citrate using an enzymatic method[11] and 2) the tartaric acid (tartrate) using another chemical method as reported by Underhill et al[12]. Both citrate and tatrate determinations had intra-variations of 4.6% CV. Uric acid and oxalate were determined using an enzymatic method[13,14]. Urine-calcium was analyzed by a standard method using atomic absorption. Sodium, potassium, creatinine, phosphorus, and magnesium were analyzed using a Synchron Clinical System CX7 (Beckman Instruments INC, Brea, CA. USA).

The concentration product ratio (CPR) of $CaPO_4$ (brushite) was determined by a method published elsewhere[15,16]. 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 to calculate CPR was:

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

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

The potential of calcium or oxalate inhibition was assessed by PI in calcium or oxalate. An increasing value of PI indicates the inhibitory activity is increasing in the urine. The PI was measured as per Nicar et al[17]. 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 was done and the pH, glucose and protein were determined with a Labstix from Bayer Diagnostics Aust. Pty. Ltd.

The data were expressed as means (SD). The mean values of urinary chemical composition, CPR and PI were analyzed using analysis of variance with repeated measurement and multiple comparison tests between the parameters on Day 0, 2, 5 and 8. A 95% significance level was accepted for the present study.

Results

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

The urinary excretion of oxalate was significantly decreased ($p < 0.05$, Fig. 1). The mean PI in calcium was significantly increased ($p < 0.05$, Fig.2) while the mean PI in oxalate and urinary citrate excretion were also increased albeit non-significantly (Table 1). Unchanged were the excretions of sodium, phosphate, calcium, magnesium, uric acid, tartrate, citrate per creatinine ratio and CPR of $CaPO_4$. The urine osmolality showed no significant change (Table 1).

Discussion

The amount of citrate and tartrate in fresh aloe gel were mid-range compared with tamarind and other Thai fruits[18].

In humans, oxalic acid is an end-product of metabolism through the ascorbic acid and glyoxylic acid pathways. Calcium oxalate is a major constituent of all stones in Northeast Thailand[19]. Low urinary oxalate excretion in the present study indicates its low availability for precipitation.

A urine sample with a CPR value of > 3 suggests abnormal super-saturation[20]. Sriboonlue et al[21] reported a comparison of mean CPR values for municipal dwellers, villagers without stones and villagers with

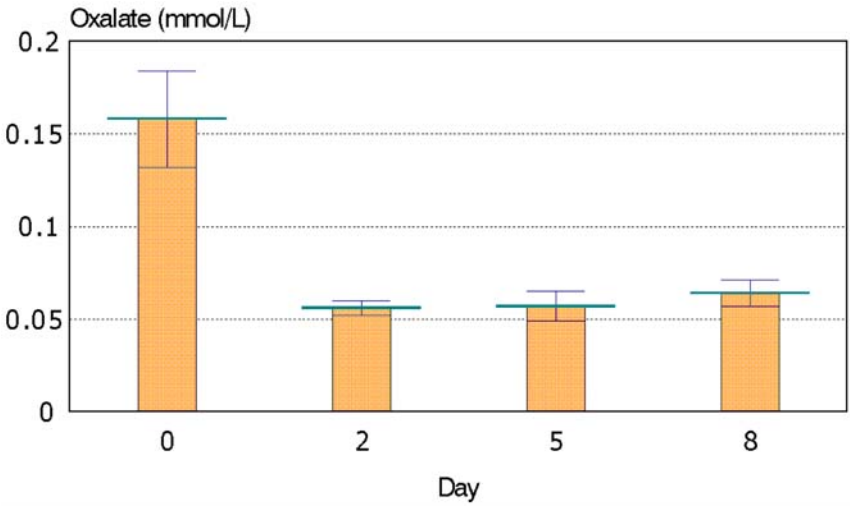

Fig. 1 Decreased urinary oxalate excretion after aloe consumption. A significant decrease occurred between Day 0 and 2, Day 0 and 5 and Day 0 and 8 at $p < 0.05$

