

PAPER • OPEN ACCESS

Effect of Turmeric Rhizome Extract (*Curcuma longa* L.) on Liver Histology of Preeclampsia Rat (*Rattus norvegicus* L.)

To cite this article: S Ilyas *et al* 2019 *IOP Conf. Ser.: Earth Environ. Sci.* **305** 012077

View the [article online](#) for updates and enhancements.

Effect of Turmeric Rhizome Extract (*Curcuma longa* L.) on Liver Histology of Preeclampsia Rat (*Rattus norvegicus* L.)

S Ilyas*, S Hutahaean, Elimasni, D K Ar-roisyi

Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Sumatera Utara, Medan, Indonesia

*Email: syafruddin6@usu.ac.id

Abstract. Turmeric is usually consumed routinely and for a long time, so it cannot be ascertained that the use of turmeric is safe or toxic especially in the liver because there are as many as 64 compounds in turmeric which are thought to be hepatotoxic, The prevalence of preeclampsia is around 5% -15% of all pregnancies in the world, where cases of hypertension in pregnancy including preeclampsia are found in numbers that tend to increase and are the most common medical complication in pregnancy. About 70% of women diagnosed with hypertension in pregnancy are cases of preeclampsia. This study used a type of analytic research with quasi-experimental design in pregnant female rats consisting of 4 treatments with 6 replications each. This study consisted of a negative control group (k-) with only feed given ad libitum, positive control (k+) in injection of LPS intervena with a group dose of 0.2 / kgBW and a group giving turmeric extract (*Curcuma longa* L.) with doses of 400mg / kgBW (P1) and 600mg / kgBW (P2) respectively. After that, histological preparations were carried out on the liver of rats (*Rattus norvegicus*). From the results of observations of the liver morphology in the negative (-) and P2 treatment the liver color was found to be dark red, whereas in the positive control group (k+) a pale red color was found. Then histological observations showed an increase in the percentage of liver necrosis from P1 and a decrease in necrosis in P2.

1. Introduction

Consumption of turmeric in the community is often uncontrolled, especially for turmeric in the form of traditional herbal preparations or herbal medicine which is usually consumed regularly and for a long time, so it cannot be ascertained that the use of turmeric is safe or toxic. Especially in the liver because there are as many as 64 compounds in turmeric which is thought to be hepatotoxic. Besides that, also because the liver is the main target of drugs and xenobiotics, so there needs to be a test related to toxicity in turmeric. Tests conducted to determine the toxicity of a compound include acute toxicity test, subchronic toxicity test and chronic toxicity test, where each test has a different observation time span. Subchronic toxicity test is a long-term toxicity test with observation for 1-3 months [1-4]

Preeclampsia is a disease that has a different incidence in each country. The incidence of preeclampsia is more prevalent in developing countries than in developed countries. This is because developed countries have better parental care. The incidence of preeclampsia can be influenced by factors and the environment. Age is very influential in gestational age and in labor [5-7].

Continuous use of drugs and inappropriate doses can cause liver damage. Where the function of the liver is related to the body's metabolism, especially regarding its influence on food and blood. The liver is the largest chemical plant in the body in that it becomes an "introduction to metabolism"



meaning that it converts food substances that are absorbed from the intestine and stored somewhere in the body, to be made suitable for use in the tissue. In addition the liver also converts waste and toxic substances to be easily excreted into bile and urine [8].

However, there are no known negative effects due to Turmeric extract (*Curcuma longa* L) [9] on liver histology as well as liver function by Rats (*Rattus norvegicus*) induced by Pre-eclampsia. Therefore further research is conducted in order to find out whether Turmeric extract (*Curcuma longa* L) affects liver histology and also liver function by Rats (*Rattus norvegicus*) induced by Preeclampsia. Liver disease have a high risk of pregnancy disorder, although until now no reports of maternal death [10-13].

2. Methods

2.1. Experimental design

This study used the Complete Randomized Design Method which was divided into 4 treatments with 6 replications in accordance with the Federer formula:

$$(t-1)(n-1) \geq 15$$

Description:

t = treatment group

n = replications

The following treatment groupings can be seen in table 1.

