ORIGINAL ARTICLE

# *Apium graveolens* accentuates urinary $Ca^{+2}$ excretions in experimental model of nephrocalcinosis

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Nephrocalcinosis (NC) is a state characterised by deposition of calcium phosphate or oxalate in the renal parenchyma due to different clinical conditions. *Apium graveolens* (Celery) is a popular vegetable added to salads and many cooked dishes, used in Chinese medicine to reduce high blood pressure and in Arabic medicine to relieve renal pains. To evaluate the effect of *A. graveolens* in reducing calcium deposits from renal parenchyma in rabbit models with induced NC by a large dose of oxalic acid. *A. graveolens* produced a significant reduction of blood urea nitrogen (5.7±0.05 *vs* 7.3±0.2) mmol/l, serum creatinine (87.2±0.63 *vs* 97.3±0.5) mmol/l and serum $Na^+$ levels (136.8±0.2 *vs* 142.16±0.7) mmol/l with non-significant reduction in serum $K^+$ (3.3±0.8 *vs* 3.8±0.03). There is a significant reduction in calcium deposition in renal parenchyma in comparison to the control group after ten days of treatment. *A. graveolens* showed a significant diuretic effect that accentuates the excretion of urinary calcium.

**Key words:** Acetylenics, allantoins, nephrocalcinosis, Vitamin D intoxication

## INTRODUCTION

Nephrocalcinosis (NC) is a condition of deposition of calcium in the form of phosphate or oxalate in the renal parenchyma that can impair kidney functions.[1] It is liable to occur in patients with renal tubular acidosis, hyperparathyroidism, vitamin D intoxication and healing of renal tuberculosis.[2] If the calcium deposits break from the kidney tissue, it will provide nuclei that are ready for the formation of different types and sizes of stones[3] which may be consequences of genetic, dietary, water intake, environmental and occupational factors.[4] In traditional medicine, some medicinal plants like corn silk, barley and celery were used to relieve some renal pains.[5] Few studies were made determining the diuretic effect of Corn silk and Barley[6] but without an available data to evaluate the possible nephroprotective effect of celery.

## MATERIALS AND METHODS

Sixteen healthy rabbits weighing 1000 to 1300 g were used in this study which was approved by the ethical committee in the college of pharmacy. The rabbits were supplied by animals' house of college of medicine. Each animal was kept in a separate cage which provided with a wide wire mesh floor. They fed standard oxoid pellets and were given water ad libitum. The animals were allocated to two groups (each group contained eight animals).

G1 (control group) received 3 ml of water orally at 9 a.m. followed by oxalic acid as a single oral dose of 333 mg/kg using gastric tube at 11 a.m. for induction of NC.

G2 was given fresh celery 8 g/kg[6] added to the animal food, half the amount was given at 9 a.m. (2 hours before induction) while the other half of fresh celery was given half-an-hour after induction. They were continued feeding the same amount for the next ten post-induction days. Daily blood samples were collected from marginal ear vein for biochemical analysis and renal functions at these occasions, before induction of NC to determine the normal values of blood urea nitrogen (BUN), serum creatinine, $Na^+$ and $K^+$ by using spectrophotometer method[7] and in the 1st, 5th and 10th day after induction. Urine samples were taken from the animals by catheterisation after anaesthetising them in the last day of the study to determine the urine $Ca^{+2}$ levels and crystals that may be present in urine. The histopathological examination was carried to check for crystal deposits in renal tissues by using polarised microscope after fixation and staining the specimens.[8]

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The obtained results were collected for analysis and assessment.

## RESULTS

The results of this study revealed significant elevation in the levels of BUN, both serum creatinine and $K^+$ with significant reduction of serum $Na^+$ levels in control group as compared to the levels of pre-induction state [Tables 1-4]. The results of celery (group 2) showed significant reduction of BUN levels (5.7±0.05 *vs* 7.3±0.2) mmol/l, serum creatinine (87.2±0.63 *vs* 97.3±0.5) mmol/l with $P<0.05$, and non-significant reduction in serum $K^+$ (3.3±0.8 *vs* 3.8±0.03) with significant decrease in serum $Na^+$ levels (136.8±0.2 *vs* 142.16±0.7) mmol/l with $P<0.05$ in comparison to the control group after one day and ten days when results became more evident.

**Table 1: Mean BUN, S. creatinine, $K^+$, $Na^+$ and urine $Ca^{+2}$ levels of the studied animals measured before induction of NC**

| Analyte | Measured levels (mmol/L) |
|---|---|
| BUN | 4.0±0.07 |
| S. creatinine | 65.0±8.9 |
| S. $K^+$ | 3.3±0.8 |
| S. $Na^+$ | 160.0±4 |
| Urine $Ca^{+2}$ | 2.05±0.07 |

## DISCUSSION

NC was induced in the experimental model by using a single large dose (333 mg/kg) of oxalic acid (a highly oxidising and strong $Ca^{+2}$ chelator) and this dose had been selected after several trials.[9] In this model of NC, significant elevation in BUN and serum creatinine levels were observed after induction of NC [Tables 2 and 3]. The idea to use some herbals like celery is to evaluate its effect in improvement of NC. Celery is an alkalising food, contains some active ingredients like alkaloids, high level of vitamin C, phthalides (lower cholesterol),[10] coumarins (prevent free radicals from damaging cells and enhance the activity of immune defenders that eliminate potentially harmful cells including cancer cells), acetylenics (stop the

