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EFFECTS OF NATURAL EXTRACT OF CELERY LEAVES ON THE KIDNEYS OF WHITE RATS (*Rattus novergicus*) AFTER ASPIRIN INDUCTION

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Abstract

Herbal plants can be used as a treatment option, including the treatment of kidney disease. The administration of herbal remedies such as celery is a more natural and safe treatment healing alternative. The study aims to determine the effect of celery extract in repairing the damage to the kidney cells of aspirin-induced white mice. This study used a completely randomized design (CRD) consisting of 5 groups with 3 replications: K- (aspirin 12.6 mg/kg BW), K+ (feed normal), P1 (celery extract 200 mg/kg BW + aspirin 12.6 mg/kg BW), P2 (celery extract 100mg/kg BW + aspirin 12.6 mg/kg BW) and P3 (celery extract 50 mg/kg BW) + aspirin 12.6 mg/kg BW). From the results of observations on kidney histology of rats after giving aspirin, it is known that there is damage to the nucleus of cells undergoing pyknosis and swelling of the glomerulus, which is characterized by narrowing of the Bowman's space. This suggests that the celery extract at a stratified dose may affect the histopathological kidney of aspirin-induced mice.

Keywords: *Aspirin, Celery (Apium graveolens L Sylvester), Kidney*

INTRODUCTION

Aspirin is a drug in the salicylate group that is widely used in the treatment of mild to moderate pain, such as headaches, toothaches, muscle aches, and joint pains in arthritis, and is also used to reduce fever (Pradhan et al., 1993). However, on the other hand, aspirin also has several side effects that are risky to the body, including overdose, which causes tinnitus, abdominal pain, hypokalemia, hypoglycemia, pyrexia, hyperventilation, dysrhythmia, hypotension, hallucinations, and even kidney failure (Bjarnason et al., 2018; Cahill et al., 2017; Kennedy et al., 2016).

Kidneys are vital organs that are very susceptible to the toxic effects of drugs and chemicals (Schreuder et al., 2011). The kidney is also an

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obligatory excretory pathway for most drugs so that the inappropriate use of the drug can lead to renal insufficiency resulting in accumulation and increased concentration in the renal tubular fluid. (Wilson, 2006). Continuous use of drugs such as aspirin can cause kidney damage (Segal et al., 2006).

Kidney disorders due to aspirin occur due to inhibition of renal prostaglandin biosynthesis (PGE2) in renal physiological processes (Li et al., 2018). Renal disorders due to aspirin use include azotemia with oliguria which can progress progressively to papillary necrosis syndrome, tubular necrosis I, inflammation of the renal interstitial tissue, and acute renal failure (Yunita et al., 2020).

Pharmacological therapy can treat kidney damage using acetazolamide, bumetanide, chlorothiazide, hydrochlorothiazide, and chlorthalidone drugs. However, its use is feared to have side effects that are risky for the body. Therefore, there is a need for pharmacological therapy that uses natural ingredients from plants to carry out therapy effectively and safely.

Herbal plants have many benefits, one of which is celery. The content of flavonoids in celery can produce natural antioxidants that can prevent atherosclerosis by inhibiting oxidative processes and reducing the effects of free radicals in the body.

The protective effect of celery on kidney damage caused by aspirin needs to be proven through preclinical testing by observing the histology of rat kidneys. The results of this study are expected to provide information for the public about the use of celery as a natural and safe kidney therapy ingredient.

MATERIALS AND METHODS

Animals and Dosing Preparation Test

A total of 15 rats were grouped into five cages. The number of rats needed was 3 for each group. Make celery extract by grinding using a mortar until smooth. The resulting celery extract was filtered and added with 1 ml of distilled water based on a predetermined dose for each treatment. Celery extract produced from 500 grams of celery is 800 ml/500g=1,6 ml/g. The following is the treatment used in this study:

1). P1: 50 mg/kg body weight (BW) = 0,05 g x 1,6 ml/g =0,08 ml
BB 200 g = 0,2 kg x 0,08 ml = 0,016 ml/kg BW + 1 ml aquades
2). P2: 100 mg/kg BW = 0,1g x 1,6 ml/g = 0,16 ml
BW 200 g = 0,2 kg x 0,16 ml = 0,032 ml/kg BW + 1 ml aquades
3). P3: 200 mg/kg BW = 0,2 g x 1,6 ml/g = 0,32 ml
BW 200 g = 0,2 kg x 0,32 ml = 0,064 ml/kg BW + 1 ml aquades

