E-ISSN: 2476-9606
Abstract Proceedings International Scholars Conference
Volume 7 Issue 1, October 2019, pp. 804-813

https://doi.org/10.35974/isc.v7i1.2085

Effectiveness of Boiled Figs Leaf (Ficus Carica L) Towards Ureum and Creatinin Serum of Male Wistar Strain Rats with Acute Renal Failure Model

Ralda christina ursula pelealu[1], Untung Sudharmono[2]
[1] Student of Nursing Faculty, Adventist University, Bandung
[2] Faculty of Nursing, Adventist University, Bandung
raldap98@gmail.com

ABSTRACT

Acute renal failure is a set of clinical symptoms characterized by increased levels of creatinine and blood urea nitrogen and a rapids decrease in the rate of glomerular filtration. The Objectives of this study was to determine the effectiveness of brewed tin water (Ficus Carica L) against urea and creatinine serum of male Wistar strain rats in acute renal Failure. The subject of the research were 30 male rats weighing 180-200 grams and 2-3 months old, which were divided into 3 groups, namely the negative control group, the positive control group and the treatment group. Each group consisted of 10 rats. The negative control group was only given food and drink as usual. The positive control group and the treatment group were induced with gentamicin 12 mg / intraperitonial for 7 days to increase urea and creatinine serum levels. The treatment group was given steeping treatment of 0.65 grams of boiled figs leaf in 100cc of given 3.6cc/orally for 7 days. One way ANOVA test was conducted to analyse the study using SPSS version 24. The results found there are no significant differences in urea serum levels between the treatment group and negative control group ($p = 0.252$) but there were significant differences in the urea serum value between the treatment group and positive control group ($p < 0.05$). There was a significant difference in the value of creatinine serum between the treatment group, the positive control group and the negative control group ($p < 0.05$). As Conclusions boiled figs leaf (Ficus Carica L) has an effect on decreasing urea and creatinine serum levels in male wistar rats with acute renal failure.

Keywords: Gentamicin, Urea Serum, Creatinine Serum, Ficus Carica L.

INTRODUCTION

Kidney is a very vital organ that functions for the excretion of several substances resulting from the body's metabolism, maintains plasma pH in the range of 7.4 and maintains fluid balance in the body (Prebowo, & Pranata, 2014). The kidneys also function to maintain the balance of the composition of the blood by way of preventing the buildup of wastes

metabolism, and maintain the stability of the level of electrolytes in the body such as sodium, potassium and phosphate, as well as producing the renin \ enzyme that helps to control blood pressure, produce the erythropoietin hormone to arouses an cell red blood and converts the calcitriol hormone to keep bones strong. Kidneys disorders can cause health problems that have a poor prognosis and high costs. In Indonesia, kidney disease treatment is the second largest financing from health BPJS after cardiac disease (Ministry of Health, Republic of Indonesia, 2017). Acute renal failure is a set of clinical symptoms characterized by an increase in blood creatinine and urea nitrogen levels and a decrease in glomerular filtration rate (Price, Sylvia A. & Wilson, L., 2012). Each year is estimated that 1.7 people die from acute kidney failure and 2.4 people die from chronic kidney failure. More than 13 million people worldwide and 85% found in low- and middle-income countries experience acute kidney failure which, without the right treatment, this problem will become chronic kidney failure. Early diagnosis, prevention of disease, and slowing the progression of the disease from acute kidney failure to chronic kidney failure, is very helpful in reducing treatment costs, risks to the disease itself and for the welfare of individuals and countries (World Kidney Day, 2019)