Table 1. Grouping of research treatments

Treatment	Control	LPS	Extract of <i>Curcuma longa</i>	
			100 mg/kg BW	200 mg/kg BW
K	√			
P1		√		
P2		√	√	
P3		√		√

2.2. Acclimatization of experimental animals

Female (healthy) rats (*Rattus norvegicus*) age 10 weeks with a weight of 150-250 grams as many as 24 individuals. Rats were divided into treatment and control groups. Rats were given ad libitum food and drink, and kept in a clean cage with sufficient moisture and light. Handling rats according to the experimental animal code of ethics (Ethical clearance from the USU FMIPA Animal Research Ethics Commission).

2.3. Injection of LPS and Extract administration

Rats were fed with pellets and drank ad libitum. then rats were injected with LPS through intervena on the tail to become a model of preeclampsia. After that, proteurina is checked every day (at 08-10 am) and monitoring systolic blood pressure every three days in rats injected with LPS. then given an extract (*Curcuma longa* L.) orally at a dose of 400 mg / kgBW and 600 mg / kgBW. Administration of extracts were carried out orally using gavage needles and 1 mL syringe [14-16].

2.4. Organ Harvesting and Making Preparations

Rats were anesthetized using chloroform and then dislocated neck. After the abdominal cavity was opened, the liver was taken and inserted into a sample bottle that contained 10% Formalin Neutral Buffer. The liver cut and put in a cassette or place of specimen. Then the dehydration process is carried out on alcohols with multilevel concentrations, 70% alcohol, 96% and absolute alcohol. Paraffin blocks are then thinly cut into 5-6 μm thickness using a microtome. The preparation is then lifted and placed on a glass object to do Hematoxylin and Eosin (HE) staining, observed under a microscope with 400x magnification.

2.5. Test Parameter Analysis

2.5.1. Visual Morphological Analysis

Rats were surgically removed at each treatment and liver extract was then weighed by each organ using a balance sheet and recorded. Observation of the heart color was done and compared to each treatment [4,17-23].

2.5.2. Histological Analysis of Liver

The liver was taken to make histopathological preparations using the paraffin method. Histopathological studies were carried out under a microscope with magnifications of 4 x10, 10 x10 and 10 x 40 x [24]. Liver histological preparations were observed under a light microscope in 5 different field fields, with a magnification of 40x10 times. Each field counted 20 cells randomly so that in one preparation 100 liver cells were found. Then the mean weight of liver histopatologic change scores in five fields of each - each rat with the Manja Roenigk Histopathology scoring model. The liver structures observed were normal hepatocytes and hepatocytes which suffered damage to both necrosis, parenchymal degeneration, and hydropic degeneration. Then recorded and calculated the percentage of damages occurred.

Table 2. Modified Hepatocyte Damage Assessment Score for Manja Roenigk Cretaceous.

Damage Rate	Score
Normal	1
Parenkimatosa Degeneration	2
Hydropic Degeneration	3
Necrosis	4

2.6. Data analysis

Data will be presented in the mean \pm standard deviation if the distribution is normal. If the distribution is not normal, the data will be presented in quartile form. Data is processed and analyzed using SPSS with a significance limit of $p < 0.05$. To assess whether the sample is normally distributed or not carried out by Shapiro-Wik test because the sample is ≤ 50 . if the data is distributed abnormally.

3. Results and Discussion

The results of this study will be discussed in two parameters, namely histopathological analysis and hepatocyte damage in rats.

3.1. Histopathological analysis

Based on the histology of liver hepatocytes in rat after administration of turmeric extract and LPS, results were obtained in Figure 1.

