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DOSE AND SAFETY OF *HYPOETES POLYTHYRSA MIQ* ETHANOL EXTRACT FOR DISSOLVING RENAL CALCULI: an affordable medication

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ABSTRACT

Renal calculi develops when the urine contains more crystal-forming substances, such as calcium, uric acid and a compound called oxalate. Most renal calculis are calcium-based, usually in combination with oxalate. *Hypoetes Polythyrsa* Miq has been used empirically to prevent or treat renal calculi. This study aims to identify toxicity or side effect of *Hypoetes Polythyrsa* Miq ethanol extract for dissolving renal calculi, therefore this extract can be applied safely and effective for curing renal calculi.

An in vitro research with pre-post control group design was conducted at Pharmacy Department Faculty of Medicine Udayana University. In addition, to determine as to whether the extract is safe orally, LD50 test was also conducted using mice strain BALB/c.

The results showed that ethanol extract of *Hypoetes Polythyrsa* Miq leaves has dissolved renal calculi significantly ($\alpha < 0.05$). Five percent of the extract was effectively dissolving calcium stone 3.36 times higher than control positive (BE). It was also proven that an acute LD_{50} was achieved at a dose of 0.694 g extract (139% of usual dose). It can be concluded that the use of ethanol extract per oral in short term therapy is safe.

Keywords: traditional medicine, hypoetes polythyrsa Miq, renal calculi.

INTRODUCTION

According to current estimates, kidney stones will develop in one in 10 people during their lifetime. This translates into nearly 30 million people in the United States. The prevalence is highest among those aged 30-45 years.[1] The incidence rate of renal calculi in Indonesia in the year of 2002 was 37,636 with number of visit around 58,959 people. Number of hospitalize patients are 19,018 people with mortality of 378 people.[2,3] This incidence will be increased in line to time and changes way of life, especially food lifestyle.

High urinary calcium can be the cause of kidney calculi in upwards of 80% of cases. The most prevalent stone composition is calcium oxalate. In recent years, natural cures for diseases and sicknesses have become more popular, as some people have taken a dislike to man-made drugs and chemicals. Kidney stones are an ailment with possible herbal treatments. However, diet change is also an effective way to combat kidney stones. Reducing calcium and sodium intake will help treat calcium stones. For oxalate stones, high oxalate foods will need to be limited. These include peanuts, beets, beans, berries, chocolate, among many other foods.[4] Uric acid stones are found in overly acidic urine.

Cherries, strawberries, apple juice, asparagus and nettles help make urine more alkaline. One thing that can cause overly acidic urine is too much of protein. The herbs meadowsweet, sarsaparilla, joe-pye weed and plantain (which is widely used by the Chinese to treat kidney problems) help rid the kidneys of excess uric acid.[5]

Various herbs have been reported to inhibit CaOx crystallization. Atmani and Khan have reported that an extract from the herb Herniaria hirsuta L., a plant that traditionally is used in Morocco for the treatment of lithiasis, promoted the nucleation of calcium oxalate crystals, increasing their number but decreasing their size.[6] In a follow-up study the authors could demonstrate that H. hirsuta could block crystal binding to cultured renal cells.[7] Similar effects on calcium oxalate crystallization in vitro have been shown for an aqueous extract from Phyllantus niruri L., a plant which is used in traditional Brazilian medicine for the treatment of stone disease.[8] The authors could show that the extract interfered with the CaOx crystallization process by reducing CaOx crystal growth and aggregation.[8]

MATERIALS AND METHODS

In this study, three steps of experiments were performed. Firstly, in this study, the ability of *Hypoetes Polythyrsa* Miq extract for dissolving calcium stone was performed. This was carried out by immersing the calcium stone with the extract for 6 h. The ability was compared towards aquabidest for injection as a

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control negative and a commercially medicine for cure renal calculi, BE as a control positive. Secondly, the safety application of *Hypoetes Polythyrsa* Miq extract for curing renal calculi was performed by providing LD_{50} data. This was carried out by applying an experimental study using BALB/c mice. A number of 25 mice were divided into 5 groups, i.e. first group was treated with 0.5 mL of 20% *Hypoetes Polythyrsa* Miq extract, second group treated with 0.5 mL of 40% *Hypoetes Polythyrsa* Miq extract, third group treated with 0.5 mL of 60% *Hypoetes Polythyrsa* Miq extract, fourth group treated with 0.5 mL of 80% *Hypoetes Polythyrsa* Miq, and the fifth group treated with 0.5 mL of 100% *Hypoetes Polythyrsa* Miq extract. Then, by applying linier regression, the LD_{50} of the extract was gained. Thirdly, to observe the extract activity for dissolving renal calculi compare to a commercial phytopharmcy/BE.