Many factors can cause acute kidney failure, one of which is an aminoglycoside antibiotic. One side effect of aminoglycosides are a class of drugs is nephrotoxic effect that initiate a apoptosis and intracellular edema, impaired basal membrane, narrowing the glomeruli Bowman space and necrosis tubules acute (Souza et al., 2008). Aminoglycosides inhibit some lysosomal phospholipase such as phosphatidylinositol-specific phospholipase C activity in the cytosol of the renal cortex and the proximal tubular epithelial cell border membrane brush. This barrier of phospholipase changes the composition amount of subcellular and plasma membranes in the proximal tubule. Changes that occur in the renal cortex have to do with phospholipids leading to symptoms of impaired kidney function. Gentamicin inhibits the action of the phospholipase-dependent enzyme, Na + -K + -ATPase, and adenylate cyclase. In addition, this aminoglycoside group also interferes with the activity of supplying oxygen to the mitochondria. There is disturbances in the function of mitochondria, create more severe, and it damage the process of supplying energy to the cell. Gentamicin also inhibits the accumulation of calcium and increases free cytosolic (Ca2 +). In this situation sequelization of aminoglycosides in lysosomes causes the formation of myeloid bodies due to degradation of phospholipid action, and the consistency of the lysosome membrane is disrupted (Hewitt, R., Goldstein, S., Hook, B., 1991 in Lintong, P., Kairupan, C., Sondakh, P., 2012).

Gentamicin is an antibiotic that is classified in aminoglycosides that are widely used by the public and has a broad spectrum (Rosmiati, H. & Gan, V. H. S., 2003).

In this modern era, the economic condition of Indonesian people is categorized as low, middle and upper, still use traditional medicine therapy as an alternative to modern medicine for health maintenance and healing of diseases. Some of the factors that people make people still use traditional drug therapy is the price, cultural factors, social factors and marketing factors (Andriati, A., & Wahyudi, R., 2016). In the social and cultural aspects, Indonesian people get a lot of information about the use of traditional medicinal plants from one's personal experience which is then shared for generations (Julung H. et al., 2018). There are still many Indonesians, especially the elderly to the elderly, grow traditional medicinal plants in the yard or if they do not have a yard, they will grow medicinal plants using potting media (Sari, I., et al, 2015). The reaction process of traditional medicine is fairly slow but has constructive properties, whereas the process of reaction of modern medicine is fairly fast but has destructive properties (Herdiani, E., 2012). The tin or ara plant, in English is called fig, belongs to kingdom of Plantae , Magnoliophyta division , the order of Urticales , Moraceae family , and genus Ficus (Umadevi S. et al., 2011). Fig Leaf (Ficus Carica L) is bright green colored, single, and large up to 1 foot. Fig leaf has lobes that in approximately 1-5 sinuses, rough hairy on the upper surface and fluffy on the bottom (Joseph, B., & Raj, J., 2011). Fig leaves (Ficus Carica L) can easily found in tropical and subtropical countries, this plant have many functions including immunomodulatory, antioxidant, anti-inflammatory, antipyretic, antidiabetic, anticancer, anti-inflammatory, hepatoprotektan, and anti-micro bacteria (Ahaddin, Y., 2014). Immunomodulator in tin leaf extract work very effective in improving cellular and humoral responses (Patil, S., Bhangale, C., Patil, R., 2010). Anti-inflammation in tin leaf extracts has been studied to show a maximum anti-inflammatory effect of 75.90% in acute inflammation and in chronic case studies showing 71.66% reduction in granuloma weight (Patil, V., Patil, R., 2011). Tin leaves contain ingredients such as flavonoids, lcaloid, saponins, polyphenols (Sirisha, N., Sreenivasulu, M., Sangeeta, K., Chetty, M., 2010). Tin leaves also contain several bioactive compounds such as arabinose, β-amirin, β-carotene, glycosides, β- setosterol and xanthol (Joseph, B., & Raj, J., 2011).

Indonesian people are very familiar with tea brewing. Apart from the short manufacturing time, the way of brewing tea is also very practical. Brewing dried fig leaves with boiling water will not damage its containment level of tin leaf itself (Princess, OK, 2018).

