



Effectiveness of Boiled Comfrey Leaf (*Symphytum Officinale L*) and Urea Creatinine Serum in Male Wistar Strain of Acute Kidney Failure Model

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ABSTRACT

Acute kidney failure is a decrease in kidney that occurs only in matter of hour's even days which can be seen from decreased urine production and increased blood urea nitrogen and creatinine. This study aims to determine the effectiveness of boiled comfrey leaf (*symphytum officinale L*) on urea creatinine serum in male wistar strain of acute kidney failure model. This research used 30 male wistar strain rats weighing 180-200 grams and aged 2-3 months that were divided into 3 groups, namely negative groups (only given minerals), positive groups (kidney damaged by gentamicin 0.3cc IP / day) and the treatment group (the kidneys were damaged with gentamicin 0.3cc IP / day and 2.8 g of boiled comfrey leaf in 150 cc of water and 2.7 cc were given orally for 7 days). Data were analyzed with SPSS version 24, one way ANOVA test was performed to compare the levels of urea and creatinine. The results showed that there was a significant difference in the urea of the treatment group and the positive group ($p < 0.05$) but there was no significant difference in the ureum value between the treatment group and the negative group. There was a significant difference in creatinine values between the treatment group, positive group and negative group ($p < 0.05$). As a Conclusion boiled comfrey leaf (*symphytum officinale L*) water has an effect on decreasing serum levels of ureum creatinine in male rat's wistar strain of acute kidney failure model.

Keywords: Gentamicin, Ureum, Creatinine, *Symphytum Officinale L*.

INTRODUCTION

The purpose of this research is to know the effectiveness of boiled comfrey leaves (*symphytum officinale L*) to urea and creatinine serum in acute renal failure of male wistar rats. This research was conducted on the grounds that herbal medicine is still very important to be developed with good benefits, easy to reach and low cost for the wider community, especially for people who are far from the reach of health workers. Comfrey leaf (*symphytum officinale L*) is one of a plants that can be made into traditional medicine, thus it is necessary to know the effectiveness of Comfrey leaf (*symphytum officinale L*) which is boiled directly with fresh

leaves and is induced in trials of Wistar strain male rats with an increase in serum urea and creatinine levels in the acute renal failure model.

LITERATURE REVIEW

Now a days, there are many Indonesian people who still use herbs as herbal medicines which believed to prevent disease, increase endurance and fitness and become a beauty ingredient that is still adhered by wider community in Indonesia and even outside the country. In this millennial era, there are some traditional medicines that are still trusted by the wider community in overcoming health problems, the main reason is they assume that this kind of medicine has low side effects and low costs. (Sudharmono, 2014)

Comfrey leaf (*symphytum officinale* L) is a type of plant that is believed by the wider community as traditional medicine. Komfrey leaf (*symphytum officinale* L) commonly found tropical area, and it very easy to find. Komfrey leaves are not only in Indonesia but also in various countries with different names, there are also foreign names of comfrey is *symphytum officinale* L (latin), "knit bone" (English), "k'ang fu li" (Chinese), "Kompri", "kompering", "gomfri" (Java) . (Jangga and Suriani. 2016)

Comfrey Leaves (*symphytum officinale* L) is one of the perennial herb of the boraginaceae family which is known as a medicine for cardiovascular system (hypertension, hypotension), respiratory system (bronchitis, pneumonia), digestive system (diarrhea, appendicitis, ulcers, typhoid, hemorrhoids), the musculoskeletal system (fracture, rheumatism, aching rheumatic pain), immunological system (cancer), reproductive system (infertility in women), urinary system (kidney stones, hematuria) and endocrine system (DM). (Norm, Latif, Usman, 2014). Comfrey leaf (*symphytum officinale* L) can also act as anti-inflammatory which has been proven to have an effect on the treatment process (Seigner et al., 2019).

