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KERSEN LEAF TEA'S EFFECTS ON MALE MICE'S LIVER AND KIDNEY FUNCTIONS INDUCED BY ALLOXAN

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ABSTRACT

Kersen leaf is a tree native to Southern America and Southern Mexico. In Indonesia, this tree is very easy to get because it grows a lot on the side of the streets. Empirically, Kersen leaves have been widely used by the public as one of the herbs or herbs to overcome various diseases, including DM disease. The study used True Experimental design with Pre and post Control Design design. The purpose of this study was to test the effect of using Kersen Leaf Tea on Hepar and Kidney function. Hepar function will be measured by assessing levels of Alanain Transminerase (ALT) Aspartate aminotransferases (AST). For kidney function is assessed by measuring Creatinine and Ureum levels. The results of the Shapiro test normality test obtained data that were not normally distributed so that the Bivariate test used alternative tests, namely the Kruscal Walis test and the Wilcoxon Test. The results of the study on the administration of kersen leaf tea there were differences between the Control group with the dose group of 2%, dose 4% and dose 6% at ALT levels (p = 0.000), AST levels (p = 0.005), and creatinine levels (p = 0.007) but there was no difference in Urium (P = 0.447). The results of the Wilcoxon test showed the effect of giving kersen leaf tea on ALT levels (p = 0.018), AST levels (p = 0.000), Urium levels (p = 0.37) and creatinine levels (p = 0.038). The administration of kersen leaf tea improves liver and kidney function in Alloxan-induced male mice.

INTRODUCTION

Diabetes Mellitus is one of the non-communicable diseases with a prevalence of 9.3% or equivalent to 463 million people aged 20-79 years in 2019 and Indonesia ranks 8th with 10.7 million sufferers and increases to 5th place with 19.47 million sufferers in 2021 (Ministry of Health RI, 2020) (IDF, 2021). Based on Riskesdas in 2018 East Kalimantan ranks second after DKI Jakarta with a prevalence of 3.1% (Ministry of Health RI, 2020). It shows that DM sufferers experience a significant increase every year (IDF, 2021). The increase in the prevalence of DM especially in developing countries follows patterns of urbanization and lifestyle changes including western-style diets related to obesity or better survival (Forbes & Cooper, 2013; Saeedi et al., 2019). This shows that environmental factors also contribute to this disease in addition to genetic factors (Forbes & Cooper, 2013).

DM disease is a disorder of carbohydrate, lipid and protein metabolism caused by damage to pancreas cells as insulin products as a result of experiencing insulin deficiency or insulin activity with symptoms of increased blood sugar levels (hyperglycemia) (Lestari et al., 2021; Pippitt et al., 2016; Wu et al., 2014). Symptoms that often occur in people with DM include polyuri, polydipsy, polypagi and weight loss (Lestari et al., 2021).

People with DM are not a few who fall into complications. DM has been proven to impact the functions of liver and kidney (Bahirwani & Reddy, 2009; Targher et al., 2018). Complications that often arise include diabetic ketoacidosis, angiopathy, retinopathy and nephropathy (Forbes & Cooper, 2013). Hemodynamic changes are considered as a result of changes in the metabolic environment, the release of vasoactive factors, changes in signal transduction as well as intrinsic defects in the glomerular arterioles as a cause of the onset of diabetic neoropathy (Forbes & Cooper, 2013; Lestari et al., 2021).

METHOD

Tool

The tools used in this study include a mice cage, oven, blender, laminating, teabag container, NGT sonde, 1 cc syringe, mice drinking water bottle, analysis scales, micro pipettes, incubators, test tubes and stationery.

Material

The material used in this study was kersen leaf tea (*Muntingia calabura* L) which was added from the Poltekkes page of the Ministry of Health of East Kalimantan. Kersen leaves are taken at the ends of twigs that are dark green.

