DIPONEGORO MEDICAL JOURNAL
(Jurnal Kedokteran Diponegoro)
Online : http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
Volume 9, Nomor 6, November 2020

THE EFFECT OF CORIANDER LEAVES EXTRACT ON THE DEGREE OF WISTAR RATS LIVER MICROSCOPIC DAMAGE WAS GIVEN MERCURIC CHLORIDE ORALLY

Zefania Regina Ardiani*)[1], Sudaryanto[2], Hermawan Istiadi[3], Hadi[4]
[1]Student of Faculty of Medicine, Diponegoro University, Semarang,Indonesia
[2]Staff of Parasitolgy Departement Faculty of Medicine, Diponegoro University, Semarang,Indonesia
[3]Staff of Anatomical Pathology Departement, Faculty of Medicine, Diponegoro University, Semarang,Indonesia
[4]Staff of Forensic Departement, Faculty of Medicine, Diponegoro University, Semarang,Indonesia
*)Corresponding author : zefaniareginard@gmail.com

ABSTRACT

Background Mercury is a heavy metal that is widely used in various aspects of human life. However, mercury exposure can damage the liver. The high antioxidant found in coriander leaves is expected to be a solution to the problem in preventing liver damage due to mercury exposure. **Aim** Proving that administration of coriander leaf extract can reduce the degree of wistar rats liver microscopic damage due to mercury exposure. **Methods** Experimental study with post test only control group design for 14 days, used 24 male Wistar rats, divided randomly into 4 groups : C (-), C (+) (given mercury orally 10 mg / kgBW), X1 (given mercury orally 10 mg / kgBW and coriander leaf extract 100 mg / kgBW) and X2 (given mercury orally 10 mg / kgBW and coriander leaf extract 200 mg / kgBW). On the 15th day, rats were terminated, the livers were harvested, microscopic preparations were made and stained with Hematoxylin-Eosin. Observed with a magnification of 400x in 5 different fields of view of each sample and were assessed using Manja Roenigk's score. **Results** Were obtained normal, mild damage, moderate damage, and severe damage respectively in the group: C (-): 80%, 20%, 0%, 0%; C (+): 0%, 3%, 67%, 30%; X1: 47%, 33%, 17%, 3%; X2: 77%, 23%, 0%, 0%. Spearman test found significant correlation (p = 0,000) with storng correlation (r = 0.781) and the direction between the two variables is negative (-) . Kruskal Wallis test found significant differences (p = 0,000). Continued Mann Whitney test found significant differences between groups C (-) with C (+) (0,000), C (-) with X1 (0.004), C (+) with X1 (0,000), C (+) with X2 (0,000)), and X1 with X2 (0.007) and the difference is not significant between C (-) and X2 (0.756). **Conclusion** Giving coriander leaves extract can reduce the degree of microscopic damage of Wistar rat liver due to mercury exposure.
Keywords : mercury, coriander leaves , liver microscopic

INTRODUCTION

Mercury (Hg) is a heavy metal with high toxicity.[1,2] Mercury exposure in humans, most often occurs due to inhalation of mercury vapor during industrial or mining processes and through the consumption of fish and shellfish that have been contaminated with mercury.[3] The impact of excessive mercury exposure on humans, causing damage to cells in the body such as the liver, kidneys, digestive tract or disrupt metabolism so that it affects the physiological functions of an organ, and can cause death. [4,5]

Liver is the center of the body's metabolism. One of the functions of the liver is to protect the body against toxic substances through the detoxification process. But not all toxic substances can be completely detoxified, so they are buried in the blood and can cause damage to liver cells. [6]

Coriander (Coriandrum sativum L.) is one of the plants that is easily found in Indonesia and has antioxidant content and potential for heavy metal detoxification. Based on antioxidant test results, ethanol extract of coriander leaves has the highest antioxidant content compared to other parts so coriander leaf extract can anticipate the harmful effects of mercury poisoning especially reducing the degree of liver

DIPONEGORO MEDICAL JOURNAL
(Jurnal Kedokteran Diponegoro)
Online : http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
Volume 9, Nomor 6, November 2020

damage.[7]

This study is relevant because there has been no research on the effect of coriander leaf extract on the degree of liver damage given mercury. Researchers hope that through this study can provide information about the effect of coriander leaf extract on liver of rats given mercury, so that it can be used effectively as a protective antioxidant agent against the liver damage.