**Table 2: Mean BUN and S.creatinine levels of the studied groups measured after induction of NC**

| Group | Agent | Dose | BUN (mmol/L) | | | S.Creatinine (mmol/L) | | |
|---|---|---|---|---|---|---|---|---|
| | | | After 1 day | After 5 day | After 10 day | After 1 day | After 5 day | After 10 day |
| 1 | Oxalic acid (control) | 333mg/kg | 7.3±0.2 | 7.9±1.1 | 9.6±0.2 | 97.3±0.5 | 99.5±0.8 | 100.3±1.2 |
| 2 | Celery | 8gm/kg/day | 5.7±0.05 | 5.1±0.3 | 4.4±0.06 | 87.2±0.63 | 81.7±0.3 | 80.1±0.12 |

**Table 3: Mean S. $K^+$ and S. $Na^+$ levels of the studied groups measured after induction of NC**

| Group | Agent | Dose | S. $K^+$ (mmol/L) | | | S. $Na^+$ (mmol/L) | | |
|---|---|---|---|---|---|---|---|---|
| | | | After 1 day | After 5 day | After 10 day | After 1 day | After 5 day | After 10 day |
| 1 | Oxalic acid (control) | 333mg/kg | 4.2±0.05 | 5.1±0.24 | 5.7±0.08 | 142.16±0.7 | 139.3±1.0 | 0137.6±0.4 |
| 2 | Celery | 8gm/kg/day | 4.1±0.07 | 3.9±0.13 | 3.8±.03 | 136.8±0.2 | 134.9±0.7 | 134.3±0.4 |

**Table 4: Mean urine $Ca^{+2}$ levels of the studied groups measured 10 days after induction of NC**

| Group | Agent | Urine $Ca^{+2}$ levels after 10 days (mmol/L) | Crystals in urine examination |
|---|---|---|---|
| 1 | Oxalic acid (control) | 4.1±0.03 | Amorphous urate, uric acid, stellar phosphate, ca and oxalate |
| 2 | Celery | 5.01±0.05 | Amorphous urate |

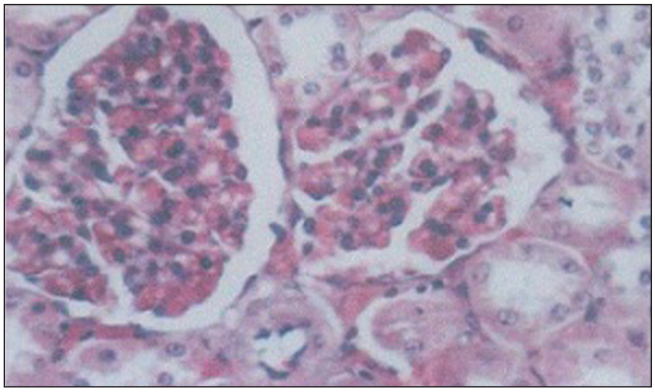

**Figure 1:** Normal histological appearance of the renal tissue of rabbit (crystal free) in the control group. ×40

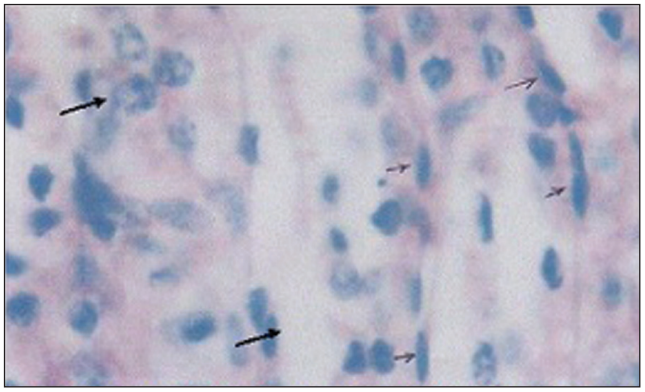

**Figure 2:** Heavy calcium oxalate crystals deposition in the renal tissues of the rabbits receiving oxalic acid. ×100

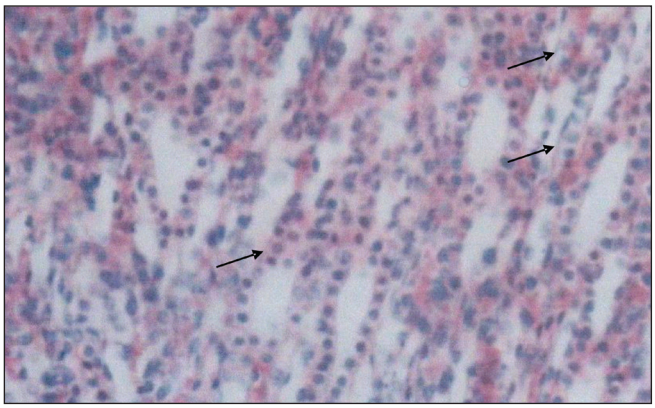

**Figure 3:** Mild calcium oxalate crystals deposition in the renal tissues of rabbits receiving oxalic acid and Celery. ×100

growth of tumour cells)[11] and plant enzymes that aid in maintaining a more alkaline balance.[12] It produces significant lowering effect in BUN, serum creatinine level and an increase in urine $Ca^{+2}$ levels than normal values[13] and a reduction of its concentration in renal tissue [Figures 1-3]. This is due to its diuretic effect which may be related to its constituents, particularly allantoins that have diuretic action.[14]

## CONCLUSION

*A. graveolens* have a significant diuretic and attenuating effect in reducing calcium deposits from renal tissues.

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