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PROCEEDING
INTERNATIONAL SEMINAR

CHALLENGES OF THE DEVELOPMENT OF NATURAL COMPOUND AS DRUG FOR INFECTIOUS & DEGENERATIVE DISEASES

Faculty of Pharmacy & Sciences
University Of Muhammadiyah Prof. DR. HAMKA
(UHAMKA)
Jakarta, January 10, 2015

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Remarks of the Dean of Faculty of Pharmacy & Sciences (FFS) UHAMKA

Assalamu'alaikumWr.Wb.

Distinguished ladies and gentlemen

First of all, on behalf of FFS UHAMKA, I would like to welcome to all of you in FFS UHAMKA Jakarta. Thank you very much for your attention to come and attend the international seminar in FFS UHAMKA. I hope we are all in health condition and in the shadow of God.

The conference is organized by FFS UHAMKA in collaboration with sponsors like PT. Triasindo Jaya , Indolab and UHAMQUA. This event is as part of the routine activities with the purpose are: discuss an update on the challenges of drug development for infectious and degenerative diseases based on natural product and provide a forum for exchange of information on the latest technologies involved in the development of natural compounds as drug.

In this seminar participants from student, lecturer, researchers have been attanded and 4 speakers within field of Pharmaceutical sciences will be presented paper with theme "Natural Compound as Therapy for Infectious and Degenerative Diseases". Besides that, this conference followed by presentation researchers in form of oral and poster presentation. Herewith we would like to express our gratitude to all participants, presenters, and special thanks to plenary speakers for joint us to day to share advance knowledge and expertise in this scientific event in FFS UHAMKA.

The FFS gratefully acknowledges the Rector of UHAMKA University, minister of Health of Indonesia, and sponsors for the nice collaboration in bringing this seminar. Furthermore, personally, I would like to express my deep appreciation to members of the Organizing Committee, for the good teamwork and their great effort to bring success to the seminar.

Finally, I wish all participants could benefit from the seminar and have an enjoyable moment in FFS UHAMKA Jakarta.

I look forward to thank you all for attending this seminar

Wassalamualaikum Warrohamatullahi Wabbarokatuh

Drs. H. Budi Arman, M. Kes, Apt.

Remarks From Rector

Bismillahirahmanirrahim,

Your Excellency, Minister of Health Republic of Indonesia
Respected Resource Persons
Respected Participants, Ladies and Gentlemen

On behalf of University of Muhammadiyah Prof. Dr. HAMKA (UHAMKA), I would like to warmly welcome you all to attend and participate in the International Seminar on "Challenges of the Development of Natural Compound as Drug for Infectious and Degenerative Disease," on Saturday, January 10, 2015 at Auditorium UHAMKA.

This international seminar is a very prestigious and academic event which has to be appreciated since the topics and sub-topics such as Natural Product Chemistry, Pharmacology, Molecular Biology and Biotechnology and Pharmaceutical Technology & Compound are crucial issues today, particularly in the pharmaceutical discipline.

This academic event becomes more significant as there are some respected experts and resource persons who know how in the field of pharmacology, biotechnology, pharmaceutical technology and compound. Through this seminar, they present their research findings and scientific experiences and share them to the participants. We wish that all participants will get valuable lesson learned from these resource persons and experts.

In addition to the presentation from keynote speaker and experts, there are also poster sessions which display the research findings which, hopefully, inspire other participants to make further research dealing with the current issue in the development of natural compound as Drugs for Infectious and Degenerative Diseases.

To make this international seminar successful, I do hope that all participants are very active to quest and explore the given ideas occurred during this seminar so that this will provide significant contribution to the development of pharmacy in particular and drugs or medicines in general for the sake of humanity health.

At last, I would like to express my sincerely thank all resource persons, Prof. Dr. Nila Djuwita F. Moeloek, Sp.M (K) (Minister of Health Republic of Indonesia) , Prof. Dr. Ibrahim Jantan (UKM), Prof. Dr. Endang Hanani, SU., M.Si (UHAMKA), Prof. Dr. Oliver Kayser (The Technical Biochemistry, TU Dortmund, Germany), and Prof. Dr. Krisana Kraisintu (Faculty of Oriental Medicine, Rangsit University, Thailand).