METHODS

Experimental study with a post test only control group design. Research has been conducted at the Animal Biology Laboratory-FMIPA UNNES. The process of making microscopic preparations has been made at the Animal Laboratory of FK UNDIP. Sample was male Wistar rats with inclusion criteria, age 2-3 months, body weight 150-250 grams and in good health without anatomical abnormalities. The criteria for exclusion of the study sample were sick or dead wistar rats.

Wistar rats were obtained from the population of Wistar rats at the center for breeding of rat Animal Biology Laboratory-FMIPA UNNES. The mercury used is mercuric chloride (HgCl2) produced by Pudak Scientific which is obtained from a chemical store. Mercury is stored in a tightly closed container, made of glass and dry. Store away from sources of ignition, without lighting and at room temperature.[8] 5 kg of coriander leaves used in this study were obtained from plantations in Bandung. Coriander leaves were dried for 5 days then mashed into powder and continued with the process of making coriander leaf extract at the UNDIP Integrated Laboratory using the maceration method. The coriander leaf extraction process uses food grade ethanol so that the coriander leaf extract can be consumed. The ketamine used is Ivanes Ketamine injection produced by PT. Ikapharmindo Putramas Jakarta in 10 ml packs with a dose of 1000mg / 10 ml.

Samples selected using simple random sampling were grouped into four groups: group C (-), C (+) (given mercury orally 10 mg / kgBW), X1 (given mercury orally 10 mg / kgBW and coriander leaf extract 100 mg / kgBW) and X2 (given 10 mg / kgBW of oral mercury and 200 mg / kgBW of coriander leaf extract). Based on the calculation of the sample size, the number of samples needed is at least 24 samples and the sample is adapted for 7 days before treatment.

The independent variable in this study was coriander leaf extract and the dependent variable was the degree of liver microscopic damage of wistar rats induced by mercury orally. For 14 days, in the morning groups C (+), X1 and X2 were given mercury orally at a dose of 10 mg / kgBW. Groups X1 and X2 were given coriander leaf extract with doses of 100 mg / kgBW and 200 mg / kgBW after oral mercury administration, the C (-) group was only given standard feed and drink. After 14 days of treatment, the sample was terminated, the liver was taken and put in 10% formalin buffer then microscopic preparations were made and painted using HE. The preparations were read using a light microscope with a magnification of 400x in 5 different fields of view of each sample and were assessed using Manja Roenigk's score. Data that has been obtained, was coded and then entered into a computer and processed using SPSS ver. 25.

RESULTS

Descriptive analysis of the frequency and proportion of degrees of liver microscopic damage of Wistar rats obtained from microscopic observations on 5 different fields of view of the whole group

DIPONEGORO MEDICAL JOURNAL
(Jurnal Kedokteran Diponegoro)
Online : http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
Volume 9, Nomor 6, November 2020

Table 1. Amount of each degree of liver microscopic damage

Group	Degree of liver microscopic damage				
	Normal	Parencyhmatous degeneration	Hydropic degeneration	Necrosis	Number of Fields of View
(C -)	24 (80%)	6 (20%)	0 (0%)	0 (0%)	30 (100%)
(C +)	0 (0%)	1 (3%)	20 (67%)	9 (30%)	30 (100%)
(X1)	14 (47%)	10 (33%)	5 (17%)	1 (3%)	30 (100%)
(X2)	23 (77%)	7 (23%)	0 (0%)	0 (0%)	30 (100%)
Number of Fields of View	61 (51%)	24 (20%)	25 (21%)	10 (8%)	120 (100%)

Based on table, microscopic liver in group C (-) is dominated by normal hepatocytes by 80%, there is also a parenchymatous degeneration of 20%. In group C (+) there was mostly hydropic degeneration by 67% and even necrosis by 33%, then there was a slight parenchymatous degeneration of 3%. In group X1 there was a normal hepatocyte of 47% and parenchymatous degeneration of 33% but hydropic degeneration was still obtained by 17% and there was still a small amount of necrosis with a percentage of 3%. The X2 group was dominated by normal hepatocytes at 77% but parenchymatous degeneration was still found at 23% and hydropic degeneration and necrosis were not found.