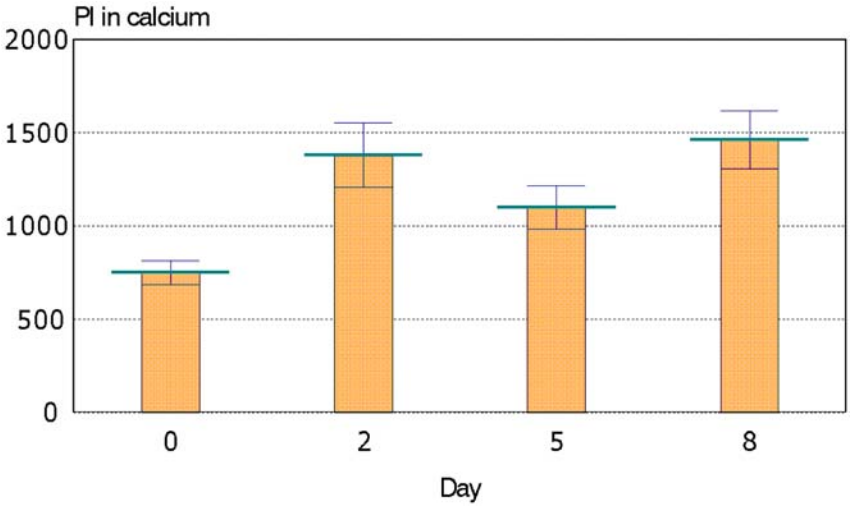

Fig. 2 Increased PI in calcium after aloe gel consumption. A significant increase occurred between Day 0 and 8 at $p < 0.05$

Table 1. 24-hr urine volume, and urinary compositions before and after aloe gel consumption (n = 31)

Parameters	Day 0	Day 2	Day 5	Day 8	p-value
Volume (ml)	1,364.52±95.16	1,389.68±79.94	1,381.61±90.15	1,383.87±85.92	>0.05
Osmolality	572.90±40.78	547.03±40.99	545.65±39.22	559.94±39.78	>0.05
Potassium (mmol/l)	26.92±2.44	24.69±1.90	25.92±1.92	24.45±2.00	>0.05
Sodium (mmol/l)	126.35±10.62	106.16±7.62	118.16±11.03	116.97±11.91	>0.05
Phosphate (mmol/l)	55.17±8.31	59.54±8.31	55.45±7.67	39.23±5.84	>0.05
Calcium (mmol/l)	2.04±0.2	2.05±0.19	2.10±0.2	1.99±0.16	>0.05
Magnesium (mmol/l)	1.72±0.17	1.73±0.16	1.72±0.17	1.64±0.11	>0.05
Uric acid(mmol/l)	2.75±0.25	2.46±0.2	2.59±0.22	2.67±0.21	>0.05
Citrate(mg/d)	270.95±24.3	286.74±21.75	285.90±22.57	303.65±23.99	>0.05
Tartrate(mmol/d)	2.31±0.13	2.32±0.12	2.27±0.12	2.31±0.11	>0.05
Oxalate (mmol/l)	0.16±0.03	0.06±0.00*	0.06±0.01*	0.06±0.01*	<0.05
PI Calcium	750.00±61.87	1,379.03±171.44	1,098.39±116.20	1,461.29±154.40*	<0.05
PI Oxalate	71.61±4.87	75.48±5.54	85.81±15.43	81.94±11.27	>0.05
CPR CaOx	0.44±0.0.10	0.68±0.12	0.42±0.10	0.38±0.10	>0.05
CPR $CaPO_4$	5.18±0.93	2.05±0.37	1.63±0.28	2.16±0.48	>0.05
Citrate/Creatinine	0.23±0.02	0.22±0.02	0.23±0.03	0.21±0.02	>0.05

Data were presented as X ± SE
*statistical significance of that day was with respect to Day 0

stones. All groups had mean CPR values for calcium oxalate and brushites suggestive of supersaturated states. The CPR values of calcium oxalate and brushites among municipal dwellers were higher than the villagers with and without stones.

Kirdpon et al[22] studied the consumption of Roselle juice and its effects on urinary changes. They observed that the mean CPR values of calcium oxalate were either increased or decreased, depending on the concentration of Roselle juice consumed.

The mean CPR values of brushites in the current study fell from a value of 5 to 2, indicating that the condition of super-saturation in the urine of normal volunteers was reduced to a safer saturation after aloe consumption. This means that the urine condition has a tendency not suitable for salt precipitation.