RESULTS

The ability of *Hypoetes Polythyrsa* Miq extract, pure aquadest, and a commercial phytopharmacy/BE to dissolve a calcium rock as a model of renal calculi was listed in Table 1.

Table 1
Dissolving ability of *Hypoetes Polythyrsa* Miq extract, pure aquadest, and a commercial phytopharmacy/BE

No	Solution	Dissolving ability (mg/L)
1.	5% of *Hypoetes Polythyrsa* Miq extract	136.79 ± 0.49
2.	10% of *Hypoetes Polythyrsa* Miq extract	156.84 ± 2.83
3.	20% of *Hypoetes Polythyrsa* Miq extract	297.21 ± 0.27
4.	BE solution	40.72 ± 11.88
5.	Aquadest (pa)	2.82 ± 0.27

LD_{50} of the *Hypoetes Polythyrsa* Miq extract was determined by applying liniear regression method, as presented in Figure 1.

DISCUSSION

All of the data observed were normally distributed and their variance also homogenous. Based on statistic analysis, in this study, it was gained that there were different between treatment and control group ($p< 0.05$). The dissolving ability are increase as the increase of the dose, i.e. 20% extract > 10% extract > 5% extract > BE solution > aquabidest.

In this study, it was observed that the LD_{50} of *Hypoetes Polythyrsa* Miq extract was at extract concentration of 0.5 mL which was similar to concentration of 129 % and equal to 0.694 g of the extract. When this dose was applied to the human, it was very safe, since by calculation the human dose become 266 g of extract which was concideraly very safe.[9]

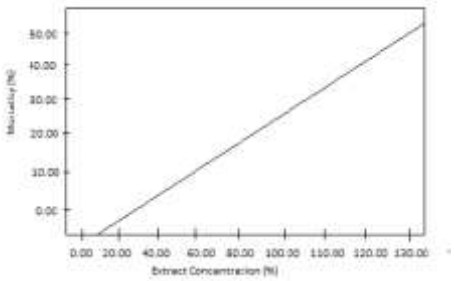

Figure 1
Correlation between *Hypoetes Polythyrsa* Miq Extract and Mice Mortality

As can be seen from Figure 1, 50% of mice died in athanol extract at concentration of 0.5 mL similar to 129 % extract.

The effectivity of *Hypoetes Polythyrsa* Miq extract for dissolving renal calculi compare to commercial phytopharmacy/BE was calculated by comparing the number of renal calculi dissolved in each treatment. The data were presented in Table 3.

Table 3
Effectivity of *Hypoetes Polythyrsa* Miq extract to dissolve real calculi compare to a commercial phytopharmacy/BE

No	Extract	Renal calculi dissolved (mg/dL)	Effectivity (%)
1	5% *Hypoetes Polythyrsa* Miq extract	136.79	3.36
2	10% *Hypoetes Polythyrsa* Miq extract	156.84	3.84
3	20% *Hypoetes Polythyrsa* Miq extract	297.21	7.30
4	BE	40.72	1

In this study we found that the *Hypoetes Polythyrsa* Miq extract was effective for dissolving renal calculi. The ability was started in 5% concentration of the extract. Increase concentration was followed by increase dissolving renal calculi ability. Therefore, 20% concentration of the extract gives the highest dissolving ability within 7.3 times higher compare to commercial phytopharmacy/BE.

CONCLUSION

Hypoetes Polythyrsa Miq extract was effective for dissolving renal calculi. The extract was safe within a lethal dose (LD_{50}) for mice 129%. We observed that in 5% concentration of the extract have already potent to dissolve renal calculi. Therefore, this herb was potent for curing renal calculi.

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