How to make kersen leaf tea

1) Material preparation: Kersen leaves that have been taken from a tree with criteria that are old or dark green are separated from the stalk.
2) Sorting: Kersen leaves are separated from damaged or light or yellow hiiau colored and are not eaten by caterpillars. Kersen leaves that are from prepared materials are then sorted or sorted. Kersen leaves of the highest quality to be used as a material for making tea are dark green and not yellowish, and do not have holes.
3) Washing: The selected kersen leaves are then washed in running water so that dirt in the form of dust and fine hairs on the kersen leaves disappear.
4) Withering: Washed kersen leaves are then drained. Then heated to a temperature of 105 0 C-130 ^{0}C for 15 minutes so that a withering process occurs to reduce the moisture content.
5) Plowing: Kersen leaves that have withered, then chopped thin thin, to optimize the drying process.
6) Drying: Chopped leaves are then dried using a cabinet dryer oven for 170 minutes with a temperature of 50^{0}C (Lolok et al., 2019).

The dried kersen leaves are then puree using a blender. The already smooth tea is packaged in teabag containers weighing 2 grams each. Kersen leaf tea is then brewed with hot water as much as 100 ml of perdose and given as much as 0.52 ml morning and evening (2 times a day).

Experimental Animals

The experimental animal (study subject) used in this study was the white male mice (*Mus Musculus*). There were 40 mice divided into 4 groups (K1 = Control group, K2 = dose group 2%,

K3 = dose group 4%, and K4 = dose group 6%). The mice (*Mus Musculus*) used in this study were 11-12 weeks old and weighed between 20-30 grams.

Research Design

This study used a true experiment design with a pre-post control group design. The treatment and maintenance of experimental animals is carried out at the Medical Laboratory Technology Laboratory of the Poltekkes of the Ministry of Health, East Kalimantan. Male mice (*Mus Musculus*) were randomized into 4 groups with each group consisting of 10. Mice (*Mus Musculus*) are acclimatized for 7 days to condition the animal to the environment before treatment. Mice (*Mus Musculus*) are placed in separate cages according to their respective groups and given standard dietary pelleted feed and drink adlibitum water. On the 8th day of mice, induction was carried out with Alloxan dose 65 mg / kg BB intravenously on the tail of the mice (Lucchesi et al., 2015). Mice are made chronic DM for 1 week, on the 15th day an examination of blood sugar and insulin levels is carried out. On the 16th day, kersen leaf tea began to be given for 14 days, which was given morning and evening at a dose of 0.52 ml. On the 29th day (14 days of treatment) blood sampling was carried out to check the levels of AST, ALT, Urium and Creatinine after treatment. Levels of AST, ALT, Urium and Creatinine were examined at the Medical Laboratory Technology Laboratory of the Poltekkes of the Ministry of Health, East Kalimantan.

Data Analysis

The data that has been collected was tested for Normality with Saphyro-Wilk because the sample was less than 50. If the Saphyro-Wilk p> 0.05 test hail is obtained, the data is considered normal and the One Way ANOVA test is carried out, the p<0.05 value is obtained, the data is abnormal and the Kruskal Wallis alternative test is carried out. Then a pre and post test is carried out using the Paired T Test test when the data is normal and if it is not normal, the Wilcoxon Test is carried out.

RESULT AND DISCUSSION

In this study, the normality test results obtained a P value of <0.05 which means that the data is abnormally distributed so that it uses the Kruskal-Wallis alternative test with the following results.

Table 1. Test Results differ between groups with the Kruskal-Wallis Test

	PostAST	**PostALT**	**PostUreum**	**Postcreatinin**
Kruskal-Wallis	29.195	12.807	2.660	12.237
Asymp. Itself.	.000	.005	.447	.007

Based on the results of the Kruskal-Wallis test in the table above, there are significant differences between dose groups (P< 0.05) except for Urium levels (P> 0.05) meaning that there is no difference between groups.

