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The use of hyperuricemia herbs at "Hortus Medicus" herbal medicine clinic Tawangmangu

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ABSTRACT

Background: Hyperuricemia has become a health problems in Indonesia lately. The use of traditional medicine, especially herbs, has been used in the treatment of hyperuricemia. Hortus Medicus Herbal Medicine Clinic Tawangmangu has several herbal formulas that are applied in the care of hyperuricemia patients.

Objective: This study aims to determine the description of the mostly used medicinal plants for hyperuricemia and the percentage of efficacy of hyperuricemia therapy using medicinal plant.

Methods: This study was a retrospective cross-sectional study using purposive sampling. The total sample was 120 medical records and prescriptions for hyperuricemia patients at Hortus Medicus clinic for the period July-December 2020.

Results: There were 3 hyperuricemia herbs formulas used in Hortus Medicus. Based on the calculation of the doctor's prescription for hyperuricemia, the first herbal formula consisting of secang (*Caesalpinia sappan*) bark, tempuyung (*Sonchus arvensis*) herb, kepel (*Stelechocarpus burahol*) leaf was prescribed as many as 72 prescriptions (60%). The second herbal formula consisting of cabe jawa (*Piper retrofactum*), daun sendok (*Plantago mayor*) leaves, celery (*Apium graveolens*) herbs with 36 prescriptions (30%), and the third herbal formula consisting of rumput bolong (*Equisetum debille*) herb, temulawak (*Curcuma xanthorizza*), turmeric (*Curcuma domestica*) with 12 prescriptions (10%). The therapeutic efficacy of herbal formula 1st, 2nd and 3rd were 80%; 60%; 50%. There was no significant relationship between sex and the outcome of hyperuricemia therapy (p= 0.804).

Conclusion: Among three hyperuricemia herbal formulas used in Hortus Medicus, the 1st formula was mostly used. The percentage of therapeutic efficacy was also higher compared to the other two formulas.

Latar Belakang: *Penyakit degeneratif menjadi permasalahan kesehatan di Indonesia akhir-akhir ini. Salah satu penyakit degeneratif dengan prevalensi yang cukup tinggi adalah hiperurisemia. Penggunaan obat tradisional khususnya herbal telah dipakai dalam terapi hiperurisemia. Rumah Riset Jamu Tawangmangu telah memiliki beberapa formula jamu yang diaplikasikan dalam pelayanan terhadap pasien hiperurisemia*

Tujuan: *Penelitian ini bertujuan mengetahui gambaran tanaman obat untuk hiperurisemia yang paling banyak digunakan dan persentase efikasi terapi hiperurisemia menggunakan tanaman obat di Rumah Riset Jamu (RRJ) Hortus Medicus Tawangmangu pada tahun 2020.*

Metode: *Penelitian ini termasuk* cross-sectional *retrospektif dengan menggunakan* purposive sampling*. Total sampel sebanyak 120 rekam medik dan resep pasien hiperurisemia di RRJ Hortus Medicus periode Juli-Desember 2020.*

Hasil: *Terdapat 3 ramuan herbal hiperurisemia yang digunakan di RRJ Hortus Medicus. Formula herbal 1 terdiri dari kulit kayu secang (Caesalpinia sappan), herba tempuyung,(Sonchus arvensis), daun kepel (Stelechocarpus burahol) dengan 72 resep (60%), formula herbal 2 terdiri dari buah cabe jawa (Piper retrofactum) daun sendok (Plantago mayor) herba seledri (Apium graveolens) dengan 36 resep (30%), dan ramuan herbal 3 terdiri dari herba rumput bolong (Equisetum debille), temulawak (Curcuma xanthorizza), rimpang kunyit (Curcuma domestica) dengan 12 resep (10%). Efikasi terapi ramuan herbal 1, 2, dan 3 berturut-turut adalah 80%; 60%; 50%. Tidak ada hubungan yang signifikan antara jenis kelamin dan outcome pengobatan hiperurisemia (p=0,804).*