Oral giving of Celery Extract

After the rats were induced by aspirin for seven days, they were given celery extract. Celery extract was given in different doses for each treatment, namely: P1 (200 mg/kg BW), P2 (100 mg/kg BW), and P3 (50 mg/kg BW) according to 200 grams of rats body weight. 4 ml volume of rat stomach and 1 ml volume of distilled water.

Data analysis

Histological observations were

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carried out by looking at the macroscopic and microscopic images, which were analyzed descriptively. Microscopic data were analyzed by calculating five fields of view per cell. For each visual field, the percentage of the number of damaged cells was calculated to the total number of cells. The data obtained were analyzed using ANOVA (Analysis of Variance), with the Duncans Multiple Range Test (DMRT) further tested with the SPSS for Windows program at a significant level of 5% (Mattjik & Sumertajaya 2002). The percentage of damage is calculated using the formula and parameters:

$$Percentage\ cell\ damage\ (\%) = \frac{Percentage\ cell\ damage\ (\%)}{Total\ Cell\ Count}$$

RESULTS AND DISCUSSION

Testing of the protective effect of celery leaf extract was carried out by observing and calculating the damage to the kidneys in the histology of the kidney of white rats (Figure 1). Observing microscopic kidney preparations was carried out using 400x magnification with five fields of view.

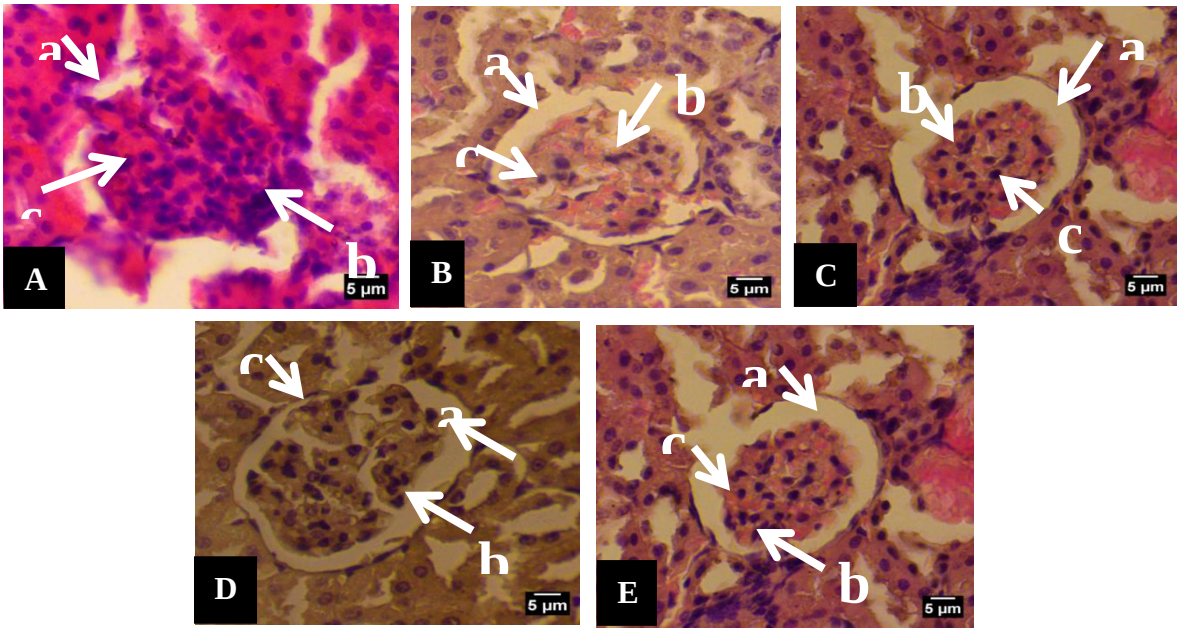

Figure 1. Microscopic structure of the Bowmani capsule of the White Rat (Rattus norvegicus). Hematoxylin-Eosin staining. 400x magnification. Description : A: Negative Control; B: Positive Control; C: Treatment 1; D: Treatment 2; E: Treatment 3.
a: Bowmen's space, b: necrosis c: pyknosis