Comfrey leaves (*symphytum officinale* L) have a slightly bitter taste and it's regarded as a cold plants, and rich with antioxidants. The chemicals contained are symphytine, echimidine, anodaline, pyrolizidine alkaloid (pas), tannin, essential oils, allatonin, and vitamins (B1, B2, C and E). Comfrey leaves are anti-inflammatory / anti-inflammatory plants. (Gonzalez, Perez, Nunez. 2016)

Comfrey Leaves (*symphytum officinale* L), forming clumps as high as 20-50 cm tall. Pseudo-shaped rods are has not wood but have stems. It has a Single leaf, shaped like an oval with the ends of the base tapering at the edges it has flat and rough surfaces (fluffy) leaves, with the

length of the leaves 27-50 cm, a width leaves of 4-14 cm long, it has pinnate shaped, and has green leaves. Composite flower, shaped like small funnel, with numbers of five, has white yellowish color, purple. Fruit shape is round; every fruit consists of 4 seeds. (Kurds, A. 2010)

Kidney is one of the important organs that become the main secretion in the body that functions as a primary vital tool that regulates the volume of and filter the blood chemical in the body. If the kidney has a problem that can reduce its function it will cause fatal things to the body. (Situmorang. 2015). Kidney can be damaged by various causes, namely sepsis, dehydration, acute glomerulonephritis, drugs (gentamicin). (Davis CP, 2015)

Based on data from the World Health Organization or the World Health Organization (WHO), it shows that patients with acute and chronic kidney failure reach 50%, while only 25% and 12.5% are known to get treatment. (Indrasari, Nur, Denita. 2015)

Kidney failure is damage to most of the nephrons in both kidneys and no longer functions normally. Kidney failure occurs when the GFR is suddenly reduced to 50% or more, so that it can trigger oliguria and anuria with the accumulation of metabolic waste in the blood (azotemia). Acute renal injury can trigger acute kidney failure caused by a decrease in perfusion, internal damage, and obstruction of the urinary flow that is based on its location and pathological processes. (Hurst, 2016)

About 5% to 7% of patients treated have acute kidney failure; this incidence increased by 30% in critical and special care units. Acute kidney failure occurs suddenly and is often reversible with rapid therapy and there is still a possibility that the kidneys will function properly if given good or regular therapy or treatment. (LeMone, Burke, Bauldoff. 2016)

Acute kidney failure occurs due to complex kidney disorders, so that the kidneys decrease to clean up toxins in the blood, which is caused by decreased the kidney function that occurs only in days or even hours which can be seen from decreased urine production and increased blood urea nitrogen (BUN) and creatinine. In which, the kidney filtration function decreases rapidly with the injury to the kidneys. It should be noted that changes in blood urea nitrogen and serum creatinine can represent not only kidney injury, but also normal responses from the kidneys to extracellular volume depletion or decreased renal blood flow. (Putra, Hafiz. 2018)

Gentamicin is an aminoglycoside type of antibiotic that has nephrotoxic side effects that cause damage to the kidneys with marked increase in urea and creatinine serum caused by nephrotoxic agents. (Endriastuti, Wahyono, Sukarno. 2015). Toxicity aminoiglikosida can synthesize mitochondrial proteins and form free radicals to actively increase the synthesis of nitric oxide, when nitric oxide binds with O₂ then activates superoxide radicals are converted

by the body's enzymes into superoxide dismutase (SOD) and produce hydrogen peroxide (H₂O₂) which is the beginning of the occurrence of free radicals in the body. (Normasari, Dewi, Rachmania. 2017). In this study gentamicin proved to show a decrease in kidney function characterized by an increase in the level of creatinine urea serum in tested animals of male Wistar strain rats.

The problem that arises from the above description is whether the water of Comfrey (*Symphytum officinale* L) decoction can reduce the levels of urea and creatinine serum in male Wistar strain rats with acute renal failure model that has been induced with gentamicin 0.3 cc intra peritoneal for 7 day.

The objectives of this study was to prove the effectiveness of comfrey leaf (*Symphytum officinale* L) decoction toward urea creatinine serum in male wistar strain with acute kidney failure. This research was conducted with Laboratory experiments, since it's directly tested to male wistar strain rats as an object of research.