Kesimpulan: *Ramuan herbal 1 merupakan ramuan yang paling banyak digunakan dalam pengobatan hiperurisemia dan memiliki persentase keberhasilan terapi tertinggi.*

INTRODUCTION

Indonesia is currently experiencing an epidemiological transition which has led to a shift in disease patterns with an increase of degenerative diseases. Degenerative disease is a chronic non-communicable disease due to deterioration in organ function due to the aging process.[1] Gout, which is characterized by an increase in uric acid levels in the blood or hyperuricemia, is a degenerative disease that has an increasing prevalence with increasing age. The prevalence of hyperuricemia ranges from 2–13.2% in the general population.[2] Hyperuricemia is a condition with an increase in uric acid levels more than normal, which is caused by overproduction of uric acid or the kidneys are not efficient at filtering uric acid out of the blood and excreting it through urine. Someone is said to have hyperuricemia if the uric acid level in the blood is more than 6.8 mg/dl. Symptoms that appear in hyperuricemia are pain accompanied by repeated arthritis, and can result in permanent joint damage, in which the joint cannot move normally. Apart from the big toes, pain also occurs in many joints in the body, such as the elbows, fingers and wrists, and heels.[3] Complications that often occur due to hyperuricemia are gout, arthritis, hypertension, and kidney stones. Hyperuricemia can be caused by environmental, genetic, and anthropometric-metabolic factors. Foods rich in purines, fructose, and alcoholic beverages are consumption factors that increase blood uric acid levels. From an anthropometric point of view, age, sex, and adiposity affect blood uric acid levels.[4]

Hyperuricemia treatment in conventional medicine aims to reduce blood uric acid levels, reduce pain and suppress inflammatory reactions. Treatment of hyperuricemia by administering drugs, to relieve symptoms and prevent recurrence of the disease. The types of gout drugs that doctors usually prescribe to treat gout are colchicine and nonsteroidal anti-inflammatory drugs (NSAIDs). In patients who cannot take the two drugs, corticosteroids are also sometimes given. To reduce recurrence, Allopurinol can also be given which works by inhibiting uric acid production in the body. Other types of drugs that can also be given are drugs to increase the removal of excess uric acid from the body such as probenecid. The administration of NSAIDs drugs often causes side effects in the form of pain in the stomach, gastrointestinal bleeding, nausea, and diarrhea.[5]

The use of traditional medicine can be an alternative in treating hyperuricemia. The Saintification of Jamu Program as a flagship program of the Ministry of Health is an effort to provide scientific evidence on native Indonesian herbs or what is known as jamu through service-based research.[6] The Tawangmangu Hortus Medicus Herbal Medicine Clinic has implemented the Jamu Saintification program and produced several herbal formulas used for the treatment of hyperuricemia. The hyperuricemia herbal ingredients used in Rumah Riset Jamu (RRJ)/ Herbal Medicine Clinic "Hortus Medicus", There were 3 hyperuricemia herb formulas used in Hortus Medicus. The first

herbal formula consisting of secang (*Caesalpinia sappan*) bark, tempuyung (*Sonchus arvensis*) herb, kepel (*Stelechocarpus burahol*) leaf. The second herbal formula consisting of cabe jawa (*Piper retrofactum*), daun sendok (*Plantago mayor*) leaves, celery (*Apium graveolens*), and the third herbal formula consisting of rumput bolong (*Equisetum debille*) herb, temulawak (*Curcuma xanthorizza*), turmeric (*Curcuma domestica*). This herbal formulas have been used since 2010 at Hortus Medicus when the "Jamu Saintification" program was implemented. The formulation of medicinal plants for hyperuricemia is based on several functions according to the purpose of hyperuricemia therapy in reducing uric acid production through inhibition of the xanthine oxidase enzyme, increasing uric acid excretion and relieving symptoms of inflammation and pain.