After the frequency and proportion of each group have been known, then proceed with the correlation test using the Spearman test. From the results of the Spearman test, the value of p = 0.000 (p<0.05) was obtained, which means that there is a significant correlation. Then the r = 0.781 was obtained, which means that there is a strong correlation between the dosage of coriander leaf extract and the microscopic degree of liver damage. The direction between the two variables is negative (-), which means that the higher the dose of coriander leaf extract, the lower the degree of microscopic damage to the liver, and vice versa.

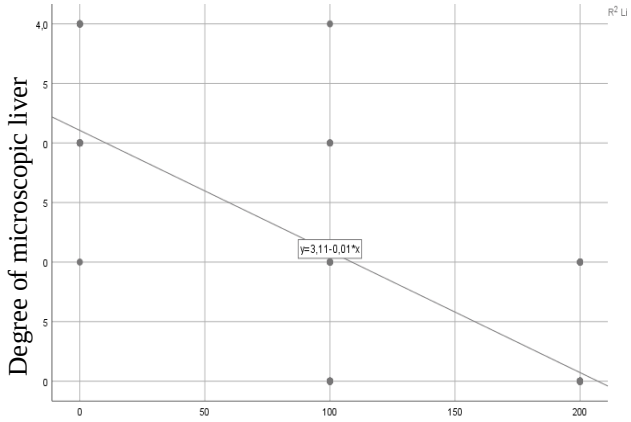

Chart 1. The relationship between coriander leaf extract dosage and degree of microscopic liver damage

Based on chart, the higher the dose of coriander leaf extract (200 mg / kgBW), the lower the degree of microscopic damage to the liver, and the lower the dose of coriander leaf extract (0 mg / kgBW), the higher the degree of microscopic liver damage.

Hypothesis testing with Kruskall-Wallis has been conducted to find differences in all population groups. From the Kruskall-Wallis test results obtained p = 0,000 (p <0.05) which means that there are significant differences. Then the data analysis is then continued using the Mann-Whitney test to assess differences between the 2 groups.

Table 2. Result Mann-Whitney test between the 2 groups

Group	C (-)	C (+)	X1	X2
C (-)	-	0,000*	0,004*	0,756
C(+)	0,000*	-	0,000*	0,000*
X1	0,004*	0,000*	-	0,007*
X2	0,756	0,000*	0,007*	-

* Mann-Whitney test analysis results are significant if p <0.05

DIPONEGORO MEDICAL JOURNAL
(Jurnal Kedokteran Diponegoro)
Online : http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
Volume 9, Nomor 6, November 2020

Based on the Mann-Whitney test, it was found that there were significant differences between groups C (-) with C (+) (0,000), C (-) with X1 (0,004), C (+) with X1 (0,000), C (+) with X2 (0,000), and X1 with X2 (0.007). While there is no significant difference between C (-) and X2 (0.756).

DISCUSSION

Based on the literature, liver damage can be caused by mercury exposure and has been proven in various studies, some studies can also prove that coriander leaves have benefits as liver protective agents.[9–13] Statistical test results showed that there were significant microscopic differences in liver between group C (-) and group C (+) (0,000). In group C (-) microscopic observations were obtained that most cells were normal. But parenchymatous degeneration can also be obtained which can occur due to the oxidation disturbance process during and after the animal is terminated due to the death process[14]. In group C (+) showed that the treatment can affect the liver microscopic that is the degree of damage starting from the stage of parenchymatous degeneration, hydropic degeneration to necrosis and no normal cells. This is appropiate with previous studies that the administration of mercury can cause damage to the liver. Mercury metabolism in the liver uses a variety of intrahepatic enzymes and the metabolic process produces free radicals, which cause liver damage. [2,9]