METHODS

The research method is an experimental laboratory within 22 days of research, this research use 30 male wistar strain rats weighing 180-200 grams and 2-3 months of age divided into 3 (three) groups, namely the negative control group (only in give food and drink as usual), the positive control group (the kidneys were damaged by giving gentamicin 0.3 cc intra peritoneal per day) and the treatment group (the kidneys were damaged by giving gentamicin 0.3 cc intra peritoneal per day and given boiled water 2, 8 gr. Comfrey leaves in 150 cc of water and give as much as 2, 7 cc orally for 7 days). Wistar strain male rats in adaptation for 7 days in a state of 12 hours of light and 12 hours dark with highly expected that Wistar strain male rats do not show any change for $\pm 10\%$. Wistar strain male rats were divided into 10 individuals per group, namely 10 Wistar strain male rats for the negative control group, 10 Wistar strain male rats for the positive control group and 10 Wistar strain male rats for the treatment group.

The comfrey leaf (*symphytum officinale* L) used was taken from the Parongpong area, West Bandung, West Java with the characteristics of fibrous roots, long-shaped leaves, round like eggs and downy in all parts of the leaves, green, has purple flowers and has a small funnel shape. The sample used was only the leaf of comfrey plant (*symphytum officinale* L) taken in the morning around 06.00-07.00 WIB. Comfrey leaves (*symphytum officinale* L) used are which are still fresh and then washed using clean water and flowing afterwards in a dried way. The comfrey Leaf (*symphytum officinale* L) taken wa measured to 2.8 grams am and in boiled

water in a 200 cc to 150 cc of water. Then the cooking water was cooled down so that it could be given to the male wistar strain rats as much as 2.7 cc orally for 7 days when treated with the treatment group.

Way to make a male Wistar strain rats into a model of acute kidney failure is by giving gentamicin 0.3 cc Intra peritoneal for 7 days. Kidney function will decline or suffered damage on the mark with an increase in serum urea and creatinine levels after at induction gentamicin 0.3 cc of intra peritoneal every day for 7 days. Gentamicin is given to the positive control group and the treatment group with the same dose, namely gentamicin 0.3 cc intra peritoneal per day, so that differences can be obtained at the time of laboratory examination to find the levels of urea and creatinine serum.

Research Procedure

The object of research were 30 male Wistar rats adapted on day 1 to day 7 (12 hours dark and 12 hours light). Wistar strain male rats in divided into 3 groups with each group consisting of 10 male rat's wistar strain and the study lasted for 22 days, namely:

1. Negative control group (only given food and drink as usual)
2. Positive control group (kidney damaged by administration of 0.3 cc intra peritoneal gentamicin per day) and
3. The treatment group (in the kidneys damaged by administration of gentamicin 0.3 cc intra peritoneal per day as well as at the given therapy boiled water of 2.8 gram of comfrey leaves (*symphytum officinale L*) in 150 cc of water and give as much as 2, 7 cc orally for 7 days).

In the 8th to the 15th day, Male wistar strain rats grouped as the positive control group and the treatment group in damaged on the kidneys by inducing gentamicin as much as 0, 3 cc Intra peritoneal for 7 days to see changes in the amount of urea and creatinine serum in acute renal failure models. On the 15th day all groups were checked for urea and creatinine serum levels to obtain pre-therapeutic results. The treatment group in the given therapy by administering 2.8 gram of leaves comfrey decoction (*symphytum officinale L*) in 150 cc of water and give as much as 2, 7 cc orally for 7 days to obtain the result of changes in urea and creatinine serum levels. In the 22nd day the subjects was rechecked in order to find the level of urea and creatinine serum as a result of post-therapy, so that the difference amount of the urea and creatinine serum levels were obtained. The final data from pre and post therapy were analyzed

using the one-way ANOVA SPSS program version 24 test to compare the levels of urea and creatinine in an acute renal failure model toward male wistar strain rats as tested animal

RESULTS

Table 1. Results of examining the UREA and CREATININE level before and after inducing comfrey leaves (*symphytum officinale L*) decoction in tested animal's namely male Wistar strain rats.