This study aims to determine the description of the mostly used medicinal plants for hyperuricemia and the percentage of efficacy of hyperuricemia therapy using medicinal plant in RRJ Hortus Medicus in the period July-December 2020.

METHODS

This study was a retrospective cross-sectional study using purposive sampling. The total sample was 120 medical records and prescriptions for hyperuricemia patients at RRJ Hortus Medicus. The research was carried out at the Hortus Medicus Clinic of the Medicinal Plant and Traditional Medicine Research and Development Office, Tawangmangu in July-December 2020. The independent variable in this study was hyperuricemia therapy in the form of herbal formulas consisting of several medicinal plants that have anti-hyperuricemic effects. The dependent variable in this study was the therapeutic outcome as assessed by the decrease in uric acid levels in hyperuricemia subjects after the giving therapy of using herbal ingredients. Therapeutic outcome was assessed as achieved if the patient's uric acid level reached the expected uric acid target of <6.8 mg / dl. Conversely, the outcome of the therapy was declared not achieved if the patient's uric acid level did not reach the therapeutic target through observation by recording the data needed for research from medical records. The data was collected using a summary of the results which included: Patient demographic data, including medical record number, age and sex, patient clinical characteristics data, including uric acid values before receiving therapy, treatment history, medical history, and observational data, including traditional medicines given and blood uaric acid levels of patients after treatment carry out therapy. Medicinal plant preparations used for the treatment of hyperuricemia at RRJ Hortus Medicus are in the form of simplicia prepared by the infudation method, sympilisia from medicinal plants extracted using water solvent, then boiled at 90°C for 15 minutes. How to use this herbal concoction is the simplicia of medicinal plants put in 5 cups of boiling water (1.25 l). Wait for 15 minutes (until the water remains 3 cups, stirring occasionally with low heat). Then, let stand until warm and filter the extract of the herbal concoction.

RESULTS

In Table 1, the demographic characteristics of research subjects are presented, patients with hyperuricemia (blood uric acid levels> 6.8 mg / dl) based on age and gender. Characteristics of age, patients were classified into groups> 40 years and <40 years.

The composition of herbal ingredients for hyperuricemia is obtained from a doctor's prescription at the Hortus Medicus Herbal Medicine Clinic for the diagnosis of hyperuricemia. There are 120 doctor prescriptions with a diagnosis of hyperuricaemia in the period July-December 2020. From the 120 doctor's prescriptions, there are 3 herb formulas used to treat hyperuricemia.

In each hyperuricemia herbal formula, the outcome of the therapy was assessed at the end of December 2020. Data were viewed

Table 1. Distribution of demographic characteristics of hyperuricemic patients

Characteristics	Amount (n)	Percentage (%)
Gender		
Women	48	40
Man	72	60
Total	120	100
Age		
<40 years	36	30
> 40 years	84	70
Total	120	100

Table 2. Composition of anti-hyperuricemia herbal formula in RRJ Hortus Medicus

Herbal formula 1	Antihyperuricemia mechanisms	n (%)
Tempuyung (*Sonchus arvensis*)	Uricosuric	72 (60%)
Kepel (*Stelechocarpus burahol*)	Xanthine oxidase inhibitor	
Sappan wood (*Caesalpinia sappan L.*)	Xanthine oxidase inhibitor	
Herbal formula 2	**Antihyperuricemia mechanisms**	**n (%)**
Javanese chili (*Piper retrofactum*)	Anti-inflammatory	36 (30%)
Spoon leaf (*Plantago major*)	Xanthine oxidase inhibitor	
Celery (*Apium graveolens*)	Uricosuric	
Herbal formula 3	**Antihyperuricemia Mechanisms**	**n (%)**
Perforated grass (*Equisetum debille*)	Anti-inflammatory	12 (10%)
Temulawak (*Curcuma xanthoriza*)	Analgesics	
Turmeric (*Curcuma domestica*)	Analgesics	

by analyzing the subjects' medical records. Outcome was achieved if at the end of the assessment of blood uric acid levels, the normal value was reached, which was below 6.8 mg/dl. The success of therapy for each ingredient can be seen in Table 3.

