ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 12, Issue, 01, pp.9281-9284, January, 2020

DOI: https://doi.org/10.24941/ijcr.37708.01.2020

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

POTENCY OF GINGER EXTRACT *(ZINGERBER OFFICINALE ROSCOE)* AS ANTIOXIDANT AND HEPATOPROTECTOR FOR LIVER AND PULMONARY TISSUE IN EXPOSED MICE *(MUS MUSCULUS)* BY ORGANOPHOSPHATE PESTICIDES

***Umi Rahayu, SKM. M.Kes, Imam Thohari ST, MMKes, Ngadino, S. Si., M.Psi**

Health Polytechnic of Ministry of Health in Surabaya

ARTICLE INFO

Article History:
Received 14th October, 2019
Received in revised form
28th November, 2019
Accepted 29th December, 2019
Published online 30th January, 2020

Key Words:
Pesticides, Ginger,
Liver and Pulmonary.

ABSTRACT

Pesticides as bioactive substances contain poison for killing plant-disturbing organism. Pesticides exposure can cause damage for liver and pulmonary tissue. Each active substance that is contained in pesticides causes different symptoms of poisoning. The symptoms of poisoning (subjective complaints) which are caused as the impact of pesticides will be improved by us through providing ginger extract. Moreover, this research will be applied to mice *(Mus musculus)*. This research aimed at analyzing the influence of providing ginger extract *(Zingiber officinale Roscoe)* as antioxidant against the protection of liver and pulmonary damage due to pesticides exposure in mice. Design of this research was Quasi Experimental research by using simple experimental design (Post Test Only Control Group Design). Sample in this research was healthy male Swiss Webster white mice. An examination was conducted in order to investigate tissue damage on experimental animals' liver and pulmonary. The research result showed that there was liver cell damage in K0 group (without any treatment). Besides, there were normal cell and the lightest damage (less than 25%). In K1 group, it was occurred cell degeneration and hepatotic damage in mild, moderate, and chronic hepatocyte damage. In K3 group, it was occurred cell degeneration and hepatocyte damage in mild, moderate, and chronic level. However, improving liver cells was through providing ginger extract. Through adding ginger extract, improving damage on pulmonary organ cells was also much better. In conclusion, by providing ginger extract in mice which were exposed by pesticides had no role in repairing liver cell damage. In contrary, in pulmonary organ, it was occurred an improvement of mice's pulmonary organ cell. Nevertheless, for further research, it needs to be conducted a research in smaller dose of ginger extract.

Citation: ***Umi Rahayu, SKM. M.Kes, Imam Thohari ST, MMKes, Ngadino, S.Si., M.Psi,*** **2020.** "Potency of ginger extract *(zingerber officinale roscoe)* as antioxidant and hepatoprotector for liver and pulmonary tissue in exposed mice *(mus musculus)* by organophosphate pesticides", *International Journal of Current Research*, 12, (01), 9281-9284.

INTRODUCTION

The use of organophosphate pesticides in Indonesia is conducted by spraying after the attack of pests and this is worsened by unconcern from the farmers regarding the use of organophosphates which is dangerous for bodily health. Farmers in Indonesia need pesticides in their life, but they are less care regarding the impact of pesticides. The symptoms of being poisoned (subjective complaint) from organophosphate and carbamate groups are such as arising certain muscle movements, blurred vision, watery eyes, foaming mouth, sweating much, salivating much, dizziness, nausea, convulsions, vomiting, fast heart, shortness of breath, and rapid heartbeat.

****Corresponding author:*** **Umi Rahayu, SKM. M.Kes,**
Health Polytechnic of Ministry of Health in Surabaya.

Several substances which are contained in pesticides (such as organophosphate and carbamate groups) can reduce the ability of cholinesterase enzyme to hydrolyse acetylcholine. Thus, rate of stimulation delivering in nerve impulses is hindered and finally, it will cause abnormality of nervous system (Rasyid, 1995).Furthermore, main function of liver is detoxification of toxic substances in the body. Liver disfunction will impact on the hindered formation of red blood cells and the disruption of food substances metabolism. Liver is an organ that can metabolize and excrete several chemicals (Mansur, 2008). In order to increase the improvement of liver function, particularly for farmer who is exposed by pesticide poison, it needs to be looked for natural substances which are easy to be obtained, cheap, easy to be processed, and non-toxic. Ginger is one of the most used spices in society. It contains antioxidant-gingerol as food ingredient and Indonesian traditional beverage / medicine.