Jakarta, January 2015

Rector,

Prof. Dr. H. Suyatno, M.Pd.

CONTENT

SUBCHRONIC TOXICITY TEST OF COMBINATION OF GINGER (*Zingiber officinale* Rosc.) EXTRACT AND *ZINC* ON SWISS WEBSTER MICE

Hadi Sunaryo. Siska. Dwitiyanti. Rizky Arcinthya Rachmania. Roja Fathul Mubdy

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ABSTRACT

The combination of ginger *(Zingiber officinale* Rosc.*)* extract and *zinc* has the effect of lowering levels of glucose. triglycerides. cholesterol and anti-oxidants. This study aimed to determine the safety administration of combination ginger extract and zinc. through subchronic toxicity test. Parameters measured were body weight. liver and kidney histopathology. SGOT. and SGPT. The study used a sample of 20 male mice. divided into one control group and one treatment group. The extract was given orally through a sonde for 75 days. The treatment group were given a combination of ginger extract and zinc (ginger 30mg / 20g BW + zinc 0.4mg / 20g BW) and control group was given a water. After 75 days of treatment sample blood the heart and then checked SGOT and SGPT. Collected statistical from result with the method of independent samples T test showed no significant difference between the levels of SGOT ang SGPT control group to the treatment group. It can be concluded combination ginger extract and zinc did not show any toxic effects in subchronic and did not cause toxicity and damage to vital organs. such as liver and kidney.

Keywords*:* subchronic toxicity . ginger extract and zinc. SGOT. SGPT

INTRODUCTION

Studies on medicinal plants need to be done so that it can be used safely and effectively. Pre-clinical trials is one of step drug testing.

Subkronic toxicity test is one of preclinical trials for test the toxicity and safety of a given compound With repeated doses in animal specific. for less than three months. This test is intended to reveal the toxic effects of test compounds as well as to show whether the toxic effects related to measure of the dose (Donatus. 2005).

Diabetes mellitus is a chronic disorder of the metabolism of carbohydrates. fats. and proteins (Robbins 2007). Lipids in diabetics caused by insulin deficiency. It occurs due to disruption of the function of insulin because of the complications of high blood

lipid levels. especially cholesterol and triglycerides (Widyastuti 2001). DM is a degenerative disease. so patients need treatment special diet. lifestyle regularly and heavily dependent on drugs hypoglycemic (Baines 1999).

Ginger (*Zingiber officinale* Rosc.) is one of medicinal plants in Indonesia which has a high economic value and has many benefits. Ginger contains essential oils With major components zingiberen zingiberol. and gingerol oleoresin With the major components (POM RI 2004) useful for pain relief. anti-inflammatory. and antibacterial (Latif 2002).

Zinc (Zn) is one of micro minerals needed for each cell in the body. Adequacy of these minerals essential in keeping optimal health. Zn deficiency in diabetics can lead to disruption of the immune system (Jacobus 2000). In addition to antioxidant properties of zinc can also reduce levels of cholesterol and triglycerides (Reiterer *et.al* 2005).

In previous study mentioned that the combination of 70% ethanol extract of ginger (*Zingeber officinale* Rosc.) and zinc at a dose of 3 mg / 20g BW + Zn 0.4 mg / 20g BW can lower blood glucose levels. triglycerides. total cholesterol. LDL. and raise levels of HDL (Sunaryo Hadi *et al*. 2013; Sunaryo Hadi *et al*. 2014). If the activity is given the combination of ethanol extract of ginger and zinc have activity as antihipercolesterol antihiperglicemia and this can contribute to the development of drugs by utilizing the results from natural materials. But still uncertain safety of the compound. Therefore. it was conducted one of the pre-clinical trials that subchronic toxicity tests for ensure the safety and the highest dose in the repeated use of a compound. By using the highest therapeutic dose administered repeatedly for 75 days for determine the effect of the combination of ethanol extract of ginger and zinc.