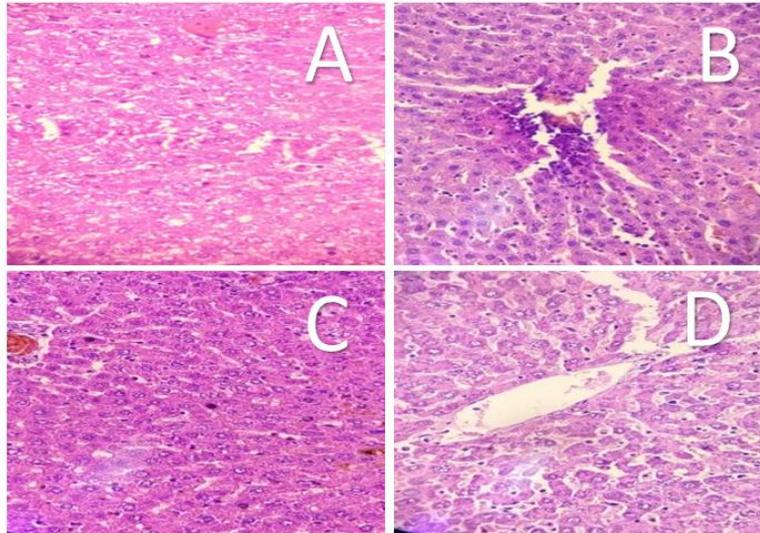


Figure 1. Structure of histological structure of hepatocytes in rat liver

In Figure 1 shows the observations of histological structure of hepatocytes in rat liver found cell changes in the form of parenchymatic degeneration, hydropic degeneration, and necrosis in each group, both in the control group and in the treatment group. In the control group this can happen, this is probably because the liver organ is infected, which is caused by natural physiological conditions in the rat so that it can cause damage to the hepatocyte treatment of hepatocyte damage is likely due to the treatment causing disruption of cell permeability in the cell membrane. The disruption of permeability in cell membranes is due to the effects of giving turmeric and LPS rhizome extract which can cause disruption of permeability in cell membranes which are most important cell components.

3.2. Normal Hepatocytes

Based on observations of normal hepatocyte histological structures in rat liver after administration of turmeric and LPS rhizome extract combinations, the results are shown in Figure 2. It can be seen that the number of normal hepatocytes in the control (+) tends to be lower than the treatment group. This might occur because the administration of LPS has a significant effect on the growth and development of hepatocyte cells ($p < 0.05$). Liver damage is closely related to bleeding and a smaller unit arrangement of liver sinus, which is the latest concept of the smallest unit and functional liver. Hepatocytes are polyhedral in shape, with at least six sides, large and round nuclei, the core membrane has a flat surface [8]. The accumulation of toxic materials and other metabolites can cause cell degeneration. Substances that have toxic properties will cause interference with mitochondrial organelles in producing energy Adenosine Triphosphate (ATP) [10].

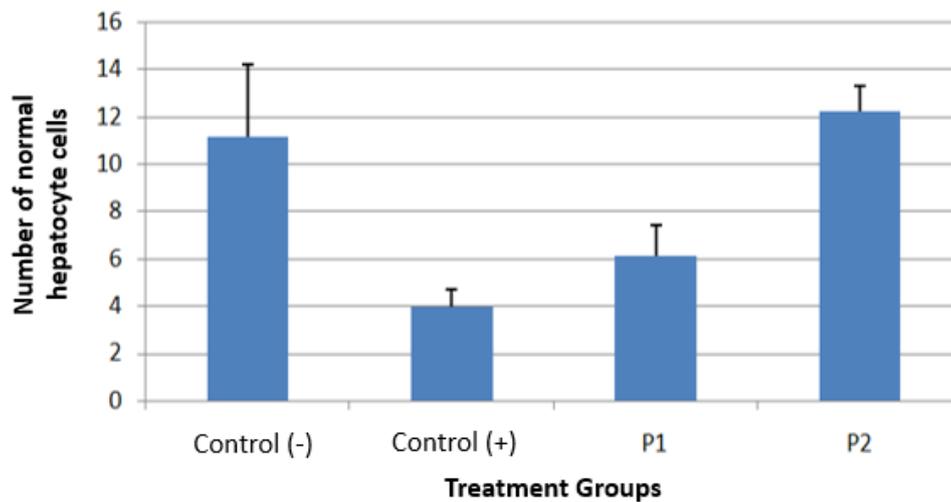


Figure 2. Mean of number of normal hepatocytes in the treatment group.

3.3. Parenchymatic Degeneration

Based on observations of parenchymaic degeneration in rat liver after administration of turmeric and LPS rhizome extract combinations, the results are shown in Figure 3.

