PROTECTIVE EFFECT OF JAVANESE BARK EXTRACTS (LANNEA COROMANDELICA) ON MALONDIALDEHYDE LEVELS (MDA), UREUM LEVELS, SERUM CREATININE AND KIDNEY HISTOPATHOLOGY IN MONOSODIUM GLUTAMATE (MSG) INDUCED MALE WISTAR RATS)

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Abstract

Monosodium glutamate is associated with kidney toxicity because it has normal glutamate levels. Lannea coromandelica extract contains secondary metabolites such as alcohols, steroids, triterpenoids, phenolics, flavonoids, tannins, and saponins. This compound is a group of bioactive compounds that produce antioxidant, anti-inflammatory, antibacterial, anticancer and immunomodulatory activities.There are effects of Monosodium Glutamate (MSG) on organ damage, increase in cardiovascular risk factors and result in oxidative stress due to ROS. To prevent the unwanted effects of free radicals, antioxidants are needed. One of the plants that can be used as a natural medicine and is rich in antioxidants is the Java Wood plant (Lannea coromandelica). This study aims to determine the protective effect of Lannea Coromandelica extract on MDA, urea, and serum creatinine levels and renal histology induced by MSG. Rats were divided into five treatment groups (KS = 0 mg, KN = 3 ml/gBB, KPA = 250 mg/KgBB, KPB = 500 mg/KgBB, and KPC 750 mg/KgBB), each group consisted of 6 rats. Administration of MSG was carried out for 28 days, then examination of serum MDA, urea and creatinine levels and renal histology. Results of MDA levels, urea, serum creatinine were analyzed using one way ANOVA test while the percentage of histological damage was analyzed using the Kruskal-Wallis test. The results showed that there were significant differences in blood levels of urea and creatinine ($p<0.05$), while blood MDA levels did not show significant differences ($p>0.05$).

Keywords:Monosodium Gluatamate, Histology, MDA, Ureum, Creatinine

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1. Introduction

One of the food additives functions as a flavor enhancer. There are two types of flavoring, namely natural flavoring and synthetic flavoring. One of the famous synthetic flavor enhancers is monosodium glutamate or commonly abbreviated as MSG. Monosodium glutamate or MSG is a food additive used to produce a better taste in cooking (Suryanto, 2015). Monosodium Glutamate (MSG) is a sodium salt of one of the non-essential amino acids glutamic acid, which will function as a flavor enhancer and flavor enhancer when added to food, especially foods containing protein. The composition of the MSG compound is 78% glutamate, 12% sodium and 10% water. MSG when dissolved or saliva will dissociate into free salts and anion forms of glutamic acid (Sukmaningsih et al., 2011).

Monosodium glutamate is often used as a flavoring agent, such as mushrooms and tomatoes which have normal levels of glutamate. The human body also produces glutamate and plays an important role in normal body functions (Yonata, 2016). Monosodium glutamate is widely used around the world, consumption of MSG in the world varies greatly, for example in Indonesia the average consumption of MSG is 0.6 gr/day, in Taiwan it is 3 gr/day, in Korea 2.3 gr/day, in Japan 1.6 gr/day, in India 0.4 gr/day, and in America 0.35 gr/day. China, which is a country that consumes and produces the most MSG in the world, consumes 52% - 57% more MSG than the total consumption in the world (Elpiana, 2011). In 1995 MSG was classified as a safe food additive such as salt, vinegar and baking powder. but its use is limited to 120 mg/kg body weight per day by the FDA and WHO (Yonata, 2016). (Food and Drug Administration, 2012) states that the average daily consumption in adults is around 13 grams of glutamate from protein in food, while the addition of MSG is around 0.55 grams. A survey conducted by the Association of Indonesian Monosodium Glutamate and Glutamate Acid Factories estimates that consumption of MSG in 2004 reached 1.53 grams/capita/day in Indonesia (Kurtanty et al., 2019).