MATERIALS AND METHODS

Materials:

Ginger was obtained from the Institute for Medicinal Plant Research. Bogor. Material after drying in a temperature of about 50°C. powdered extract was then made thicker with the maceration using ethanol 70%.

Test Animal:

White male mice *Swiss webster* strain. aged 2-3 months weighing about 20-30 grams. As many as 20 mice were divided into one control group and one treatment group.

Methods:

Extract Preparations

As much as 25 kg of dried ginger produces 2.5 kg of powder ginger. Then ginger powder was extracted using maceration method using 70% ethanol as a liquid maserate and produced 18.8 L maserat. Maserate results obtained using a vacuum rotary evaporator and the resulting extract in the oven until viscous.

The test material was administered orally via sonde each day for 75 days. The health condition of the test animals was checked every day to know the symptoms of toxic effects and weighed every day. The control group was given food and drink and the standard treatment group received a dose (ginger 30mg / BW + zinc 0.4mg/20g BW). At the end of 75 days the animals were anesthetized with ketamine then try surgery for blood sampling through the heart to be examined SGOT and SGPT. After the blood was collected through the heart followed by taking the liver and kidneys for making preparations for histopathology as macroscopic observation in a standard way using hematokisilin eosin staining for the presence or absence of histopathologic abnormalities.

RESULTS

The experimental results Subchronic toxicity combination ginger extract and zinc are listed in the table.

Table 1. The average weight observations mice for 75 days.

Groups	Days								
	1	10	20	30	40	50	60	70	75
Controls	32.7	34.1	39.8	40.4	40.9	41.1	42	44.2	44.5

Treatments	31.9	33	36.5	36	36.9	36.9	38.5	37.5	37.7

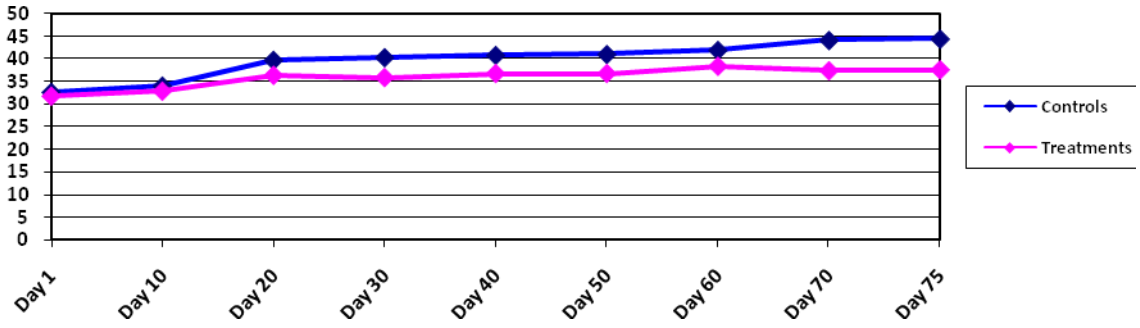

Figure 1. The average weight observations mice for 75 days.

Table 2. Results of macroscopic examination of the liver and kidneys of mice after 75 days.

Groups	Macroscopic Observation	Liver	Kidney
Control	Color	Normal	Normal
	Form	Normal	Normal
Treatment	Color	Normal	Normal
	Form	Normal	Normal

Table 3. The average yield SGOT and SGPT examination mice.

Groups	SGOT	SGPT
Control	13.9794 u/L	8.79 u/L
Treatment	17.6026 u/L	16.5476 u/L

DISCUSSION

Early stages of this research is the determination. Determination aims to get the true identity of the plants that will be tested its efficacy. so it can be provide the certainty about the truth of these plants. Based on the results of determination of plants

that will be used as the main substance in this study is completely ginger (*Zingiber officinale* Rosc.).

Making the ginger simplicia begins with sorting so ginger wet clean of impurities such as soil attached. then be washed using water flowing. After cleaning ginger sliced with the aim of expanding the material surface to accelerate the drying process. The drying process was done by aerated in order not damage the active substance content of ginger.