METHODS

The method used in this study is an experimental laboratory. The dependent variable of this study was urea and creatinine serum of male rats and the independent variable was tin leaf decoction. The tin leaves (Ficus carica L) used were obtained from the Cimenyan area of Bandung regency. The research object used was 30 male Wistar strain rats weighing 180-200 grams and 2-3 months of age which were adapted for 7 days with 12 hours of bright light and 12 hours of dark. After which, they were randomly divided into 3 groups, namely negative groups control, positive control group and treatment group. Each group consisted of 10 rats. The negative control group was only given food and drink as usual. The positive control group and the treatment group were induced with gentamicin 12 mg / intraperitonial for 7 days to increase the level of urea and creatinine serum. The treatment group was given treatment of 0.65 grams of figs leaf in 100cc and then induced at a dose of 3.6cc / orally for 7 days. The research objects criteria did not experience more than 10% decrease or increase in body weight during the adaptation to its initial body weight.

The subject of research that was adapted for 7 days that met the inclusion criteria was used in the study, the test material namely Figs leaves decoction was given orally to the treatment group only. The treatment in the three study groups was as follows:

1. Negative control group: 10 rats were given food and drink as usual during the study.
2. Positive control group: 10 rats induced with gentamicin 12 mg / intraperitonial for 7 days and given food and drink as usual during the study.
3. Treatment group: 10 rats were induced with gentamicin 12 mg / intraperitonial for 7 days, given 0.65 grams of tin leaf decoction therapy in 100cc of water given 3.6cc / oral for 7 days and also given food and drink as usual.

Day 1 to day 7 the rats were adapted. Day 8 to day 15 the positive control group and the treatment group was induced with gentamicin 12 mg / intraperitonial. The 15th day of blood sampling was taken by cutting the tip of the tail, this activity was carried out on all research objects to obtain urea and creatinine serum levels as pre-therapeutic data. The 15th day until the 22nd day the treatment group was given 0.65 grams of tin leaf decoction therapy in 100cc water as much as 3.6cc / orally. On the 23rd day all research objects were examined for urea and creatinine serum levels for the second time as post-therapy data

RESULTS AND DISCUSSION

Research data (Table 1, Table 2, Table 3, and Table 4) were analyzed with SPSS version 24 using the one way ANOVA statistical test.

Table 1. **Results of comparison of serum urea levels of male rats in the acute Wistar strain of kidney failure before administration of tin leaf steeping therapy.**

Parameter	Comparison among groups		Mean Difference (IJ)	Standard Error (SE)	p-value
	Groups (I)	Groups of Comparison (J)			
Urea Pre	Negative Control Group	Positive Control Group	-44.52000 *	2. 47165	0,000
		Treatment group	-48.47000 *	2. 47165	0,000
	Positive Control Group	Negative Control Group	44.52000 *	2. 47165	0,000
		Treatment group	-3.95000	2. 47165	0. 264
	Treatment group	Negative Control Group	48.47 000 *	2. 47165	0,000
		Positive Control Group	3.95000	2. 47165	0.264

Referring to the results of the data that has been analyzed for serum urea levels pre therapy there is a significant difference from the negative control group compared to the positive control group and the treatment group ($p < 0.05$), this condition is caused by giving gentamicin 12 mg / intraperitonial for 7 days for the group positive control and treatment groups in male wistar rats that resulted in an increase in serum urea levels while in the negative control group no gentamicin was given 12 mg / intraperitonial for 7 days so that the serum urea levels did not increase . However, there was no significant difference between the positive control group and the treatment group ($p = 0.264$), because the positive control group and the treatment group were each given gentamicin 12 mg / intraperitonial for 7 days so that the serum urea levels of these two groups increased.