Glutamate receptors are found in various organs, one of which is the kidney. Glutamate receptors trigger a variety of different responses and can trigger cell death, so consumption of Monosodium Glutamate can potentially damage the kidney structure. Monosodium Glutamate can also cause damage to the kidneys through the mechanism of oxidative stress. Oxidative stress is characterized by decreased antioxidant enzymes, increased lipid peroxidase and can cause tubulo-interstitial fibrosis in the kidneys (Sharma, 2015). Administration of monosodium glutamate can result in functional changes in the kidneys due to the presence of glutamate receptors (Mathieu et al., 2016). Administration of MSG can also cause an increase in plasma glutamate levels followed by an increase in glutamate levels in the filtrate. The glutamate is distributed to the renal cortex via arterial branches to the glomerulus which are attached to the tubules. The function of the glomerulus is as a filter and the tubules as a place to collect waste materials and excess water (Savira, 2021). Increased ROS causes kidney damage. Kidney damage causes impaired kidney function, namely the excretion of waste products of the body's metabolism, such as urea and creatinine. Impaired excretion of urea and creatinine through the urine causes an increase in the levels of these two substances in the serum (Sharma, 2015). such as urea and creatinine. Impaired excretion of urea and creatinine through the urine causes an increase in the levels of these two substances in the serum (Sharma, 2015). such as urea and creatinine. Impaired excretion of urea and creatinine through the urine causes an increase in the levels of these two substances in the serum (Sharma, 2015).

Java wood plants are known to contain secondary metabolites such as alcohol, steroids, triterpenoids, phenolics, flavonoids, tannins, and saponins. This compound is a

group of bioactive compounds that produce antioxidant, anti-inflammatory, antibacterial, anticancer and immunomodulatory activities (Anggreini et al., 2018). Natural Research (2012) has reported that methanol extraction of Javanese bark has biological activities such as antibacterial and antioxidant against Candida albicans. Lannea coromandelica has not been widely studied in Indonesia, most research on this plant has been carried out in India. Lannea coromandelica has several properties, including: curing sprains, bruises, kidney disease, dysentery, canker sores.

Phytochemical tests showed that the ethanol extract of Java wood contained flavonoids, steroids, terpenoids, saponins, tannins and phenolics. Research on the toxicity of medicinal plants in Indonesia has not been widely carried out, on the other hand, many people have used medicinal plants. (Sumardika, 2012).

Based on the descriptions above, it is known that the effects of excessive MSG can initiate the occurrence of free radicals and cause various damage to kidney tissue. Due to the increase in free radicals in the body, antioxidants are needed to counteract these free radicals. therefore the Lannea coromandelica plant might be an alternative to prevent damage to kidney tissue, this is because lannea coromandelica contains high antioxidant compounds. so it is on this basis that researchers are interested in conducting research on the protective effect of Lannea coromandelica on urea and creatinine levels (kidney function) in male Wistar rats induced by MSG.

2. Materials and methods

Monosodium Glutamate (MSG) Preparation

The monosodium glutamate used was obtained from the free market under the trademark Ajinomoto produced by PT Ajinomoto Indonesia, MSG is in the form of white crystalline powder containing pure monosodium glutamate. The daily dose given to rats is 3 mg/gBW rats.

Preparation of Lannea coromandelica stem bark extraction

*Lannea coromandelica*obtained from Pinrang District, South Sulawesi Province, Indonesia.A sample of 100 g is weighed and put into the reflux device. Then 96% ethanol was added until the sample was submerged. Reflux process is carried out for 3-4 hours. After that it is filtered, and the filtered results are stored to evaporate the solvent. The filtered dregs are then refluxed again for 3-4 hours.

Animal Preparation

Twenty-five male Wistar rats weighing between 180 and 300 grams and ± 3 months old were adapted for 7 days in laboratory animals before the experiment started. During this stage, all rats were given standard feed and drinking water ad libitum, the rats were housed individually in their respective cages.

Experimental Protocol

Twenty five male Wistar rats were divided into five groups, the healthy group was given standard feed, the negative group was given MSG 3 mg/grBW, the treatment group 1 was given MSG and Lannea coromandelica extract 250 mg/kgBW, the treatment group 2 was given MSG and Lannea coromandelica extract. 500 mg/kg BW while the treatment group 3 was given MSG and Lannea coromandelica extract 750 mg/kg BW for 28 days. Lannea coromandelica bark extract isgiven 1 hour before administration of MSG.In this study MSG and bark extract of Lannea coromandelica were given to Wistar rats via the gavage method, namely by giving it orally using a spin. Treatment of rats was carried out according to laboratory animal care standards, and all procedures involving animals were approved by the Animal Ethics Committee of the Hasanuddin University Faculty of Medicine.