The percentage and scoring of renal glomerular damage can be seen in Table 1, which is determined based on the evaluation of the renal tubular and glomerular evaluation parameters. The results of the ANOVA test on kidney glomerular cell damage in white rats obtained a P-value of 0.000. P-value

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<0.05 means that there is a significant difference in the percentage of kidney damage in white rats in each treatment. DMRT showed a significant difference between the administration of celery extract P1, P2, and P3 with a ratio of P0. The damage value of K+ is lower than that of P1, P2, and P3.

The scoring of glomerular cell damage in white rats shows that the damage value is 25-50%. In K- and P1, the value of glomerular cell damage they experience is 50-75%, while in P2 and P3, the value of glomerular cell damage they experience is 25-50%.

Table 1. Percentage and scoring damage to kidney glomerulus cells in white rats after DMRT test

Treatment	Damage Average (%)	Damaged Score
K- (aspirin 12,6)	$69.68 \pm 1,68^{e}$	0
K+ (Normal feed)	$25,21 \pm 1,50^{a}$	0
P1 (50mg/Kg BW)	$58,51 \pm 5,00^{d}$	0
P2 (100mg/Kg BW)	$44,58 \pm 1,10^{c}$	0
P3 (200mg/Kg BW)	$31,69 \pm 17,09^{b}$	0

Notes: K-: control 0, K+: positive control, P1: Dosage 1, P2: *Nanas Bongsai* Dosage 2, P3: *Nanas Bongsai* Dosage 3. Numbers followed by different alphabet at same coloumn is significantly different at α 5%. Damage score (0) based on Baldatina (2008).

The damage value of 0% in the positive control was caused by external factors, such as less than ideal cage conditions, less varied feeding and drinking, stress factors for rats, and the influence of other substances or diseases. The internal factors such as resistance and susceptibility of rats during acclimatization can affect the results. The increased activity of cytosolic enzymes can also cause this situation due to stress in white rats, which impacts the kidneys and heart (Sanchez et.al., 2002).

Figure 1.A shows the histological structure of the kidney of a negative control rat with aspirin at a dose of 1.6 ml. Based on observations, renal histology preparations in negative controls found large amounts of glomerular damage in the form of pyknotic cell nuclei. The damage that occurs undergoes a change in the shape of the Bowman's space which is narrowed due to the fusion of visceral epithelium and visceral epithelium. The largest percentage of damage was 69.68± 〖1.68〗 ^e (Table 1). Aspirin 0.1 mg/20 g BW with fruit extracts of Red Tomato (*Lycopersicum esculentum*) and Purple Tomato (*Lycopersicum esculentum* var *indigo rose*) cause kidney damage such as tubular necrosis because of their toxic properties if used in excessive amounts (Sicily et al., 2016). Aspirin can cause increased blood flow from the heart to the kidneys. This condition can cause the flow of various drugs and chemicals in the systemic circulation to be delivered to the kidneys in large quantities.

In Figure 1B, kidney histology preparations of positive control white rats showed some damage to the glomerulus in the form of cell nuclei experiencing pyknosis and necrosis, but still in a small percentage. Parts of the visceral epithelium and the pars parietal epithelium are still clearly

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visible, and Bowman's space covers the glomerulus.

Figure 1C shows the histological structure of the kidney of white rats with the administration of celery extract at a dose of 50 ml/kg BW found some damage in the form of pyknotic nuclei. Damage that occurs does not affect the shape of the glomerulus. This was indicated by the histological preparations of the Bowman's chamber white rat kidney not experiencing narrowing.

The visceral and parietal epithelium can still be seen clearly (Mayori et al., 2013). The damage in the glomerular cell nucleus is still a mild percentage. Research by Leto (2019) induced rats with aspirin and thistle leaf extract can reduce gastric necrosis, degeneration, and inflammation in the kidneys.