Table 3.The outcome of hyperuricemia herbal herb therapy based on prescription at RRJ Hortus Medicus in July-December 2020

No.	Hyperuricemia herbal herbs	Outcome		Total (%)
		n not reached (%)	n accomplished (%)	
1.	Herbal formula 1	14 (20%)	58 (80%)	72 (60%)
2.	Herbal formula 2	14 (40%)	22 (60%)	36 (30%)
3.	Herbal formula 3	6 (50%)	6 (50%)	12 (10%)
	Total	34	86	120 (100%)

Table 4 shows the relationship between sex and treatment outcome in hyperuricemic patients. The calculation of odds ratios is used to see differences in the outcome of therapy based on the sex of the patient.

Table 4.The relationship between gender and therapeutic outcomes in hyperuricemia patients in RRJ Hortus Medicus period 2020

Gender	Outcome		Total	P value
	n not reached	n accomplished		
Women	14 (29.2%)	34 (70.8%)	48	0,804
Men	20 (27.7%)	52 (72.3%)	72	
Total	34 (28.3%)	86 (71.7%)	120	

Odds Ratio (OR) = 1.070

DISCUSSION

The proportion of male subjects who have high blood uric acid levels was 72 respondents (60%) compared to female respondents with 48 respondents (40%). In accordance with the literature, hyperuricemia affects 1-2% of the adult population, and is the most common case of inflammatory arthritis in men. The prevalence of gout is estimated to be between 13.6 per 1,000 men and 6.4 per 1,000 women. The prevalence of gout increased with age with a mean of 7% in men aged> 75 years and 3% in women aged> 85 years.[7]

Medicinal plant preparations used for the treatment of hyperuricemia in the form of an infusion.[8] Treatment of hyperuricemia at RRJ Hortus Medicus uses 3 antihyperuricemia herbal formulas, namely 1st ,2nd, and 3rd herbal formula. Each formula have diferent ingredients.

The 1st formula consist of kepel (*Stelechocarpus burahol*) leaf, secang (*Caesalpinia sappan*) bark, tempuyung (*Sonchus arvensis*) herb. The use of kepel leaves is based on several previous studies. Pre-clinical studies on experimental animals that induce hyperuricemia have been carried out compared to allopurinol as an uric acid drug. The results showed that in vivo both the ethanol extract of kepel and the extract of hexane had the potential to reduce uric acid levels in rat blood equivalent to allopurinol. Chemical content that is estimated to have activity in reducing uric acid levels in kepel leaves is flavonoids. Hypouricemic activity is obtained through inhibition of the xanthine oxidase enzyme, an enzyme that acts as a catalyst in the oxidation process of hypoxanthine to xanthine and then to uric acid.[9–11] The components of secang wood contain phenolics, flavonoids, tannins, polyphenols, cardenolin, anthraquinone, sappan chalcone, caesalpine, resin, resorcin, brazilin, d-alfa phallandren, oscimenen, and essential oils.[12] The 70% ethanol extract of secang wood is reported to reduce uric acid levels in hyperuricemic rats. The mechanism of decreasing uric acid in secang wood is also through inhibition of the activity of the xanthine oxidase enzyme, although not higher than allopurinol.[13] The chemical content that is responsible as a hypouricemic agent in secang wood is not known. Tempuyung leaves have a diuretic effect so that they can be uricosuric by eliminating uric acid in the bladder.[14] The three components in 1st formula are synergistic in reducing blood uric acid in subjects with hyperuricemia.[15]