Enzyme Level Analysis

Serum collection was carried out on rats and then sacrificed on ± 14 days after body weight measurement. Rats were totally anesthetized using ether and then the rats were dissected. Furthermore, blood samples were taken with cardiac puncture as much as ± 3 mL. The blood sample was put into the ETDA tube and then centrifuged at 6000rpm for 15 minutes or until complete separation of serum from blood cells occurred. The serum sample obtained was transferred to a 1.5 mL micro tube and stored at -20°C until analyzed. Serum urea, creatinine levels were measured using the diagnostic kit for Humalyzer 3000 according to the kit instructions. Unlike the analysis of MDA levels, rat kidney tissue was weighed as much as 0. 4 grams then added ± 2000 µl of PBS and crushed until smooth then centrifuged at 3000 rpm for 10 minutes. The supernatant was taken using a micropipette as much as 500 µl then put in a vacutainer tube then added 10% TCA and 1% TBA 1000 µl each and homogenized. The mouth of the tube was tightly closed with aluminum foil. Then heated in a water bath at room temperature. Then it was centrifuged twice at 3000 rpm for 10 minutes. The supernatant was taken and put into a vacutainer tube and then the absorbance was measured using a UV-Vis spectrophotometer at a wavelength of 532 nm. The mouth of the tube was tightly closed with aluminum foil. Then heated in a water bath at room temperature. Then it was centrifuged twice at 3000 rpm for 10 minutes. The supernatant was taken and put into a vacutainer tube and then the absorbance was measured using a UV-Vis spectrophotometer at a wavelength of 532 nm. The mouth of the tube was tightly closed with aluminum foil. Then heated in a water bath at room temperature. Then it was centrifuged twice at 3000 rpm for 10 minutes. The supernatant was taken and put into a vacutainer tube and then the absorbance was measured using a UV-Vis spectrophotometer at a wavelength of 532 nm.

Histopathological examination

Rat kidney organs were washed with saline solution, then fixed with 10% formalin. The fixed tissue was then placed in a paraffin block and cut into sections 5 µm thick. Each section was stained using haematoxylin and eosin (H&E). Histopathological observations were carried out using a microscope. On microscopic observation, kidney damage is observed and assessed based on the score of the degree of damage, includinghypertension, necrosis, degeneration, infiltration of inflammatory cells, glomeruli, and renal tubules.

Statistical analysis was performed using IBM SPSS 22 software. Data distribution was examined using the Shapiro Wilk test to determine whether the data was normally distributed or not. If the data is normally distributed then the analysis is continued with ANOVA, whereas if the data is not normally distributed then the Mann-Whitney test is used. The difference is considered significant if the p value <0.05.

3. Results and Discussion

The results of the study used MSG as an inducer of kidney damage to see the protective effect of Lannea coromandelica extract on male Wistar rats. The samples used were serum and kidney organs from male Wistar rats and maintained during March 2023. The number of samples that met the criteria was 25 samples. Furthermore, parameters of urea, creatinine, MDA and histopathology were used to see the effectiveness of Lannea coromandelica extract.

Results Rat urea levels

In Figure 1 it can be seen that the healthy control group (KS) has urea levels, namely the average15.6000 ± 1.77764 mg/dl. then the negative control group (N) which was only given MSG increased significantly from the healthy control group (KS) with an average of 39.20 ± 6.09 mg/dl. then in the experimental group 1 (KPA) which was given MSG and

Java wood extract at a dose of 250mg/KgBW had an average urea level of 32.00 ± 1.22 mg/dl. whereas in the treatment group 2 (KPB) which was given MSG and Java wood extract at a dose of 500 mg/Kg, the average urea level was lower compared to the other groups, namely 25.50 ± 6.55 mg/dl while in the treatment group 3 (KPC) which was given MSG and Java wood extract at a dose of 750 mg/Kg BW had a urea level of 31.60 ± 5.31 mg/dl.

