The Role of *Rhaphidophora pinnata* (L.f) Schott Water Extract on Dissolution of Calcium Containing Renal Stones

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Abstract: Kidney stone disease is a common chronic disorder in humans and the most common type of renal stone is made of calcium oxalate. Calcium oxalate stones are made of calcium oxalate monohydrate and dihydrate, often combined with calcium phosphate which is the original cause of stone formation. Growth and aggregation of calcium stone inhibits by coating the surface of growing calcium crystals or by complexing with calcium and oxalate, such as potassium ion and magnesium ion. *Rhaphidophora pinnata (L.f) Schott* leaves contain high potassium mineral that is 847.9 mg / 100g and calcium 474.7 mg / 100g. This study was to investigate the effect of water extracts of *Rhaphidophora pinnata (L.f) Schott* leaves toward solubility of kidney stone. The water extract of *Rhaphidophora pinnata (L.f) Schott* leaves, simplicia, and nano-simplicia was made in three different concentration, 5%, 10%, and 20%. Dissolution of calcium-containing renal stone was performed by incubating each water extract with 0.1% calcium containing renal stone for 4 hours. Nano-simplicia water extract was shown the highest dissolution ability, 80.55% calcium of kidney stones decomposed within 4 hours of incubation.

1 INTRODUCTION

The search for the source of medicinal plants continues to produce chemical compounds used in various diseases, including from plants that have the potential in the treatment of kidney stone disease (Vina, 2010). Kidney stone disease is one of common chronic disorder in humans. Renal stone (calculi) is made of calcium oxalate, and also contain other crystals and organic component that formed in the renal *pelvis* or *calyces*. This process called *urolitiasis (litiasis renalis, nefrolitiasis)* (Pratomo, 2008), (Basavaraj, 2007), (Worcester and Coe, 2008), (Cunningham, 2016).

Treatment of kidney stones is carried out depending on the size of the stone. If kidney stones are still relatively small or medium, and still can pass through the urinary tract without surgery, doctors usually recommend drinking lots of water (Nouvenne, 2013). Handling of kidney stones with special procedures (eg laser energy, ultrasound, or surgery) is usually applied only if the stone is larger enough to clog the patient's urinary tract.

Calcium oxalate stones are made of calcium oxalate monohydrate and dihydrate, often combined with calcium phosphate which is the original cause of stone formation. Calcium oxalate monohydrate is thermodynamically most stable form and observed more frequently in clinical stones than calcium oxalate dihydrate, at a ratio of >2:1. The stone will be more quickly formed when the urine is very concentrated and cause the supersaturating of calcium oxalate. These condition will gradually form a solid mass and hard resemble a stone (Pramono, 1988), (Brown, 1989), (Basavaraj, 2007), (Worcester and Coe, 2008).

Growth and aggregation of calcium stone inhibits by coating the surface of growing calcium crystals or by complexing with calcium and oxalate, such as potassium ion, magnesium ion. citrate, pyrophosphates, inter-alpha-trypsin inhibitor family of proteins, Tamm-Horsfall protein (THP), glycosaminnoglycans, and renal lithostathine. Potassium and magnesium ions can inhibit the formation of stones by binding with oxalate, it will form a water-soluble oxalate salt. Similarly, citrate binding with calcium ions to form calcium citrate

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which is water-soluble, and these condition lead to decreasing of calcium oxalate supersaturation (Basavaraj, 2007), (Putra and Fauzi, 2016), (Maharani, 2012). Besides phytochemicals as antioxidant, dietary phyto-phenols were found to be effective for the prevention the growth of renal stone by inhibits the stone formation process in the urinary tract (Nirumand, 2018).

Supersaturation of urinary salts and crystal retention in the urinary tract initiated the formation of renal stones. Deficiency or abundance of inhibitors are almost certain to predispose to stone disease. Some herbal plants have been detected as a deterrent of kidney stones allegedly contain high potassium mineral such as tempuyung leaves, nasty shard, kapok, corn hair and lettuce (Alvin, 2015), (Girsang, 2016), (Muhgni, 2013), (Nessa, 2013), (Permata, 2017). *R. pinnata* leaves contain high potassium mineral that is 847.9 mg / 100g and calcium 474.7 mg / 100g. According to these results, allegedly the potassium ion can act as an agent to bind oxalate (water-soluble), so as not to form stones in the kidney. The kidneys will pass trough potassium oxalate and remove it through the urine.

Based on the description above, since the human nephron is a dynamic system, in vitro crystal behaviour is too simplistic a concept to entirely explain renal calculus formation. This study was to see how the water extracts of simplicia leaves of *R. pinnata* predispose to kidney stone

2 MATERIALS AND METHODS

2.1 Materials

The materials used in this research were *R. pinnata*, calcium-containing renal stone, nitric acid, distillate water, calcium standard solution. Those chemicals and solvents used were analytical grade and are commercially available from Merck. *R. pinnata* leaf plants were cleansed and dried, then crushed to obtain simplicia powder and nano simplisia powder. The nano simplicia powder was analyzed by LIPI (Lembaga Ilmu Pengetahuan Indonesia) using particle size analyzer nano.

2.2 Methods

2.2.1 Water Extract Preparation

The water extract of *R. pinnata* leaves, simplicia *R. pinnata*, and simplicia nano *R. pinnata* was made in three different concentration-5%, 10%, and 20%- in water, using infused technique according to Farmakope Indonesia 4th Edition.

2.2.2 Dissolution of Calcium-containing Renal Stone

Dissolution of calcium-containing renal stone was performed by incubating each water extract with 0.1% calcium-containing renal stone for 4 hours. The levels of calcium free ions present in the water extract before and after incubation were measured using atomic absorption spectrophotometry methods.