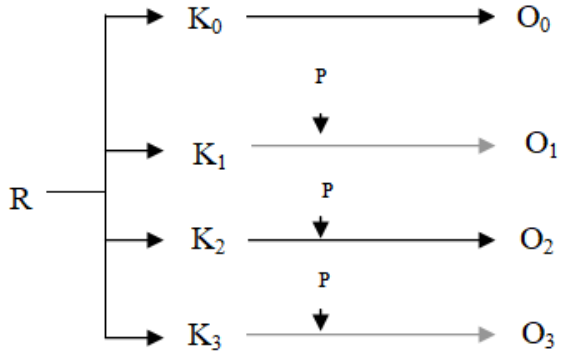
Moreover, it has been conducted a research against SGPT (Serum Glutamic Pyruvate Transaminase) level and description of hepatic histopathology due to exposure of Allaetrin by Achmad Fathir in 2010. Rachmaniyah et.al, in 2018 with the title "*Pengaruh rimpang Jahe (Zingerber officinale Roscoe) terhadap aktivitas enzim Kolinestarase akibat paparan pestisida pada mencit terpapar pestisida Organofosfat*" (Effect of Ginger rhizome (*Zingerber officinale Roscoe*) on cholinestarase enzyme activity due to pesticide exposure in exposed mice by Organophosphate pesticides) has proved that ginger has very strong antioxidant activity and can improve cholinesterase enzyme activity in mice which are exposed by pesticides. In conducted research by Fugio et al regarding the characteristic of antioxidant in chemical component of ginger was found the component of several compounds which had important role in antioxidant activity of ginger: gingerdiol, gingerol, caffeic acid, camphene, capsaicin, chlorogenic acid, curcumin, delphinidin, eugenol, ferulic acid, gamma terpinen, isoeugenol, melatonin, myrcene, sam vanilat, vanillin, and zingerone. (Utami A Meryalita Prihatin et al, 2012). Conducted research by Yuli Haryani, 2016, also proved that ginger rhizome water extract (*Zingiber off Cinale*) could reduce AgNO3 in simple biosynthesis of silver nanoparticles at room temperature simply. Result of previous research (Imam Thohari et al, 2017) explained the function of red guava extract (*Psidium Guajava L*) as antioxidant that could protect liver cell membranes damage due to exposure of cigarette smoke. This research proved that red guava extract (*Psidium Guajava L*) could improve cell membrane that was seen through how big the serosis in liver cell in white mice after being induced by cigarette smoke.

Result of conducted research by Anam(2008) proved that the poisoning level of farmers by pesticides in Batu Mediri sub-village, Karang Pule sub-district showed that from 11 farmers who did not use personal protective equipment, the 10 farmers of them (90%) suffered from mild poisoning and 1 farmer suffered from moderate poisoning. There were 13 farmers who were landowners and 112 farm laborers in Kembang Kuning Hamlet Sub-Village, Gerimax Village, Narmada Sub-District, West Lombok District, Indonesia used pesticides in organophosphate and carbamate category and type of Parathion and Selvin by spraying. Until recently, it has no research which explains that ginger rhizome can repair liver cell damage due to exposure of pesticide smoke. Moreover, according to the background above, we were interested to conduct a research with title: **"***Hipoprotektor ekstract jahe sebagai antioksidan pada mencit yang terpapar pestisida*" (Hypoprotector of ginger extract as an antioxidant on exposed mice by pesticides). This research was as an alternative of solution for the farmers who were pesticide poisoning by using ginger rhizome as the antioxidant because from preliminary research, it stated that ginger extract *(zinger officinle rosue*) as antioxidant had succeeded to improve the activity of cholinesterase enzymes and reduce SGOT (serum glutamic oxaloacetic transaminase) levels in experimental animals.

From the previous research, Lilis S 2005, proved the biggest content in ginger rhizome was gingerol 6,1% and shogaol 4,3%, which were as active substances as the antioxidant. Furthermore, this research aimed at analyzing the influence of providing ginger extract *(Zingiber officinale Roscoe)* as an antioxidant against the protection of liver and pulmonary damage due to exposure of pesticides in0,005 gr/l on white mice.