Table 2. **Results of comparison of serum urea levels of male rats in the model of acute renal failure after administration of tin leaf decoction therapy.**

Parameter	Comparison among groups		Mean Difference (IJ)	Standard Error (SE)	p-value
	Groups (I)	Groups of Comparison (J)			
Urea Post Content	Negative Control Group	Positive Control Group	-136.86000 *	13.15129	0,000
		Treatment group	-21.40000	13.15129	0.252
	Positive Control Group	Negative Control Group	136.86000 *	13.15129	0,000
		Treatment group	115.46000 *	13.15129	0.005
	Treatment group	Negative Control Group	21.40000	13.15129	0.252
		Positive Control Group	-115.46000 *	13.15129	0.005

The level of urea serum in post therapy between the negative control group and the positive control group show a significant difference ($p < 0.05$), this situation occurred because in the negative control group post urea serum levels of male Wistar strain rats did not increase, whereas in the positive control group the levels of post urea serum of male Wistar strain rats is gradually increase because it is given gentamicin 12 mg / intraperitonial for 7 days and no tin leaf water decoction therapy is given (*Ficus Carica L).* there was the significant difference between the negative control group and treatment group ($p = 0.252$), this situation is caused by the serum levels of urea post treatment groups that have been given therapy of fig leaves *(Ficus Carica L)* decoction for 7 days in male Wistar strain rats that had been inducted with gentamicin 12 mg / intraperitonial for 7 days approached the level of post urea serum of negative control group who were not given gentamicin at dose of 12 mg/ intraperitonial for 7 days. The post-therapeutic level of urea serum between the positive control group and the treatment group shows significant differences ($p < 0.05$). This situation occurs because in the positive control group that was induced gentamicin as much as 12 mg / intraperitonial for 7 days the post levels of urea serum increased, whereas in the treatment group who were given gentamicin 12 mg / intraperitonial for 7 days then given the treatment of tin leaf *(Ficus Carica L)* decoction for 7-day, post urea serum levels decreased. There was a change in the ratio of urea levels before and after administration of tin leaf *(Ficus Carica L)* decoction therapy for 7 days from the negative control group compared to the treatment group, the change was seen from a significant difference before therapy became insignificant different after therapy. It happened because of the ability of the substance contained in tin leaf *(Ficus Carica L)* decoction for 7 days in nature decreased the urea level of male wistar strain induced gentamicin 12 mg intraperitonial / day.

Table 3. **Results of comparison of serum creatinine levels in male Wistar strain models of acute renal failure before administration of tin leaf decoction therapy.**

Parameter	Comparison among groups		Mean Difference (IJ)	Standard Error (SE)	p-value
	Groups (I)	Groups of Comparison (J)			
Creatinine Levels Pre	Negative Control Group	Positive Control Group	-2.18800*	0.2 4919	0,000
		Treatment group	-2.41500*	0.24919	0 000
	Positive Control Group	Negative Control Group	2.18800*	0.24919	0,000
		Treatment group	-0.22700	0.24919	0. 638
	Treatment group	Negative Control Group	2.41500*	0.24919	0,000
		Positive Control Group	0.22700	0.24919	0.638

The levels of creatinine serum before the therapy shows no significant difference between the negative control group and positive control group ($p < 0.05$), this situation is caused by the negative control group was not given 12 mg of gentamicin / intraperitoneally for 7 days so that the levels of creatinine serum increase, whereas in the positive control group gentamicin was given as much as 12 mg / intraperitonial for 7 days so that the serum creatinine level had increased. There is a significant difference between the negative control group if with the treatment group , this condition is caused by the negative control group not being given gentamicin 12 mg / intraperitonial for 7 days so that serum creatinine levels do not experience an increase, whereas in the treatment group giving gentamicin as much as 12 mg / intraperitonial for 7 days and have not been given treatment of tin leaf *(Ficus Carica L)* decoction for 7 days so that serum creatinine levels have increased. Pre-treatment creatinine serum was not show a significant difference between the positive control group to the treatment group ($p = 0.638$), due to the positive control group and the treatment group were given gentamicin as much as 12 mg / intraperitoneally for 7 days so that the two groups show increases in its creatinine serum levels. The increase in creatinine serum before the therapy of fig leaves (*Ficus Carica L*) decoction for 7 days in male wistar strain rats occur due to administration of gentamicin 12 mg intraperitoneally / day for 7 days, it's also can be seen microscopically a swelling of cells- epithelial tubules (hydropic degeneration) in which the cells enlarged, the vacuole and granular cytoplasm, the round core is still in the middle, the membrane is still intact basement, also in part where the epithelial cells of the tubules show a dead cell and apoptosis, and the tearing of the basement membrane (Lintong, P., Kairupan, C. , Sondakh, P., 2012).