Figure 1D shows the histology of white rat kidney with celery extract given at a 100 ml/kg BW dose. Based on the observation of giving celery extract to the kidney histology of white rats, it appears that only some damage to the renal glomerular cells was found. The damage was found in the form of the core experiencing pyknosis. Damage occurred in an average percentage (Table 1. This is indicated by the Bowman's space in the glomerulus, which is still clearly visible. The pars parietal and visceral epithelium has narrowed, so they cannot be distinguished. The difference in the percentage of glomerular cell damage that occurs due to giving celery extract from each treatment can be caused by differences in the dose in each treatment. The difference in dose, of course, has a different effect or effect on the kidneys of white rats. The damage seen in histological preparations in the form of glomerular cell nuclei undergoes necrosis, namely the nuclei appear denser and dark in color. However, the damage did not affect changes in the structure of the kidney glomerulus of white rats. Bowman's space surrounding the glomerulus is still clearly visible, like a bowl marked by the visceral and parietal epithelium that is still clearly visible. Sulistyowati et al. (2013) and Fitmawati et al. (2020) stated that a normal glomerulus is characterized by Bowman's capsule, which completely covers it and looks like a bowl.

Figure (1E) shows the histology of a white rat kidney given celery extract at a 200 ml/kg BW dose. Based on observations, celery extract at a dose of 200ml/kg BW has a protective effect on the kidneys because its antioxidant content can inhibit the production of the xanthine oxidase enzyme (Yulian, 2014). Kidney histology preparation in treatment 1 (figure 1C) showed some damage found in the glomerulus in the form of pyknotic nuclei but only in small amounts. Kidney histology preparations for control are still in normal condition. It is characterized by the appearance of a rounded glomerular nucleus. In addition, the visceral and parietal epithelium are visible, and Bowman's space also covers the glomerulus. This can occur due to factors affecting the study results, such as less than ideal cage conditions, less varied feeding and drinking, stress factors for rats, the influence of other substances or diseases, and other internal factors such as resistance and susceptibility of rats (Suhita et al., 2013; Susilo & Ismail, 2014).

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The damage seen in histological preparations in the form of cell nuclei from glomerular cells undergoes necrosis in pyknosis. The nucleus looks denser and dark in color. Sulistyowati et al. (2013) stated that a normal glomerulus is characterized by Bowman's capsule covering the whole and looking like a bowl. The normal glomerulus has a polyhedral shape. The spherical nucleus is inside the cell. The cytoplasm inside the cell looks clear. The par visceral epithelium and pars parietal epithelium are still clearly visible (Septiana & Kurniati, 2009).

The damage seen in histological preparations in the form of cell nuclei from glomerular cells undergoes necrosis in pyknosis. The nucleus looks denser and dark in color. Sulistyowati et al. (2013) stated that a normal glomerulus is characterized by Bowman's capsule covering the whole and looking like a bowl. The normal glomerulus has a polyhedral shape. The spherical nucleus is inside the cell. The cytoplasm inside the cell looks clear. The par visceral epithelium and pars parietal epithelium are still clearly visible.

The kidney structure changes the glomerulus caused by frequent exposure to foreign substances and materials that enter the body. Assiam et al. (2014) stated that the narrowing that occurs in the Bowman's space is caused by an enlargement of the glomerulus, which is characterized by an increase in the volume of the glomerulus. The glomerulus is more susceptible to toxins and circulating than other tissues in the kidney, so damage to the glomerulus will interfere with the function of filtrate production and filtrate control.

CONCLUSION

Based on the results of research carried out using different serial doses, it can be concluded that the highest percentage of damage occurred in negative controls, namely 69.68 ± 1.68, and the lowest percentage of damage occurred in positive controls, 25.21 ± 1.50. The percentage of damage given celery extract at a dose (200mg/kg BW) had a lower percentage of glomerular cell damage than the administration of celery extract in treatment 3 with a dose (50 mg/kg BW) glomerular cell damage that occurred was 58.51±5.00. From the results of observations on kidney histology of rats after giving aspirin, it is known that there is damage to the nucleus of cells undergoing pyknosis and swelling of the glomerulus, which is characterized by narrowing of the Bowman's space. It is necessary to do further research on toxicological tests and the effect of giving celery extract using a more optimal dose to know the dose limit for its use.

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