The compositions of 2nd herbal formula are cabe jawa (*Piper retrofactum*), daun sendok (*Plantago mayor*) leaves, celery (*Apium graveolens*). Celery herb flavonoid compounds have been shown to reduce blood uric acid levels in mice with hyperuricemia and increase uric acid excretion. Previous research stated that the water fraction of celery herbs up to a dose of 50 mg/kgBW can reduce blood uric acid levels in mice. The bioactive compounds that this plant has are iridoid glycosides (such as aukubin), flavonoids (including apigenin) and polyphenols.[16] The ethanol extract of daun sendok has an inhibitory power of 100 ppm equivalent to 10 ppm of allopurinol.[17] Cabe jawa (*Piper retrofractum*) is widely used in the community which is proven to have analgesic effects. This effect can of course be used as pain reliever experienced by some hyperuricemia sufferers. In addition, cabe jawa also have anti-

inflammatory properties that are beneficial for people with hyperuricemia.[18]

Formula 3rd consists of rumput bolong (*Equisetum debille*) herb, temulawak (*Curcuma xanthorizza*), turmeric (*Curcuma domestica*). Temulawak rhizome contains phenols, flavonoids, tannins, saponins, terpenoids, sterols, proteins, and carbohydrates. The essential oils from ginger rhizome include: xanthorrhizol as the main component followed by camphene, curcumin, α pinene, α thujene, β pinene, linalool then zingiberene.[19] Temulawak infusion can inhibit the volume of inflammation at a dose of 480 mg/ 100 mgBW on the soles of the feet rats induced 0.2 ml/ head suspension of 1% carrageenan in physiological NaCl. The mechanism of curcumin as an anti-inflammatory is to inhibit the formation of prostaglandins.[20] Turmeric rhizome contains active compounds such as curcumin, dihydrocurcumin, desmethoxicurcumin, and bisdesmetoksikurcumin.[21] Intraperitonial administration of curcumin and sodium curcuminate showed strong anti-inflammatory activity in carrage-induced acute swelling of rats. Curcumin's anti-inflammatory activity occurs due to its ability to bind oxygen free radicals that can cause an inflammatory process.[22] Rumput bolong herbs contain flavonoids, sterols, saponins and tannins. The bioactive has anti-inflammatory activity. The anti-inflammatory mechanisms of perforated grass affect the central nervous system (such as narcotics) and peripherals (such as NSAIDs) but the exact mechanism is still in question. The bioactive has anti-inflammatory activity. The anti-inflammatory mechanisms of rumput bolong affect the central nervous system (such as narcotics) and peripherals (such as NSAIDs) but the exact mechanism is still in question. The bioactive has anti-inflammatory activity. The anti-inflammatory mechanisms of perforated grass affect the central nervous system (such as narcotics) and peripherals (such as NSAIDs) but the exact mechanism is still in question.[23]

The percentage of therapeutic efficacy of the 1st formula was higher compared to the other two formulas. In formula 1, there is a more complete combination of inhibitors of uric acid production and increases in uric acid excretion through urine / uricosurics. Although Formula 2 also has an anti-hyperuricemic effect, it is not as strong as formula 1. While formula 3 is dominated by plants with analgesic and anti-inflammatory effects compared to hypouricemic effects.

In this study, the herbal ingredients that were observed and analyzed through secondary data were in the form of simplicia. According to the Regulation of the Minister of Health of the Republic of Indonesia Number 007 of 2012 concerning Registration of Traditional Medicines, simplicia is dried natural material that is used for treatment and has not undergone processing, unless stated otherwise.

The weakness of this study is that the data used are secondary data in the form of prescriptions and medical records, meaning that the researcher cannot interact directly with the patients, so that he cannot know the patient's condition. The patient's condition in question is the factors that can affect hyperuricemia therapy using traditional medicine, such as lifestyle, diet, adherence to taking herbal medicine, and the accuracy of how to use hyperuricemia herbal concoctions.

CONCLUSION

Among three hyperuricemia herbals formulas used in Hortus Medicus, the 1st formula consist of secang (*Caesalpininia sappan*) bark, tempuyung (*Sonchus arvensis*) herb, kepel (*Stelechocarpus burahol*) was mostly used. The percentage of therapeutic efficacy was also higher compared to the other two formulas.

CONFLICT OF INTEREST

The authors declare that there is no confict of interest.

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