Table 2. Pre and Post Test Results of Kersen Leaf Tea Administration with Wilcoxon Test

	PostAST–PreAST	**PostALT–PreALT**	**PostUreum–PreUreum**	**Postcreatinin–Precreatinin**	**Postgds–Pregds**
Asymp. Sig. (2-tailed)	.000	.018	.037	.038	.000

Based on the Wilcoxon test results there is a significant difference between before treatment and after treatment on all indicators. AST levels with a value of P = 0.000 means P<0.05 ALT levels value P=0.018 meaning P<0.05, Ureum levels P=0.037 meaning P<0.05 and creatinine levels P=0.038 meaning P<0.05.

Discussion

Based on table 2 above, there is a decrease in levels of AST, ALT, Urium and creatinine. Kersen leaves contain various phytochemicals including saponins, flavonoids, tannins. Flavonoids contained in Kersen leaves have kersen leaf extract administration can reduce levels of ALT / SGPT, AST/SGOT enzymes (Lalihatu & Sudharmono, 2019; Zakaria et al., 2018). Flavonoids as antioxidants have hepatoprotective activity in the concentration range of 1-100 g/mL increasing cell viability and inhibiting cellular leakage of hepatocytes aspartate aminotransferase (AST) and *alanine aminotransferase* (ALT) (Kočevar et al., 2007). Flavonoids can inhibit inflammation in the kidneys by the pathway of decreasing urium creatinine levels and inhibition of the xanthin oxidase pathway (Panche et al., 2016; Ren et al., 2020). Saponins can protect kidney function and oxidative stress due to diabetic nephropathy through pathways as antioxidants and anti-inflammatories (Mi et al., 2022).

Based on the results of the Wilcoxon test, all indicators showed a significant relationship (P<0.05) between before the intervention and after the intervention with the administration of Kersen Leaf Tea for 2 weeks in Alloxan-induced mice. Kersen Leaf Tea contains various phytochemicals including flavonoids, saponins and tannins. Flavonoids contained in kersen leaves are of various types, namely; flavones, flavonons, flavans, and biflavans (Zahara & Suryady, 2018). Flavonoids have a wide range of activity; Anti-inflammatory, anticholinesterase, steroid genesis modulator, xanthine oxidase modulator, fights antibiotic resistance, disease-fighting activities, and anti-depressants (Jäger & Saaby, 2011; Benche et al., 2016). Giving kersen leaf extract (Muntingia Calabura L) at a dose of 50 mg / kgBB, 250 mg / KgBB, and 500 mg / KgBB Male rats (male Sprague Dawley) can reduce levels of AST, ALT and ALP (Wahhab Rofiq Hakim, 2012; Zakaria et al., 2018). The administration of kersen leaf extract can improve liver and kidney function (Fadil et al., 2017; Kholifaturrokhmah & Purnawati, 2016). Kersen leaves that contain a lot of antioxidants can improve the protective mechanism against oxidative stress (Fadil et al., 2017; Kholifaturrokhmah & Purnawati, 2016; Zakaria et al., 2018). Saponins contained in kersen leaves can be antioxidants and anti-antioxidants in improving kidney function (Mi et al., 2022). Administration of kersen leaf extract can improve proximal renal tubules in diabetic rats (Safrida & Sabri, 2019). Research by Lalihatu et al, 2019, Kersen leaf decoction can reduce SGOT and

SGPT levels in Wistar Rats with Acute Hepatitis (Lalihatu & Sudharmono, 2019). Kersen leaves have a variety of activities including antimicrobial, anti-inflammatory, antinociseptic, anticancer, antiulcer, antioxidant and gastroprotektic (Mahmood et al., 2014; Pereira et al., 2018).

CONCLUSION

In this study, the administration of kersen leaf tea can reduce levels of *AST*, *ALT*, Ureum and Creatinine. It proves that consuming kersen leaf tea is safe against liver function and kidney function. In addition, it is important to research this topic further to gain more in-depth insight regarding DM affects liver and kidney functions.

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