Table 4. **Results of comparison of serum creatinine levels in male wistar strain models of acute renal failure after administration of tin leaf steeping therapy.**

Parameter	Comparison among groups		Mean Difference (IJ)	Standard Error (SE)	p-value
	Groups (I)	Groups of Comparison (J)			
Post Creatinine Levels	Negative Control Group	Positive Control Group	-3.30800 *	0.27603	0,000
		Treatment group	-1.10900 *	0.27603	0.001
	Positive Control Group	Negative Control Group	3.30800 *	0.27603	0,000
		Treatment group	2.19900 *	0.27603	0,000
	Treatment group	Negative Control Group	1.10900 *	0.27603	0.001
		Positive Control Group	-2.19900 *	0.27603	0,000

Post-treatment serum creatinine levels were significantly different from the negative control group compared to the positive control group ($p < 0.05$), this condition was caused by post serum creatinine levels from male wistar strain rats in the negative control group who were not given gentamicin 12 mg / intraperitonial for 7 days so that serum creatinine levels did not increase, whereas in the positive control group, gentamicin was given as much as 12 mg / intraperitonial for 7 days so that serum creatinine levels increased. There was a significant difference between the negative control group and the treatment group ($p < 0.05$), this condition was caused by post serum creatinine levels from male wistar rats in the negative control group who were not given gentamicin of 12 mg / intraperitonial for 7 days so that serum creatinine levels did not experience improvement, while in the treatment group that was given gentamicin at a dose of 12 mg / intraperitonial for 7 days so that the serum creatinine levels increased and its treated by figs leaf *(Ficus Carica L)* decoction therapy for 7 days . There was a significant difference between the positive control group and the treatment group ($p < 0.05$), this condition was caused by post serum creatinine levels from male wistar rats in the positive control group which given gentamicin at dose of 12 mg / intraperitonial for 7 days resulting increasing in the creatinine serum levels, whereas in the treatment group that was given gentamicin at dose of 12 mg / intraperitonial for 7 days so that the serum creatinine levels increased and then given the treatment of figs leaf *(Ficus Carica L)* decoction for 7 days. There was a changing in the ratio of serum creatinine levels before and after administration of figs leaf water steeping therapy *(Ficus Carica L)* for 7 days from the positive control group compared to the treatment group, the change was seen from a significant difference before therapy and became insignificant after therapy. This happened because of the ability of the substance contained in figs leaf *(Ficus Carica L)* decoction in reducing creatinine levels in male Wistar strain rats that induced gentamicin at a dose of 12 mg intraperitonial / day

Conclusion and Suggestion.

The conclusion of research can be seen as follows:

1. Giving gentamicin 12 mg / intraperitonial for 7 days in male wistar rats, can increase the level urea and creatinine serum.
2. The administration of figs leaf (Ficus Carica L) decoction therapy for 7 days in male Wistar strain rats with acute kidney failure has the effect of lowering the level urea serum to normal level.

3. The administration of figs leaf (Ficus Carica L) decoction therapy for 7 days in male rats in the acute renal failure model has the effect of lowering serum creatinine levels, but did not reached normal level.

Based on the results of this study, creatinine serum levels in male wistar rats with acute kidney failure models given figs leaf (Ficus Carica L) decoction therapy for 7 days have not reached the normal value limit, this condition is caused by the relatively short research time, for subsequent studies need to increase the duration of therapy.

REFERENCES

Ahaddin Y, (2014). *Isolasi dan Sitotoksitas Ekstrak Flavonoiddaun Tin (Ficus carica Linn)*. Bogor: IPB.