RESEARCH METHOD

This research was quasi-experimental research by using simple experimental design (Post Test Only Control GroupDesign). One group in this research was given a treatment and another group was not given any treatment. For the sample collection, the researchers used simpler and omsampling method. The sample in this research was male white mice which were 3-4 weeks old and their weight were about 20-25gr.The minimum sample that was used was 7 mice for each group, thus, total sample in this research was 28 mice. Schematically, design of this research could be illustrated as below:



Notes:

R: randomization
$K_{0:}$ pretest group (without any treatment)
K_1 : treatment group 1(being given exposure of pesticide smoke in 0,001gr/l)
K_2: treatment group 2 (being given pesticide smoke and given treatment of ginger extract in 0,0001 gr/lt)
K_3: treatment group 3 (being given pesticide smoke and given treatment of ginger rhizome extract in dose of 0,005 g/lt)

Research Procedures

Preparation for Experimental Animal: Experimental animals (white mice) were adapted for 7 days by feeding, drinking, and resting naturally in a cage (being bred in Biochemistry Laboratory of Airlangga University in Surabaya, East Java Province, Indonesia). Besides, the mice were grouped randomly to be 4 treatment groups.

Providing Pesticides in Experimental Animal: The exposure of cigarette smoke was for 1 month. In a day, the experimental mice were exposed by pesticides in 0,001 gr/lt. The exposure was conducted by using nebulizer (usually was used for baby), then, it was connected to spray tool which was sprayed into the Indonesian traditionaldrum (*kendang*).

Providing ginger extract: *(Zingiber officinale Roscoe)*was given through *sonde*, into white mice's mouth every day with the dose in 0,001 and 0,005 gr/lt.

Taking the pulmonary and liver organ from experimental animal (white mice) was conducted by surgery firstly. Some organ that will be made for microscope observation object (*preparat*) was saved firstly in PFA solution (*Paraformaldehid* 4%). Producing microscope observation object (*preparat*) used HE(Hematoksilin Eosin) staining method. The observation was focused on smooth muscle tissue (conducted in Anatomy laboratory of Airlangga University Surabaya).

Observation of Histopathology of Liver: Observation was conducted by looking at the microscope observation object (*preparat*) of histopathology of liver between treatment group and control group through magnification of 400 times. Then, it was counted for average of weight score for histopathological change. Meanwhile, the criteria of assessment of cell histopathology degrees were:

Observation of Histopathology of Liver: The observation was seen from the microscope observation object (*preparat)* from staining result in magnification of 100x and the target that was read was the percentage of widening of alveolar lumen in broad field of view and presence of infiltration of inflammation cell.

RESEARCH RESULT

Histopathological damage of mice's(Musmusculus) Liver Tissue due to the exposure of pesticide in 0,0001 gr/l: One of the purposes in this research was in order to investigate cell damage of liver tissue as the influence of pesticide exposure in 0,001 gr/lt. An observation was conducted in Control Group (K0) and Treatment Group (group that was exposed by pesticides (K1)). However, there was a significant difference from both of them. In K0 group, the average of weight score was 73% and it was occurred histopathic changes in the liver from four fields of view. Meanwhile, the average in K1 group resulted58%.According to the observation result in K0 group, hepatocytes were seemed normal which were showed by the composition of liver cells and they were consisted of hexagonal units, which were known as lobules hepaticus (liver). The center of each lobule was a central vein, which was radially surrounded by a plate of liver cells and the shape of the cells were round and oval.

Rate of Change	Value
Normal	0
Damage of mild hepatocyte cells (≤ 25%)	1
Damage of moderate hepatocyte cells (25-50%)	2
Damage of chronic hepatocyte cells (≥50%)	3

Rate of Change	Value
Normal	0
Occurred damage cells/ infiltration of inflammation cell (mild) ≤ 25%from broad field of view	1
Occurred damage cells/ infiltration of inflammation cell (moderate)25-50%from broad field of view	2
Occurred damage cells/ infiltration of inflammation cell (chronic)≥50%from broad field of view	3

The damage of liver cell in K1 group (treatment 1) that was exposed by pesticides in 0,001 gr/lt showed the liver cell degenerated and underwent necrosis in around 25 – 50%. The damage of liver cell by pesticides was likely occurred as the impact of several factors, dose, exposure time, and its types. Commonly, the liver cell had high regeneration ability, tissue loss due to toxic substances that triggered the mechanism of cell division and it continued until the improvement of tissue mass was achieved. Furthermore, necrosis process was begun by weakening of blood vessel wall, inflammatory response, and the formation of plaque which was foam cells and the blood clots was formed. Foam cell was a layer that contained macrophages which was laden with lipid and smooth muscle cells whose cytoplasm was raised by lipids. This foam cell was a component in forming lipid zones and smooth muscle cells that enlarged by lipids.