These results indicate that mice given MSG could increase Ureum levels in experimental animals and rats given Java wood extract had a significant effect on decreasing Ureum levels compared to the healthy control group (without MSG and Java wood extract) which had the lowest levels.

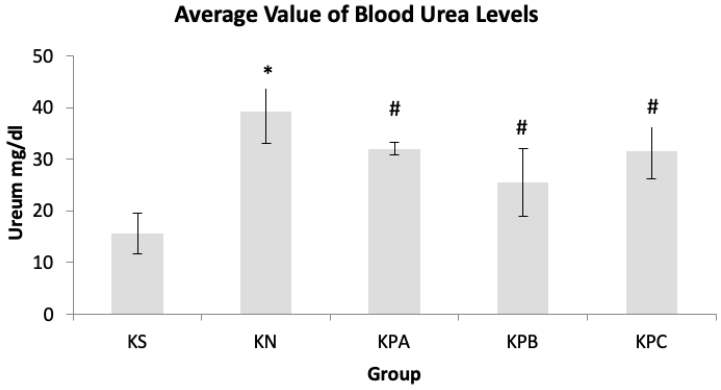

Figure 1. Diagram showing the average value of blood urea levels in each group. Data are presented as mean ± SD* indicating significantly different values from healthy controls (KS). The # symbol indicates a significantly different value to the negative control (KN)

Results of rat creatinine levels

Comparison of creatinine levels in each group can be seen in Figure 2, above shows that the healthy control group (KS) has creatinine levels with an average of 0.3280 ± 0.2864 mg/dl. Then the negative control group (KN) which was only given MSG increased significantly with an average of 0.65 ± 0.11 mg/dl. Then the treatment group 1 (KPA) which was given Java wood extract at a dose of 250 mg/KgBW had an average creatinine level of 0.57 ± 0.44 mg/dl. whereas in the treatment group 2 (KPB) which was given Java wood extract at a dose of 500 mg/kg, it was slightly lower than the previous experimental group (KPA) with an average creatinine level of 0.55 ± 1.03 mg/dl while the treatment group was the highest of the two the previous treatment group (KPA and KPB) which was given Java wood extract at a dose of 750 mg/KgBW had an average creatinine level of 0.57 ± 0.

These results indicate that rats given MSG could increase creatinine levels in experimental animals and rats given java wood extract had a significant effect on decreasing creatinine levels compared to the healthy control group (without MSG and java wood extract) which had the lowest levels.

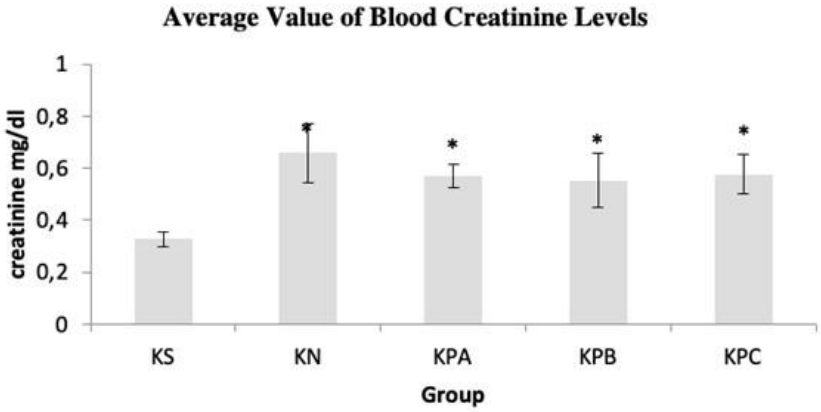

Figure 2. Diagram showing the average value of blood creatinine levels in each group. Data are presented as mean ± SD* indicating significantly different values to healthy controls (KS).

Results of Malondialdehyde (MDA) Levels

Comparison of the MDA levels of the kidneys in each group can be seen in Figure 3.