Andriati, A., & Wahjudi, R., (2016). Tingkat penerimaan penggunaan jamu sebagai alternative penggunaan obat modern pada masyarakat ekonomi rendah-menengah dan atas. *Masyarakat dan Kebudayaan Politik.* 29(3), 133-145. doi: http://dx.doi.org/10.20473 /mkp.V29I32016.133-145

Herdiani, E. 2012. Potensi Tanaman Obat Indonesia [Online]. Indonesia: BBPP Lembang. Retrieved from: http://www.bbpplembang.info/index.php/arsip/artikel/artikelpertanian/ 585-potensi-tanaman-obatindonesia

Joseph B, & Raj J, (2011). Pharmacognostic and phytochemical properties of Ficus carica Linn–An overview. International journal of pharmtech research, 3(1), 8-12.

Julung Hendrikus, Supiandi Markus Iyus, Ege Benediktus, Mahana Susriyati, Zubaidah Siti, (2018). Analisis Sumber Pengetahuan Tradisional Tanaman Obat yang Digunakan oleh Masyarakat Suku Dayak Desa. *Proceeding of Biology Education.* 2(1), 67-74. doi: https://doi.org/10.21009/pbe.2-1.9

Kementrian Kesehatan RI, (2017). *Pusat Data dan Informasi. Situasi Penyakit Ginjal Kronis.*

Prabowo, Eko & Pranata, Andi Eka (2014). *Buku Ajar Asuhan Keperawatan Sistem Perkemihan.* Yogyakarta:Nuha Medika.

Price, Sylvia A. & Lorraine M Wilson, (2012). *Patofisiologi: Konsep Klinis Proses-proses Penyakit. Edisi 6. Volume 2. Alih Bahasa.* Jakarta: EGC.

Putri, Oktavina Kartika, (2018). Kadar Fenolik Total dan Flavonoid Total Seduhan Daun Tin (Ficus carica) Segar dan Kering dengan Air Mendidih. *JC-T (Journal Cis-Trans): Jurnal Kimia dan Terapannya).* 2(2), 7-12. doi: http://dx.doi.org/10.17977/um026v2i22 018p007

Rosmiati, H. & Gan, V.H.S. (2003). *Farmakologi dan Terapi.* Jakarta: Gaya Baru.

Sari, I. D., Yuniar, Y., Siahaan, S., Riswati, M. S., (2015). Tradisi Masyarakat dalam Penanaman dan Pemanfaatan Tumbuhan Obat Lekat di Pekarangan. *Jurnal Kefarmasian Indonesia.* 5(2), 123-132. doi: 10.22435/jki.v5i2.4407.123-132

Sirisha, N., Sreenivasulu, M., Sangeeta, K., & Chetty, CM., (2010). Antioxidant properties of Ficus spesies-a review. *Int J Pharm Tech Res.* 2(4), 2174-2182.

Souza, V. B., Oliveira, R. F. L., Ferreira, A. A. A., & Araújo Júnior, R. F., (2008). Alterações renais por aminoglicosídeos. *Arq Med,* 22(4/5), 131-135.

Umadevi, S., Kumar, S., Joseph, M., Easow, M., Kandhakumari, G., Srirangaraj, S., Raj, S., Stephen, & S., (2011). Microbiological Study of Diabetic Foot Infections, *Indian Journal of Medical Specialities*. 2(1), 12-17. doi: 10.7713/ijms.2011.0004

Patil, V. V., Patil, V. R., (2011). Evaluation of anti-inflammatory activity of Ficus carica Linn. leaves. *Indian J Nat Prod Resour.* 2(2), 151-155.

Patil, V. S., Bhangale, S. C., Patil, V. R., (2010). Studies on immunomodulatory activity of Ficus carica. Int J Pharm Pharm Sci. 2(4), 97-99.

World Kidney Day, (2019). *Kidney Health For Everyone Everywhere Campaign Toolkit.* Retrieved from: https://www.worldkidneyday.org/wp-content/uploads/2018/09/2019-WKD-Campaign-Toolkit.pdf