Statistical test results in group C (+) with group X1 showed significant liver microscopic differences (0,000). In the microscopic group X1 the liver is dominated by normal cells and parenchymatous degeneration although there is still hydropic degeneration and little bit necrosis. Damage to X1 is lighter compared to C (+). Statistical test results also showed a significant difference (0,000) in group C (+) and group X2. In group X2 the microscopic picture of the liver is dominated by normal cells and partially parenchymatous degeneration. Microscopic liver in X2 is much better compared to C (+). Several studies have shown that the administration of coriander leaf extract can improve liver damage by reducing the concentration of heavy metals that accumulate in the liver and reduce levels of liver enzymes markers of liver damage. [11–13]Membrane damage characterized by necrosis can release liver enzymes markers of liver damage such as SGPT,SGOT,ALP into the circulation and can be measured through blood serum. These enzymes are quantitative markers that are useful for determining the extent and type of liver cell damage.[13] This is in line with the results of this study that coriander leaf extract can reduce the degree of liver damage due to mercury exposure.

There was a significant difference between group C (-) and group X1 (0.004). This shows that the coriander leaf extract dose of 100 mg / kgBW has not been able to reduce the degree of liver microscopic damage due to mercury chloride until it returns to normal. But there was no significant difference (0.756) between group C (-) and group X2. This shows that the coriander leaf extract dose of 200 mg / kgBW can reduce the degree of liver microscopic damage to near normal. In previous studies, it was found that the higher the dose of coriander leaf extract, the better it is to repair liver damage due to CCl4 exposure.[13] This is in line with this study that higher doses of coriander leaf extract are better at repairing liver damage that is exposed to mercury.

The mechanism of action of the active compound of coriander leaf extract which has the potential as a hepatoprotector is flavonoids.[15,16] Flavonoids are one type of antioxidant in coriander leaf extract that can reduce the production of ROS through suppression of singlet oxygen, inhibit

DIPONEGORO MEDICAL JOURNAL
(Jurnal Kedokteran Diponegoro)
Online : http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
Volume 9, Nomor 6, November 2020

enzymes that produce ROS such as cyclooxygenase, lipoxygenase, monooxygenase, xanthine oxidase and reduce free radical reactions in lipid peroxidation. From this mechanism, coriander leaf extract can prevent damage to the liver caused by free radicals from metabolism and the accumulation of toxic substances such as mercury.[17]

Significant differences were also found in the liver microscopic picture between groups X1 and X2 (0.007). So that it can prove that coriander leaf extract dose of 200 mg / kgBW can reduce the degree of liver damage better than coriander leaf extract dose of 100 mg / kgBW. In previous studies, the dose of coriander extract 200 mg / kgBW can repair tissue damage and reduce the accumulation of iron in the liver.[12] This is in line with this study that the dose of coriander leaf extract 200 mg / kgBW can repair liver microscopic damage to near normal even though exposed to mercury, a type of heavy metal that is different from previous studies.

The effect of reducing the degree of liver damage differs depending on the dose of coriander leaf extract given. Based on the pharmacokinetic theory of oral administration of the drug, if it reaches the peak point of absorption, there will be a change to the distribution, metabolism and excretion phases. The levels of active substances from coriander leaf extract in blood plasma vary according to the dose given. After achieving balance in the body, it can show a good relationship between levels of active substances in blood plasma and the effect of therapy. The relationship between bioaviability and effectiveness depends on the dose and duration of the pharmacological response to the drug given[18]

The results of this study indicate that the hypothesis about coriander leaf extract can function as hepatoprotective in reducing the degree of liver microscopic damage has been proven in accordance with previous studies.[7,11–13,15] The limitations of this study were: it cannot measure the internal condition of the rats which includes the ability to regenerate, repair body tissues and the immune status of the rats.

CONCLUSION

Administration of coriander leaf extract can reduce the degree of microscopic damage of Wistar rat liver due to mercury exposure.