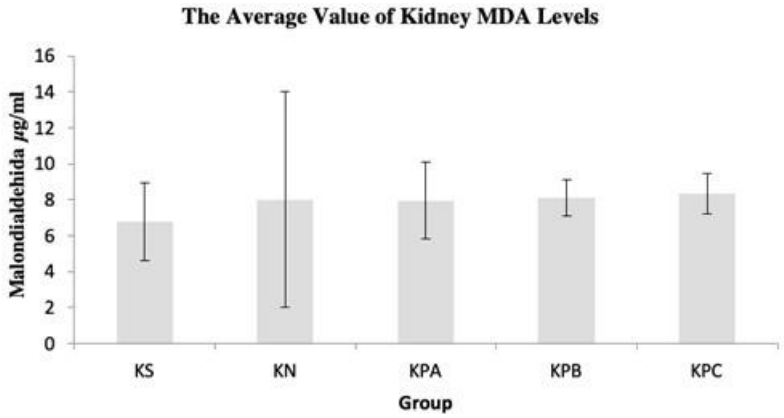

Figure 3. Diagram of average kidney MDA levels

Renal histopathology

The following is a histopathological picture of the kidneys based on the parameters of damage in each group

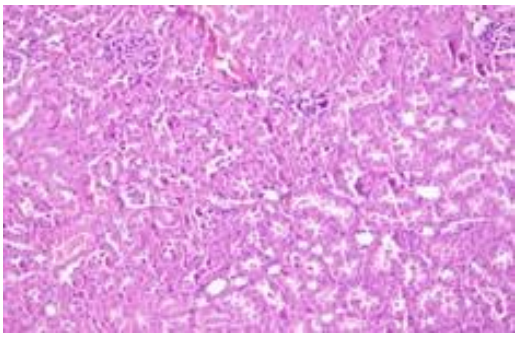

Figure 4. Renal histopathology in the healthy control group. (KS) Did not show any damage

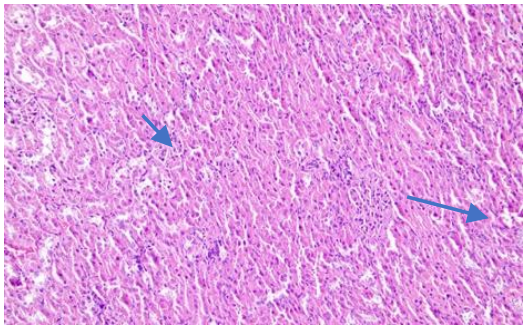

Figure 5. Renal histopathology in the negative control group (KN). The image shows the presence of hydrophilic deg (DE), and inflammatory cell infiltration with severe degree of damage:50% of the entire visual field. (Damage degree 3)

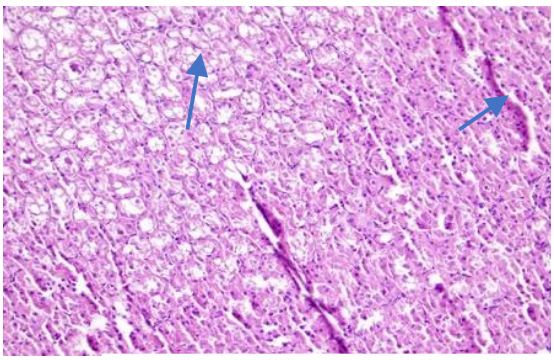

Figure 6. Kidney histopathology in treatment group A (KPA). This picture shows the presence of hydrophilic deg (DE) with a moderate degree of damage: visible 25% of the entire visual field (degree of damage 3)

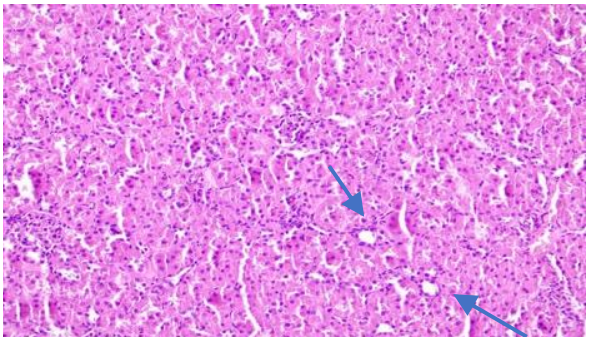

Figure 7. Renal histopathology in treatment group B (KPB). This picture shows the distance between cells with a mild degree of damage: cell damage reaches <25% of the entire field of view