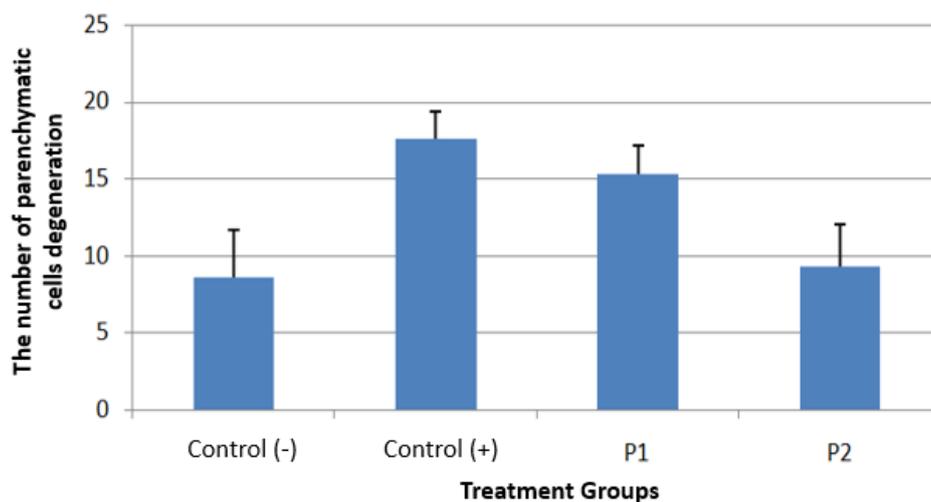


Figure 3. The number of parenchymatic cells degeneration

It can be seen that there is a very significant effect ($p < 0.05$), the number of parenchymatic degeneration in the control (+) tends to be higher than P1 and P2. This may occur because the administration of LPS has a very strong influence on the emergence of parenchymatic degeneration. But in the presentation of damage to P1 and P2 parenchymatosa degeneration tends to decrease. This might occur because turmeric rhizome extract has a very good compound to trigger a decrease in the level of parenchymatosa damage in the liver. Parenchymatic degeneration is the mildest level of degeneration category. In cells that experience parenchymal degeneration, there are granules in the cytoplasm due to deposits that cause the cytoplasm to become cloudy and followed by swelling of the

cells. This change is caused by a disturbance of mitochondrial oxidation and endoplasmic reticulum. Parenchymatic degeneration can return to its normal form if given water or substances that have antioxidants, for example EVOO has vitamin E and antioxidant (Tocopherol) which is anti-apoptotic [7,8,25-27].

3.4. Hydrophic degeneration

Based on observations of hydrophic degeneration in rat liver after giving a combination of turmeric and LPS rhizome extract, the results were obtained in Figure 4.

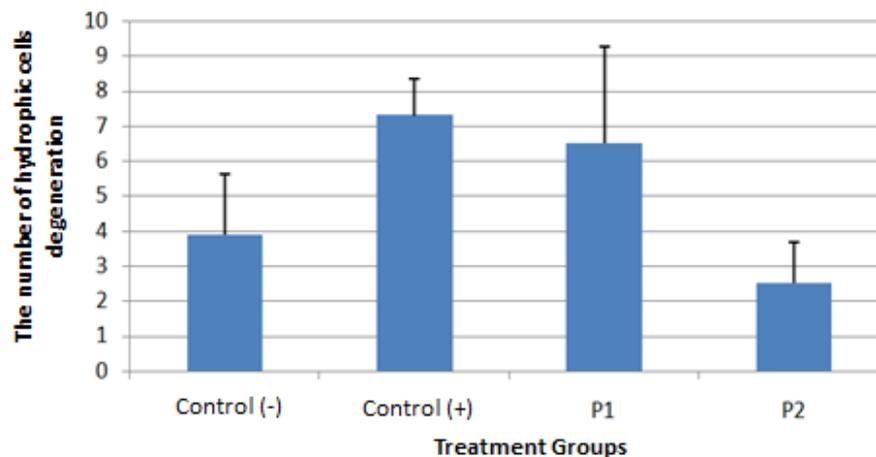


Figure 4. The number of hydrophic cells degeneration.

It can be seen that there is a very significant effect ($p < 0.05$), the number of hydrophic degeneration in the control (+) tends to be higher than P1 and P2. This may occur because the administration of LPS has a very strong influence on the emergence of hydrophic degeneration. But in the presentation of damage to hydrophic degeneration p1 and p2 tends to decrease. This may occur because turmeric rhizome extract has a very good compound to trigger a decrease in the level of hydrophic damage in the liver. Hydrophic degeneration is a more severe degree of damage, it appears vacuole containing water from the cytoplasm that contains no fat and glycogen. These changes are generally a result of metabolic disorders such as hypoxia or chemical poisoning. This degeneration is also reversible even though it is possible to become irreversible if the cause of the injury persists. Cells that have been injured can then experience plasma membrane tears and core changes [11,28].