Dependent Variable	(I) Group	(J) Group	Mean Difference (IJ)	Std. Error	Sig.
UREA_PRE	Negative Control	Positive Control	-41.02000 *	2.52371	.000
		Treatment	-44.80000 *	2.52371	.000
	Positive Control	Negative Control	41.02000 *	2.52371	.000
		Treatment	-3.78000	2.52371	.308
	Treatment	Negative Control	44.80000 *	2.52371	.000
		Positive Control	3.78000	2.52371	.308
UREA_POST	Negative Control	Positive Control	-137.03000 *	13.13514	.000
		Treatment	-18.55000	13.13514	.349
	Positive Control	Negative Control	137.03000 *	13.13514	.000
		Treatment	118.48000 *	13.13514	.000
	Treatment	Negative Control	18.55000	13.13514	.349
		Positive Control	-118.48000 *	13.13514	.000
CREATININE_PRE	Negative Control	Positive Control	-2.11800 *	.2010	.000
		Treatment	-2,398,000 *	.2010	.000
	Positive Control	Negative Control	2.11800 *	.2010	.000
		Treatment	-.28000	.2010	.376
	Treatment	Negative	2,398,000 *	.2010	.000
		Positive	.28000	.2010	.376
CREATININE_POST	Negative Control	Positive Control	-3,322 **	.22929	.000
		Treatment	-.97800 *	.22929	.001
	Positive Control	Negative Control	3.32200 *	.22929	.000
		Treatment	2,34400 *	.22929	.000
	Treatment	Negative Control	.97800 *	.22929	.001
		Positive Control	-2,344 **	.22929	.000

DISCUSSION

In this study, two measurements of serum UREA and CREATININE were taken, before and after the therapy. Looking at the data from the results of the one way ANOVA SPSS version 24 test that is used to compare creatinine urea levels in acute kidney failure models.

Tabael 2. **The results of the examination of urea serum level before the therapy of comfrey leaves (*symphytum officinale L*) decoction in wistar strain male rats.**

Dependent Variable	Group I	Group J	Mean (IJ)	Std.Error	Sig
UREA_PRE	Negative Control	Positive Control	-41.02000 *	252,371	.000
		Treatment	-44.80000 *	252,371	.000
	Positive Control	Negative Control	41.02000 *	252,371	.000
		Treatment	-378,000	252,371	.308
	Treatment	Negative Control	44.80000 *	252,371	.000
		Positive Control	378,000	252,371	.308

From the analysis of urea serum levels before administration of therapy, the negative control group was compared with the positive control group and the treatment show a significant difference ($P < 0.05$). This is happen due to the induction effect of 0,3cc gentamicin intra peritoneal per day which increase the level urea serum level of male rats with acute renal failure model. There is no significant difference between the treatment group and the positive control group ($P = 0.308$), and this is because both groups experienced kidney damage as a result in the induction of gentamicin 0, 3 cc intra peritonial for 7 days and gentamicin can make hydroptic degeneration that causes necrosis renal tubules so that the level of urea serum rises. (Siahaan, G. S et al, 2016)

Table 3. **The results of the examination of urea serum level after the therapy of comfrey leaves (*symphytum officinale L*) decoction in wistar strain male rats.**

Dependent Variable	Group I	Group J	Mean (IJ)	Std.Error	Sig
UREA_POST	Negative Control	Positive Control	-137.03000 *	1,313,514	.000
		Treatment	-1,855,000	1,313,514	349

	Positive Control	Negative Control	137.03000 *	1,313,514	.000
		Treatment	118.48000 *	1,313,514	.000
	Treatment	Negative Control	1,855,000	1,313,514	349
		Positive Control	-118.48000 *	1,313,514	.000