Citrate has an inhibiting effect on both calcium phosphate and calcium oxalate[23-,25]. The present study on citrate shows consistently increased excretion in the urine even though the difference was not always statistically significant. Thus, aloe may have a role in increasing citrate excretion with some benefit of preventing stone formation.

The increase of the PI in calcium indicates that calcium salts are more easily soluble in the urine. The PI in calcium reflects the overall condition of the urine, which does not have calcium salts available for precipitation. The present study, therefore, shows that calcium salts were made more soluble in the urine. The tendency for an increase in the PI in oxalate, albeit statistically non-significant, indicates that oxalate salts in the urine are also possibly inhibited from precipitation.

According to the low oxalate excretion in the urine and increasing PI in calcium, the authors conclude that aloe consumption has a beneficial effect for the prevention of both calcium and oxalate stone formation in adults. Further study is needed to confirm this conclusion.

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ผลต่ออาสาสมัครปรกติที่รับประทานว่านหางจระเข้: การเปลี่ยนแปลงในองค์ประกอบของปัสสาวะ

สุขชาติ เกิดผล, วิจิตร เกิดผล, วันชัย ไอรารัตน์, อโนทัย ตรีวานิช, สมทรง ณ นคร

วัตถุประสงค์: *1. เพื่อหาปริมาณสารซิเตรตและทาร์เตรตในว่านหางจระเข้และในปัสสาวะของอาสาสมัครผู้ใหญ่สุขภาพแข็งแรง ก่อนและหลังรับประทานว่านหางจระเข้*
2. เพื่อประเมินการเปลี่ยนแปลงทางเคมีขององค์ประกอบในปัสสาวะหลังจากรับประทานว่านหางจระเข้
3. เพื่อดูคุณค่าของการรับประทานว่านหางจระเข้ต่อการป้องกันการ เกิดนิ่วในไตในผู้ใหญ่

วัสดุและวิธีการ: *ได้ศึกษาในนักศึกษาแพทย์ชายที่มีสุขภาพแข็งแรงจำนวน 31 คนมีอายุระหว่าง 18-23 ปี โดยให้รับประทานว่านหางจระเข้สด ครั้งละ 100 กรัม วันละ 2 ครั้งติดต่อกันเป็นเวลา 7 วัน เก็บปัสสาวะ 24 ชั่งโมงที่ 1 วันก่อนรับประทานว่านหางจระเข้ (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, ค่าซีพีอาร์ของแคลเซียมฟอสเฟต และค่าอัตราส่วนของซิเตรตต่อครีอาตินีน*

ผลการศึกษา: *ในว่านหางจระเข้สด 100 กรัมมีความเข้มข้นของซิเตรตและทาร์เตรตเท่ากับ 96.3 และ 158.9 มิลลิกรัมตามลำดับ จากการศึกษาพบว่าหลังจากรับประทานว่านหางจระเข้สด การขับออกของออกซาเลตลดลงอย่างมีนัยสำคัญ ($p < 0.05$) ค่าพีไอของแคลเซียมเพิ่มขึ้นอย่างมีนัยสำคัญ ($p < 0.05$) การขับซิเตรตออกในปัสสาวะ และค่าพีไอของออกซาเลตในปัสสาวะเพิ่มขึ้นแต่ไม่มีนัยสำคัญทางสถิติ ค่าซีพีอาร์ของแคลเซียมฟอสเฟตลดลงอย่างมากแต่ก็ไม่มีความสำคัญทางสถิติเช่นเดียวกัน ส่วนการวัดหาค่าอื่น ๆ นอกจากนี้ไม่พบการเปลี่ยนแปลงที่มีนัยสำคัญทางสถิติ*

สรุป: *ว่านหางจระเข้สดมีปริมาณของซิเตรตและทาร์เตรตในระดับปานกลางเมื่อเทียบกับผลไม้ไทยอื่น ๆ การเปลี่ยนแปลงทางเคมีขององค์ประกอบในปัสสาวะหลังจากรับประทานว่านหางจระเข้บ่งชี้ได้ว่าว่านหางจระเข้มีศักยภาพเพียงพอที่จะป้องกันการเกิดนิ่วในไตในผู้ใหญ่ได้*