The dissolution percentage of calcium was calculated by the formula below:

$$\mathrm{DCa}\ (\%) = \frac{CAD - CBD}{CaRS} \tag{1}$$

Where DCa is the dissolution percentage of calcium; CAD is the calcium content after dissolution; CBD is the calcium content in water extract; and CaRS is the calcium contain in renal stone (1 gram of renal stone contain 10.29 mg calcium).

3 RESULT AND DISCUSSION

The following Table 1 was the result of calcium analysis in water extract of *R. pinnata* leaves, simplicia of *R. pinnata* and nano-simplicia of *R. pinnata*..

Table 1: The effect of treatments on calcium content in water extract before and after dissolution.

No	Treatments	Water extract (%)	Calcium level (µg/ml) in water extract	Calcium (µg/ml) after dissolution
1	*R. pinnata* water extract	5	2.22	2.77
		10	3.79	4.18
		20	5.11	5.70
2	Simpicia *R. pinnata* water extract	5	6.21	7.84
		10	17.57	19.78
		20	26.56	40.09
3	Nano-simplicia *R. pinnata* water extract	5	61.91	105.62
		10	112.20	169.28
		20	206.53	436.05

The effect of water extract on dissolution percentage of calcium-containing renal stone result is presented in the Figure 1.

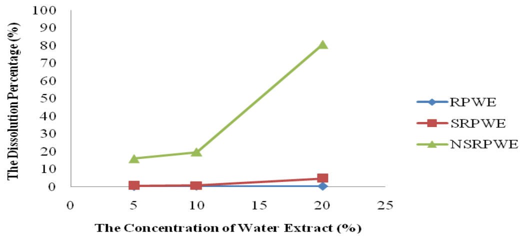

Figure 1: The effect of water extract on dissolution percentage of calcium-containing renal stone in the *R. pinnata*. RPWE = *R. pinnata* water extract; SRPWE = Simplicia of *R. pinnata* water extract; NSRPWE = Nano-simplicia *R. pinnata* water extract.

From the data Table 1 and Figure 1 can, be seen there are differences in calcium levels in *R. pinnata* water extract incubated with kidney stones. After incubation the levels of calcium in the water extract as a whole increased. The highest dissolution was shown by a 20% nano-simplicia water extract, 80.55% calcium of kidney stones decomposed within 4 hours of incubation. The lowest dissolution was shown by fresh water extract of *R. pinnata* where for the three concentrations of water extract did not show a significant difference that is below 1%.

Based on research conducted by (Alvin, 2015) and (Girsang, 2016), reports that plants with high potassium content, such as tempuyung and keji beling has good solubility to calcium oxalate. In terms of reactivity of alkaline ions, the position of potassium in the voltaic series is more left than calcium so that potassium is more reactive (the more easily the electrons are released) then the potassium gets rid of calcium to join the carbonate compound, oxalate or urate from the calcium compound to dissolve. In a supersaturated calcium oxalate solution 2 mmol/L magnesium reduced particle number by 50%. It was found that magnesium exert a fine kinetic control on the precipitation and growth of calcium oxalate monohydrate (Girsang, 2016), (Permata, 2017), (Desmars and Tawashi, 1973), (Basavaraj, 2007). Magnesium can form complexes with oxalate and decreases supersaturation. Oral intake of magnesium will decline the oxalate absorption and urinary excretion, in a manner similar to calcium by binding to oxalate in the intestines (Liebman and Costa, 2000).

The figure 2 illustrated the extrapolation of the dissolution effect of nano-simplicia of *R. pinnata* water extract, since this extract shown the highest ability to dissolve calcium contain renal stone. A hundred percent of calcium contain renal stone (1 gram of renal stone contain 10.29 mg calcium) should be dissolve in 27% nano-simplicia of water extract approximately. By this concentration, the future research of animal study of anti-nephrolithiasis of *R. pinnata* should be done.

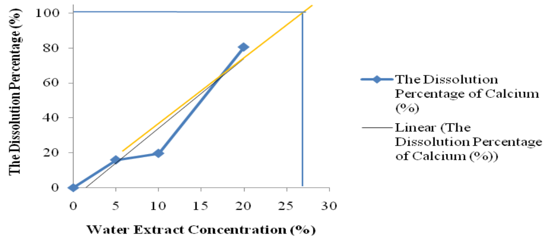

Figure 2: The Dissolution Percentage of Calcium Nano-simplicia *R. pinnata* water extract extrapolation

Calcium oxalate is the constituent component of the process of formation of kidney stones in the human body. Calcium oxalate stones are difficult to dissolve in water and clog up the urinary system. By the content of potassium ions and also high magnesium, calcium oxalate can be broken down and form new compounds that easily dissolve in water (Girsang, 2016), (Permata, 2017). After incubation with water extract of each treatments, the levels of calcium in the water extract as a whole increased. The highest dissolution was shown by a 20% nano-simplicia water extract, 80.55% calcium of kidney stones decomposed within 4 hours of incubation. But the fresh water extract of *R. pinnata* leaves and water extract of *R. Pinnata* simplicia did not show a significant difference that is below 5%. However, there is little evidence to recommend magnesium therapy in patients with renal stones.

4 CONCLUSIONS

R. pinnata water extract has the ability to dissolve calcium containing renal stone allegedly due to their potassium and magnesium contained in the water extract. Nano-simplicia shown the highest dissolution percentage, 80,55%. However, the future research of animal study of anti-nephrolithiasis of *R. pinnata* should be done.

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