The results of the analysis of urea serum levels after giving comfrey leaves (*symphytum officinale L*) decoction shows there is a significant difference between the negative control group and the positive control group ($P < 0.05$). This is because the positive control group experienced kidney damage which is characterized by an increase in ureum serum levels due to the administration of 0.3 cc intra peritoneal gentamicin per day, so the results approach the normal rate of urea serum levels in the negative control group. According to research from *Abbas et al., (2017)* gentamicin was proven to be a member of amino glycosides which causes nephrotoxicity. There was a significant difference between the positive control group and the treatment group ($P < 0.05$). This can occur because of the effect of giving 150 cc from 2.8 grams of boiled comfrey leaves (*symphytum officinale L*) as much as 2.7 cc orally for 7 days to the treatment group. There was no significant difference between the treatment group and negative control group ($P = 0.349$), due to the results of urea serum level of treatment group reach normal rate to the negative group that became the standard.

Table 4. Test results creatinine level before the therapy of comfrey leaves decoction (*symphytum officinale L*) in Wistar strain male rats as tested animals.

Dependent Variable	Group I	Group J	Mean (IJ)	Std.Error	Sig
CREATININE_PRE	Negative Control	Positive Control	-2.11800 *	.2010	.000
		Treatment	-2,398,000 *	.2010	.000
	Positive Control	Negative Control	2.11800 *	.2010	.000
		Treatment	-.28000	.2010	.376
	Treatment	Negative Control	2,398,000 *	.2010	.000
		Positive Control	.28000	.2010	.376

The results of analysis of creatinine serum levels before being given boiled water treatment of comfrey leaves (*symphytum officinale L*) in the negative control group compared with the positive control group and the treatment group there shows a significant differences (P

<0.05). The results of the comparison of the positive control group with the treatment group showed no significant difference ($P = 0.376$) because both groups experienced kidney damage which was marked by an increase in serum creatinine levels due to administration of 0.3 cc intra peritoneal gentamicin per day. The results of a study by Rajak, Z.F.W., Loho, L., Lintong, P, (2016) showed that administration of intra-peritoneal gentamicin with a toxic dose of 0.3 cc every day for 7 days showed acute tubular necrosis (NTA).

Table 5. The results of the KREATININ tilapia examination after the administration of komfrey (*symphytum officinale L*) decoction of boiled water to the wistar strain male rats.

Dependent Variable	Group I	Group J	Mean (IJ)	Std.Error	Sig
CREATININE_POST	Negative Control	Positive Control	-3,322 **	.22929	.000
		Treatment	-.97800 *	.22929	.001
	Positive Control	Negative Control	3.32200 *	.22929	.000
		Treatment	2,34400 *	.22929	.000
	Treatment	Negative Control	.97800 *	.22929	.001
		Positive Control	-2,344 **	.22929	.000

From the data above can be concluded that after administering water comfrey leaves (*symphytum officinale L*) decoction in the negative control group in comparison with the positive control group and treatment group shows significant differences ($P < 0.05$). This can occur because of the effects of giving 150 cc from 2.8 grams of comfrey leaves (*symphytum officinale L*) decoction as much as 2.7 cc orally for 7 days. The treatment group compared with the negative control group had a significant difference ($p < 0.001$), after having been given a therapy of comfrey leaf (*symphytum officinale L*) decoction as much as 2.8 grams in 150 cc of water and given as much as 2.7 cc per oral for 7 days which has the effect of lowering serum creatinine levels. But the value is still significantly different from the negative control group as the standard creatinine normal value.

Conclusions And Suggestions

Based on the results of the research data, it can be concluded that administration of gentamicin at a dose of 0.3 cc intra peritoneal per day for 7 days showed an increase in urea and creatinine serum levels in male wistar strain rats against acute renal failure models. The comfrey leaves (*symphytum officinale L*) has an effect on the decrease in creatinine urea serum levels of male rats in the acute renal wistar strain model with proven value ($P < 0.05$).

From the results of this study, advice is still needed to modify the dose and duration of therapy of comfrey leaves (*symphytum officinale L*)

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