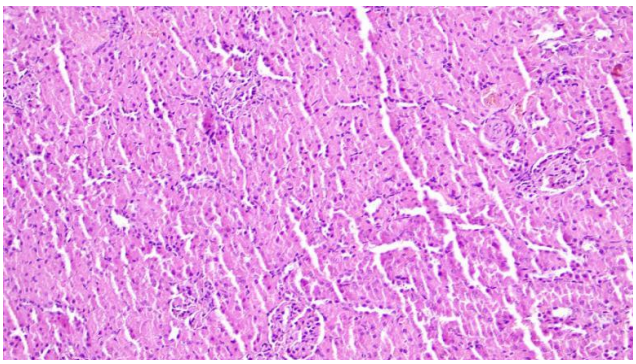

Figure 8. Histopathological picture of the kidney in treatment group C (KPC). This picture shows inflammatory cell infiltration with 0/normal damage

From the five pictures of kidney histology observations, it shows that in figure 4, the healthy control group (KS) does not show any damage (normal). Then Figure 5 shows the histology of the negative control group which was only given MSG without giving Lannea coromandelica extract first. Histopathological analysis showed severe inflammation, characterized by some inflammation on the hydrophilic deg, and inflammatory cells. The degree of damage in this group is severe (3), namely 50% of the entire visual field. In contrast to Figure 6, the MSG-induced group received lannea coromandelica extract 250 mg/kg for 28 days. Meanwhile, Figure 7 represents the MSG-induced group and received lannea coromandelica extract 500 mg/kgbb for 28 days. Then figure 8 was the MSG-induced group and received lannea coromandelica extract 750 mg/kgbb for 28 days. In all three groups, histopathological analysis showed mild-moderate damage, marked by hydrophilic deg, inflammatory cell infiltration, and also visible distances between cells. The degree of damage was seen in the three groups, namely the degree of damage 1 and 2 (KPA and KPC).

Discussion

In this study, administration of MSG and Java bark extract (*Lannea coromandelica*) was given to experimental animals at doses of 250 mg/KgBW, 500 mg/KgBW, and 750 mg/KgBW. Induction of renal fibrosis was carried out by administering MSG at a dose of 3 mg/gBB to experimental animals. Assessment of the effect of MSG and bark extract of answer wood (*Lannea coromandelica*) in reducing inflammation in kidney damage, the examination variables for MDA, Ureum, Creatinine, and histopathological levels were used.

Effect of MSG and Javanese bark extract (*Lannea coromandelica*) on Urea Levels

Urea in the blood is the main element resulting from the decomposition of proteins and other chemical compounds containing nitrogen. Urea and other nitrogen-rich waste products are normally excreted from the blood vessels via the kidneys, so an elevated urea level can indicate kidney failure.

The average value of Ureum levels in the kidneys of wistar rats that have been carried out shows that the healthy control group (KS) has urea levels with an average of 15.60 ± 1.77 mg/dl. then the negative control group (N) which was only given MSG increased significantly from the healthy control group (KS) with an average of 39.2000 ± 6.09918 mg/dl. then in the experimental group 1 (KPA) which was given MSG and Java wood extract at a dose of 250mg/KgBW had an average urea level of 32.00 ± 1.22 mg/dl. whereas in the treatment group 2 (KPB) which was given MSG and Java wood extract at a dose of 500 mg/Kg BW, the average urea level was lower compared to the other groups, namely 25.50 ± 6.55 mg/dl. As for the treatment group 3 (KPC) which was given MSG and Java wood extract at a dose of 750 mg/Kg BW, the urea level was 31.60 ± 5. 31mg/dl. These results indicate that mice given MSG could increase Ureum levels in experimental animals and rats given Java wood extract had a significant effect on decreasing Ureum levels compared to the healthy control group (without MSG and Java wood extract) which had the lowest levels. This shows that the negative control group experienced oxidative stress, because the negative control group was only given MSG and standard feed without being given antioxidant intake. The absence of intake of antioxidants causes free radicals to increase which is indicated by an increase in urea

levels. While the treatment of experimental animals using Lannea coromandelica stem bark extract which contains antioxidants can prevent the increase in Ureum levels because. Java wood plants are known to contain secondary metabolites such as alcohol, steroids, triterpenoids, phenolics, flavonoids, tannins, and saponins. This compound is a group of bioactive compounds that produce antioxidant, anti-inflammatory, antibacterial, anticancer and immunomodulatory activities (Anggreini et al., 2018).