3.5. Necrosis

Based on observations of necrosis in rat liver after administration of turmeric and LPS rhizome extract combinations, the results are shown in Figure 5. It can be seen that there is a very significant effect ($p < 0.05$), the number of necrosis cell in the control (+) tends to be higher than P1 and P2. This may occur because the administration of LPS has a very strong influence on the emergence of necrosis. However, the presentation of damage to necrosis p1 and p2 tends to decrease. This might happen because turmeric rhizome extract has a very good compound to trigger a decrease in the level of necrosis damage in the liver. Damage to the liver is cell death or necrosis. Necrosis in hepatocytes arises because of the presence of toxic compounds that enter the liver which cause infection. Damage to the liver arising from toxic compounds, is influenced by several factors including the type of chemical compound, dose, and length of exposure of the compound [29-32]. A normal heart has a flat

surface and is smooth and brownish red in color, while an abnormal liver has a surface such as connective tissue, cysts or spots and changes in color [9].

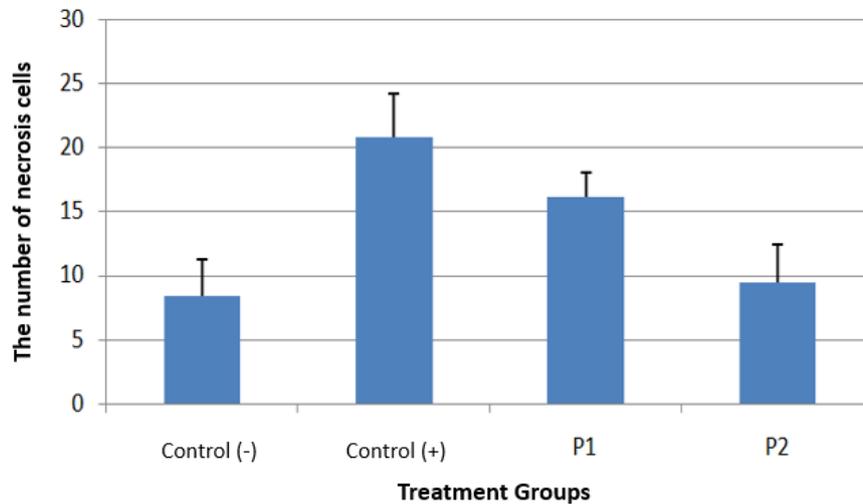


Figure 5. The number of necrosis cells.

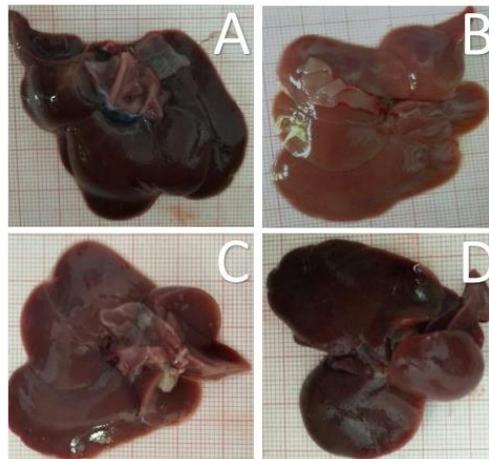


Figure 6. Normal liver has a brownish red color (A) the liver given LPS treatment has a pale color (B) liver organs given LPS and given turmeric extract 400mg/kgBW have red and slightly pale color (C) liver which is given LPS and given 600mg/kgBW turmeric rhizome extract has a brownish red color (D).

4. Conclusions

- LPS can damage hepatocyte cells, parenchyma, hydrophic, and necrosis, while turmeric rhizome extract can improve hepatocyte, parenchymal, hydrophic, and necrosis cell damage in PE rats significantly ($p < 0.05$).
- Turmeric rhizome extract can improve damage from both hepar color morphology and histology in rats given LPS.
- Turmeric extract at a dose of 400 mg / kgBW can reduce the level of liver damage and at a dose of 600 mg / kgBW can also significantly reduce the level of liver damage in PE rats ($p < 0.05$).