Fatty streak was consisted of fat-filled foam cells which were lesions that did not increase significantly, thus, it did not cause impaired blood flow. Furthermore, the correlation between fatty streak and atherosclerotic plaques was unclear although these patches could develop into plaques. Improvement of liver tissue cell as the impact of giving ginger extract *(Zingiber officinale Roscoe)* in dose of 0,0001 gr/l against cell damage in liver organ due to pesticide exposure in dose of 0,0005 gr/lt: In K2 group (treatment 2 (it was exposed by pesticide and was given ginger extract *(Zingiber officinale Roscoe))* as antioxidant against the improvement of tissue cell in histopathology of broncus that underwent cell damage due to exposure of cigarette smoke in white mice. The description of liver cell in this K2 group was seemed to degenerate cell. Degeneration change was a change whose process was reversible, which meant that it could return as what it was in the beginning. Thus, cell would return to be healthy as before being exposed by pesticides. Theoretically, the process of liver cell damage was begun from degeneration process with criteria of cell swelling. The criterion was observed in the treatment of providing ginger extract *(Zingiber officinale Roscoe)* that was as antioxidant. A treatment of providing *gingerol,* shogaol, *dhearil* heptanoite as high antioxidant caused extracellular fluid entered into the cytosol in large quantities. (Annisa, Agata 2016). In K2 group that was given ginger extract *(Zingiber officinale Roscoe)* as antioxidant was obtained data that damage of histopathological structure decreased more than in K1 group (without any providing ginger extract *(Zingiber officinale Roscoe)*). Shogaol that was as an antioxidant had role in improving liver cell damage due to pesticide exposure with recovery effect and the level of damage was mild (0-25%).

Improvement of tissue cell in liver due to providing ginger extract*(Zingiber officinale Roscoe)* in dose of 0,005gr/lt against cell damage in liver due to pesticide exposure in dose of 0,0001 gr/lt: In K3 group was different with K_1 group which had been exposed by pesticide in 0,0001 gr/lt for 30 days and it was injected with ginger extract as the antioxidant. Description of histopathological liver in K3 group was seen that the damage of histopathological structure decreased more rather than in K1 group (treatment only with pesticide). In this group, there was hepatosis that underwent microvescular steatosis (fatty degeneration). Besides, in liver cell, a central vein underwent blood containment that was seen as lumen of central vein and it was covered by a red mass which was the blood that blocked these vessels. Besides, there were also bleeding of veriver and inflammation cells around the liver cell. In this K3 group, there were central vein, hepatocyte, and lobius cells which were almost in normal condition. Although the decrease of damage had not reached the illustration of normal histopathology, result of this research had undergone cell improvement and this was possibly caused by lack of time in providing ginger extract *(Zingiber officinale Roscoe)*or a mistake in providing the dose. Compound in category of *Shogaol an gingerol*also could induce necrosis and stopped the cell cycle through the mechanism of inhibition of enzyme topoisomerase. *Shogaol an gingerol* also improved excretion of the glutathione S -tranferase enzyme which could detoxify carcinogens so that the body was eliminated quickly.

Conclusion

- There was damage of the structure of liver tissue (moderate hepatocyte damage) and pulmonary (scar

tissue) from the white mice due to pesticide exposure in 0,1. 10^{-6} gr/lt

- The improvement of damaged liver cell was through cell degeneration and the cell damage was in mild – moderate. In pulmonary organ, scarring had not occurred anymore.
- The improvement of liver tissue cells due to providing ginger extract (*Zingiber officinale Roscoe*) in dose of 0,0005 gr/l against cell damage in liver due topesticides exposure in 0,0001 gr/lt showed cell degenaration and hepatotic damage, such as damage with hepatocyte score in mild, moderate and chronic.

Recommendation

The results of this study can be used to repair lung organ cells for people who use pesticides in agricultural practices or pest eradication. Need to do research on the administration of ginger extract in mice exposed to pesticides with different types of ginger, dosage and time.

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