Effect of MSG and Javanese bark extract (*Lannea coromandelica*) on Creatinine Levels

Creatinine is an ideal substance that can be used to measure kidney function because creatinine is constantly produced by the results of the body's metabolism, which is filtered by the kidneys, not reabsorbed, and excreted by the proximal tubules (Verdiansyah, 2016).

The average value of creatinine levels in the kidneys of wistar rats that has been done, shows that the healthy control group (KS) has creatinine levels with an average of 0.32 ± 0.28 mg/dl. then the negative control group (KN) which was only given MSG increased significantly with an average of 0.65 ± 0.11 mg/dl. then the treatment group 1 (KPA) which was given Java wood extract at a dose of 250 mg/KgBW had an average creatinine level of 0.57 ± 0.44 mg/dl. whereas in the treatment group 2 (KPB) which was given Java wood extract at a dose of 500 mg/kg, it was slightly lower than the previous experimental group (KPA) with an average creatinine level of 0.55 ± 1.03 mg/dl. the treatment group that was the highest of the two previous treatment groups (KPA and KPB) who were given javanese wood extract at a dose of 750 mg/KgBB had an average creatinine level of 0.57 ± 0.75 mg/dl. These results indicate that rats given MSG could increase creatinine levels in experimental animals and rats given java wood extract had a significant effect on decreasing creatinine levels compared to the healthy control group (without MSG and java wood extract) which had the lowest levels.

In the treatment group that was given Lannea coromandelica extract it was more effective in reducing creatinine levels compared to MSG administration. This is because lannea coromandelica contains various phytoconstituents such as phenolic compounds, flavonoids, triterpenoids, tannins, and alkaloids.(Kumar and Jain, 2015)

Effect of MSG and Javanese bark extract (*Lannea coromandelica*) on MDA levels

Melondialdehyde (MDA) is a marker that shows an increase in free radicals in the body caused by oxidative damage (Matzusaki, et al., 2009). Melondialdehyde is also a product formed from lipid peroxidation in cell membranes, namely the reaction of free radicals (hydroxyl radicals) with*polyunsaturated fatty acids*(PUPA). This increase in MDA indicates a fat peroxidation process that has a high potential for both micro and macrovascular complications (Marjani, 2010). Malondialdehyde can be observed in plasma, serum, and various tissues such as kidney tissue (Tiwar, et al., 2002). MDA levels can be measured in several ways, namely by:*thiobarbituric-reactive substance*(TBARS), where the TBA measurement method can be carried out using the colorimetric method and the fluorescence method. Another MDA measurement method is HPLC (*High Performance Liquid Chromatography*) which is the most sensitive and specific method of measuring serum MDA levels (Arkhaesi, 2008). melanodialdehyde (MDA) compound which is the end product in the process of lipid peroxidation. Increased MDA levels due to peroxidation indicate the pathogenesis of a number of diseases such as diabetes mellitus, coronary heart disease, and oral cancer (Jaggi, et al., 2015).

MarkThe average kidney MDA level in rats is the healthy control (KS) which shows an average kidney MDA level of 6.7860 ± 2.16911µg/ml.then the negative control (KN) after being given MSG increased, namely the average value of pulmonary MDA levels was 8.01 ± 6.00µg/ml.then in the treatment group 1 (KPA) which was given MSG and Java wood extract at a dose of 250 mg/Kg BW, the average kidney MDA level was slightly lower, namely 7.96 ± 2.13µg/ml.while the treatment group 2 (KPB) which was given Java wood extract at a dose of 500mg/KgBW had an average kidney MDA slightly higher than the previous treatment group (KPA), which was 8.11 ± 1.00µg/ml.while the treatment group 3 (KPC) which was given MSG and Java wood extract at a dose of 750 mg/KgBB had the highest average kidney MDA of the 2 previous treatment groups (KPA and KPB) which was 8.34 ± 1.14µg/ml.