REFERENCES

1. Clarkson TW, Magos L. The toxicology of mercury and its chemical compounds. Crit Rev Toxicol. 2006;36(8):609–62.
2. Broussard LA, Hammett-stabler CA, Winecker RE. The Toxicology of Mercury. Lab Med. 2002;33(8):614–25.
3. WHO. Exposure to Mercury: A major public health concern [Internet]. 2006 [cited 2020 Mar 1]. p. 4. Available from: https://doi.org/10.1016/j.ecoenv.2011.12.007
4. Sutomo AH, Suwarni A. Kadar Mercury Dalam Rambut Dan Kesehatan Nelayan Di Pantai Kenjeran Surabaya. J Tek Lingkung P3TL-BPPT. 2004;5(1):17–24.
5. Sentra Informasi Keracunan Departemen Kesehatan RI. Merkuri dan Dampaknya Terhadap Kesehatan Manusia. 2015 [cited 2020 Mar 1];1–2. Available from: http://ik.pom.go.id/v2016/artikel/MERKURI-UTK-KORAN-TERBIT
6. Sherwood L. Fisiologi Manusia: Dari Sel ke Sistem. 8th ed. Octavius H, Agung Mahode A, Ramadhani D, editors. Jakarta: EGC; 2012.
7. Bani F, Serang Y, Safitri. Kajian efektivitas filtrat perasan, minyak atsiri dan ekstrak etanol daun ketumbar (Coriandrum sativum L.). J Farm dan

DIPONEGORO MEDICAL JOURNAL
(Jurnal Kedokteran Diponegoro)
Online : http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
Volume 9, Nomor 6, November 2020

Sains Indones. 2016;1(1):39–47.
8. National Center for Biotechnology Information [Internet]. PubChem Compound Summary for CID 24085, Mercuric chloride. 2020 [cited 2020 Aug 2]. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/Mercuric-chloride.
9. Johan J, Hadi, Amarwati S. Pengaruh Pemberian Merkuri Per Oral Terhadap Gambaran Histopatologis Liver Tikus Wistar. J Kedokt Diponegoro. 2016;6(2):673–81.
10. Amdalia PR, Anwar C, Kurnijasanti R. Pengaruh Pemberian Ekstrak Daun Kelor Terhadap Gambaran Histopatologi Sel Hepar Mencit Jantan yang Dipapar Merkuri. J Basic Med Vet. 2017;6:1–7.
11. Nishio R, Tamano H, Morioka H, Takeuchi A, Takeda A. Intake of Heated Leaf Extract of Coriandrum sativum Contributes to Resistance to Oxidative Stress via Decreases in Heavy Metal Concentrations in the Kidney. Plant Foods Hum Nutr. 2019;74(2):204–9.
12. Talaei A, Kheirollah A, Rezaei HB, Mansouri E, Mohammadzadeh G. The Protective Effects of Hydro- Alcoholic Extract of Coriandrum sativum in Rats with Experimental Iron-Overload Condition. Jundishapur J Nat Pharm Prod. 2017;2(13):1–9.
13. Pandey A, Bigoniya P, Raj V, Patel KK. Pharmacological screening of Coriandrum sativum Linn. for hepatoprotective activity. J Pharm Bioallied Sci. 2011;3(3):435–41.
14. Ramachandran R, Kakar S. Histological patterns in drug- induced liver disease. J Clin Pathol. 2009;62(6):481–92.
15. Momin A, Acharya S, Gajjar A. Coriandrum sativum Review of advances in phytophaymacology. Int J Pharm Sci Res. 2012;3(05):1233–9.
16. Laribi B, Kouki K, M'Hamdi M, Bettaieb T. Coriander (Coriandrum sativum L.) and its bioactive constituents. Fitoterapia. 2015;103:9–26.
17. Mierziak J, Kostyn K, Kulma A. Flavonoids as important molecules of plant interactions with the environment. Molecules. 2014;19(10):16240–65.
18. Utami VN, Hadisaputro S, Rahayu S. Pengaruh Ekstrak Ketumbar *(Coriandum Sativum)* terhadap Perubahan Tekanan Darah Tikus Pasca Melahirkan. J Keperawatan Soedirman. 2016;11(3):1