References

- [1] Lubis, R., Ilyas, S., Panggabean, M. 2018. The effectivity test of *Aloe vera* leaf extract to larvae AEDES sp. Asian Journal of Pharmaceutical and Clinical Research 11(7):262.
- [2] Weny, WNF., S Ilyas, S., Panggabean, M., 2018. The effectivity test of *Aloe vera* leaf extract to larvae culex species. Asian Journal of Pharmaceutical and Clinical Research 11(7):255
- [3] Situmorang PC and Ilyas S. 2018. Description of Testes Histology of *Mus musculus* after giving nano herbal *Rhodomyrtus tomentosa* (Haramonting). Asian J Pharm Clin Res. 11(11)
- [4] Satria D, Silalahi J, Haro G, Ilyas S, Poppy Anjelisa Z Hsb. 2017. Antioxidant and Antiproliferative Activities of an Ethylacetate Fraction of *Picria Fel-Terrae* Lour. Herbs. Asian Pac J Cancer Prev, 18(2), 399-403.
- [5] Ilyas, S., Hutahaean, S., Irianti, D.E. 2018. Transforming growth factor expression (TGF- β) correlate with serum level of malondialdehyde (MDA) after EVOO administration in preclinical rat models of preeclampsia. IOP Conf. Ser.: Earth Environ. Sci. 130 - 012048.
- [6] Allaire AD, Ballenger KA, Wells SR, McMahan MJ, Lessey BA. 2000. Placental Apoptosis In Preeclampsia. Obstet Gynecol 96:271-6
- [7] Irianti, E., Ilyas, S., Hutahaen, S., Rosidah. 2018. The role of EVOO (extra virgin olive oil) in serum MDA concentration and blood pressure of pregnant mice (*Rattus norvegicus*) with pre-eclampsia. Research J. Pharm. and Tech, 11(3):1053-1057.
- [8] Braha MIA, 2003. Effect of 30-Day Percent Doses of Coffee on Winstar Mouse Liver Histology. [Final report]. Semarang: Diponegoro University.
- [9] Ikpeama, Ahamefula, Prof. Onwuka, G. I. and Nwankwo, Chibuzo. 2014. Nutritional Composition of Tumeric (*Curcuma longa*) and its Antimicrobial Properties. International Journal of Scientific & Engineering Research, 5(10).
- [10] Situmorang PC dan Ilyas S. 2018. Study of Preeclampsia In Placenta, Kidney, And hepatic Diseases. Asian Journal of Pharmaceutical and Clinical Research. 11(11). 21-28
- [11] Ilyas S. 2018. The correlation of some of the heating of various palm oils to histologic and liver function of rats (*Rattus norvegicus*). IOP Conf. Series: Journal of Physics: Conf. Series 1116 - 052032.
- [12] SKDI. 2007. Number of Maternal Mortality. In: RI D, editor. Jakarta: Directorate of Maternal Health. 1-6.
- [13] Yoshitani T, H Yagi, N Inotsume, and M Yasuhara. 2002. Effect Experimental Renal Failure On The Pharmacokinetics of Losartan In Rats. Biol. Pharm. Bull. 25(8).
- [14] Hutahaean, S., R D Banjarnahor, P Darsini, Ilyas, S, and E Sabri. 2018. The effect of *Saurauia vulcani* Korth. leaves extract on penile corpus cavernosa microstructure and the quality of sperm in alloxan-induced diabetic mice. IOP Conf. Series: Journal of Physics: Conf. Series 1116 – 052030.
- [15] Ilyas S, Hutahaean, S., Nursal. 2018. Transforming growth factor beta of testis germinal cell in Guinea pig (*Cavia porcellus*) after exposure to methanol extract of the seeds of bitter melon (*Momordica charantia*) and depot medroxyprogesterone acetate. Asian Journal of Pharmaceutical and Clinical Research 11(12):149
- [16] Hutapea, A., Hutahaean, S., and Ilyas, S. 2018. Influence of pirdot leaf (*Saurauia vulcani*, korth.) extract on the blood glucose rate and histologic description of the retina of male mice (*Mus musculus* strain ddw). Asian J Pharm Clin Res, 11(11), 389-392.
- [17] Sari MI, Ilyas S, Tri Widyawati, Antika MA. 2018. Effect of *Lawsonia innermis* (Linn) leaves ethanolic extract on blood glucose and malondialdehyde level in alloxan-induced diabetic rats. IOP Conf. Series: Earth and Environmental Science 130 - 012034.
- [18] Ilyas, S., 2014. Effect of methanolic *Momordica charantia* seed extract and depot medroxyprogesterone acetate (DMPA) to quantity and quality of rat sperm. Syafruddin Ilyas Int.J. PharmTech Res.,6(6), 1817-1823.