Brownlee's research (2001) reported that increasing blood glucose levels would trigger an increase in the formation of ROS through an oxidation-reduction mechanism by encouraging more electron donors (NADH and FADH2) into the electron transport chain in mitochondria. Aitken and Roman (2008) reported that an increase in the rate of electron transport can trigger an increase in the formation of superoxide anion (O2-), which is an element of ROS, causing oxidative stress. The low concentration of antioxidants in tissues and the disruption of enzymatic antioxidant defense activities such as SOD, GPx and Cat are also factors for increased ROS production in hyperglycemia conditions (Poitot and Robertson, 2008).

Increased levels of MDA and protease activity can be suppressed with Java wood bark elstract therapy. Java wood bark contains secondary metabolites of polyphenols such as flavonoids, namely Quercetin, Kaempferol, Isoquercetin which have been shown to act as antioxidants. (Reddy, et al., 2011).

The presence of flavanoid compounds in Javanese bark extract can inhibit free radical reactivity in inflammatory bowel disease. Inhibition of these free radicals will suppress the occurrence of lipid peroxidation, so that MDA levels decrease. In addition, it can suppress neutrophils for protease release, so that protease activity in the ileum can decrease and tissue damage in the kidney can be suppressed.

Renal Histopathology Examination

MSG is the sodium salt of glutamic acid (glutamic acid). MSG has been consumed widely throughout the world as a food flavor enhancer in the form of L-glutamic acid, because the addition of MSG will make food taste more delicious (Rangkuti, et al., 2012).

Renal histopathological observationWhat has been done is that there are differences in kidney damage between groups of experimental rats. In the negative group (KN) which was only given MSG for 28 days showed kidney damage, when viewed microscopically it showed hydrophilic deg, inflammatory cells with degree of damage 3, namely severe damage with the lesion assessment criteria of 50-75% of the total visual field. Then in the healthy control group (KS) which was not given MSG and Java bark extract (Lannea coromandelica) viewed microscopically showed 0 (mild) damage. Furthermore, in treatment group 1 (KPA) which was given MSG and Java bark extract (Lannea coromandelica) microscopically viewed it showed the presence of hydrophilic deg and inflammatory cells, with a degree of damage of 2 (moderate). In the treatment group 2 (KPB) which was given MSG and Java bark extract (Lannea coromandelica) viewed microscopically, it showed that there was a distance between cells, with a degree of damage of 1 (mild) reaching <25% of the total visual field. Furthermore, in treatment group 3 (KPC) which was given MSG and Java bark extract (Lannea coromandelica) viewed

microscopically, it showed inflammatory cell infiltration, with a degree of damage of 0 (Normal).

The results of the observations showed that the amount of cell damage in the KN group that was only given MSG was the highest, namely severe damage. The cell damage was caused by treatment which was only in the form of giving MSG in drinking water. Damaged cells occur due to MSG which contains lots of free radicals.

Kidney histopathological examination found in the healthy control group (KS) without MSG administration and Java wood extract had a degree of damage of 0, severe damage occurred in the negative control group (KN) where rats were given MSG with a value of 1.67 ± 1.15 IU/L. then treatment group 1 (KPA) in which rats were given MSG and Java wood extract at a dose of 250 mg/KgBB also experienced severe damage and the value was the same as the negative control group (KN) but slightly lower, namely 1.67 ± 0.57 IU/L. In contrast to the treatment group 2 (KPB) which was given MSG and Java wood extract at a dose of 500 mg/Kg BW, the moderate degree of damage began to decrease significantly with a value of 0.67 ± 0.57 IU/L.

The resulting toxic response will be greater along with the high concentration of compounds that enter the body. Kidney damage caused by toxic substances that show microscopic features in the form of degeneration of tubular cells. Degeneration is a condition when a cell loses its normal cell structure due to influences from inside or outside the cell. Degeneration is characterized by metabolic disturbances, this causes accumulation of intracellular and extracellular materials which then leads to cell death and is a sign of the start of cell damage due to toxins (Fahrimal, et al., 2016).

4. Conclusion

Administration of Java bark extract (Lannea coromandelica) especially at doses of 250 mg/kg and 500 mg/kg, reduced MDA levels, urea levels, and serum creatinine, which were induced by MSG in rats, which indicated an increase in kidney function. In addition, pathological changes found in kidney tissue due to MSG administration were perfected by administering Lannea coromandelica extract at higher doses. Further research is needed to see if the benefits of Lannea coromandelica extract in animal models translate to human subjects.

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