- [19] Ilyas, S. 2018. Histological changes in the testis if the guinea pig during administration of methanol extract of bitter melon (*Momordica charantia* L.) seed and DMPA. IOP Conf. Series: Journal of Physics: Conf. Series 1116 - 052031.
- [20] Ilyas, S., Hutahaean, S., Nursal. 2018. Quantity and quality of guinea pig (*Cavia porcellus*) spermatozoa after administration of methanol extract of bitter melon (*Momordica charantia*) seed and depot medroxy progesterone acetate (DMPA). IOP Conf. Series: Earth and Environmental Science 130 - 012047.
- [21] Hasibuan R, Ilyas S, and Hannum,S. 2015. Effect of leaf extract Haramonting (*Rhodymyrtus tomentosa*) to lower blood sugar levels in mice induced by alloxan. *International Journal of Pharmatech Research*. 8(6): 284-291.
- [22] Ilyas S, Hutahaean S, Nursal. 2016. Apoptosis overview of cerebellum Purkinje cell in mice (*Mus musculus* L.) after exposure to methanol extract of the seeds of bitter melon (*Momordica charantia*) and DMPA. *International Journal of Pharmtech Research*, 9(9): 444-449.
- [23] Masyithah C, Hadisahputra S, Ilyas S. 2015. Combinational effects of ethylacetate extract of *Zanthoxylum acanthopodium* DC. With doxorubicinon MCF7 breast cancer cells. *Int.J. PharmTech Res.*, 7(4), 651-653.
- [24] Fajariyah, S. 2010. Synthetic Estrogen Delivery Effects (Diethylstilbestrol) on Hepar And Level Structure SGOT And SGPT In Mice (*Mus musculus*) Balb/C Female Strain. *Journal of Basic Science*. 11 :76-82
- [25] Ilyas S., Tanjung, R.S., Thahira, D., Wulandari, J. 2018. Effectiveness of administration haramounting leaf (*Rhodymyrtus tomentosa*) as antioxidant in preventing the damage pancreas mice (*Mus musculus* L.) after exposure of electric cigarette smoke. IOP Conf. Series: Journal of Physics: Conf. Series 1116 - 052084.
- [26] Yusuf, F., Ilyas, S., Damanik, H.A., Fatchiyah, F., 2018. Microbiota Composition, HSP70 and Caspase-3 Expression as Marker for Colorectal Cancer Patients in Aceh, Indonesia. *Acta Med Indones-Indones J Intern Med*. 289-299.
- [27] Ilyas, S., Tanjung RS, Thahira D, Wulandari J. 2018. Effectiveness of administration haramounting leaf (*Rhodymyrtus tomentosa*) as antioxidant in preventing the damage pancreas mice (*Mus musculus* L.) after exposure of electric cigarette smoke. IOP Journal of Physics : Conference Series 1116 - 052084: 1 -6.
- [28] Siribamrungwong M, Chinudomwong P. 2016. Relation Between Acute Kidney Injury and Pregnancy Related Factors. *J Acute Dis*. 5: 22-8.
- [29] Irianti, E, Ilyas,S., Rosidah, and Hutahaean, S. 2017. Hsp70 Expression Profile in Preeclampsia Model of Pregnant Rat (*Rattus norvegicus*) after Giving the EVOO. IOP Conf. Ser.: Mater. Sci. Eng. 180 - 012161.
- [30] Ilyas S, Lestari SW, Moeloek N, Asmarinah, Siregar NC. 2013. Induction of rat germ cell apoptosis by testosterone undecanoate and depot medroxyprogesterone acetate and correlation of apoptotic cells with sperm concentration. *Acta Med Indones-Indones J Intern Med*. 45(1), 32-37.
- [31] Masfria, Harahap U, Nasution MP, Ilyas S. 2014. Cytotoxic activity, proliferation inhibition and apoptosis induction of *Rhaphidophora pinnata* (L.F.) schott chloroform fraction to MCF-7 cell line. *Int.J. PharmTech Res*, 6(4), 1327-1333.
- [32] Situmorang, P., S. Ilyas. 2019. Description of Kidney Histology of *Mus musculus* After Giving Nano Herbal *Rhodymyrtus tomentosa* (Haramounting). *International Journal of Ecophysiology* Vol. 01, No. 01, 26–33.