The extraction method used in this study is maceration. This method was used because it is easy and simple and did not require heating so it is suitable to active substances which did not resistant heating. The first stage was conducted by soaking the crude drug powder with liquid extract. Extract fluid used was ethanol 70%. because ethanol is more selective against fungi and bacteria so it is difficult to grow. did not toxic and its has well absorb. The water content in 70% ethanol serves to break down the cell walls that contain the active substance resulting in swelling of the cell so that ethanol can enter the cell and the active substance attracted by the solvent. At the time of immersion occasional stirring to flatten the concentration of the solution due to the concentration difference between the solution in the cell and outside the cell solution. Maserat separation using filter paper with no pollen extracts goal that brought into maserat. Maserat obtained was concentrated using a rotary vacuum evaporator so that there was a separation between the active substance and the solvent used is based on differences in boiling point. Concentration using a low temperature process ± 50ºC in order not to affect the quality of the active substance. Then dried in an oven to remove residual solvent in order to obtain ethanol-free viscous extract.

Viscous extract obtained was conducted phytochemical screening. to determine the compounds contained in the viscous extract. Screening results was obtained a positive result in phytochemical screening are alkaloids. flavonoids and triterpenoids.

In this research sub-chronic toxicity test combination of 70% ethanol extract of ginger with zinc using white mice strains Swiss Webster. Sub-chronic toxicity test was conducted by giving a combination of ethanol extract of ginger with zinc for 75 days and once daily dosing.

The selection of the dose was based on the highest therapeutic dose that did not result in death was obtained in acute toxicity tests. Giving time of ginger extract

combination With zinc for 75 days. Selection of 75 days to fulfill the requirements of observation subchronic toxicity test which is usually between 4 weeks to 3 months (Donatu 2005). Then did the histology of liver and kidney in the control group and the treatment group and checks the value of SGOT and SGPT. It was conducted to determine the possible target organs affected by a combination of 70% ethanol extract of ginger with zinc and comparing SGOT SGPT of control group with SGOT SGPT of treatment group.

Research using animal testing young adults in a sense still in the process of growth that can be known directly and optimal effect of the test material by using parameters observation of symptoms of toxic effects and weighing during the experiment. It turns out that the results of the experiment shows that the weight of test animals during the 75-day study did not decrease. even increased and the provision of test materials for 75 days did not cause toxic effects on mice.

On macroscopic examination of the liver and kidneys of mice was not found specific abnormalities or within normal limits.

Histological examination was conducted on liver and kidney of white mice qualitatively by looking at the composition of the liver structure namely central venous cells and cells of hepatocytes.

While in the kidneys by looking at the structure of the glomerulus. Can be seen in Figure 1. 2. 3 and 4.

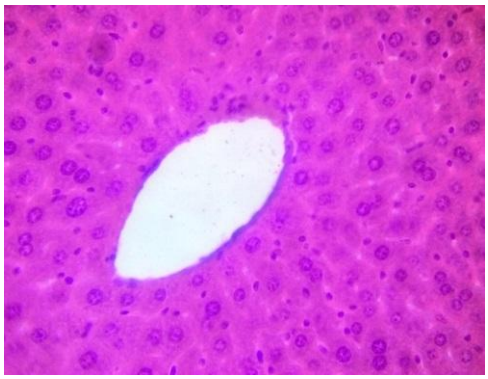

Figure 2. Preparat of histology liver of control group.

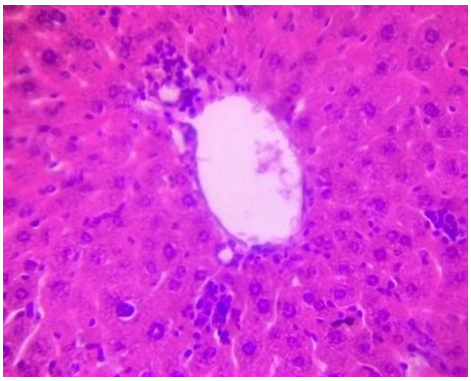

Figure 3. Preparat of histology liver of treatment group.

Histological examination of the liver preparations between the control group with treatment group found slightly difference in which in Figure 2 structure central

venous. endothelial cells look normal. while in Figure 3 the structure of endothelium damaged by inflammation so that the structure of central venous becomes damaged.

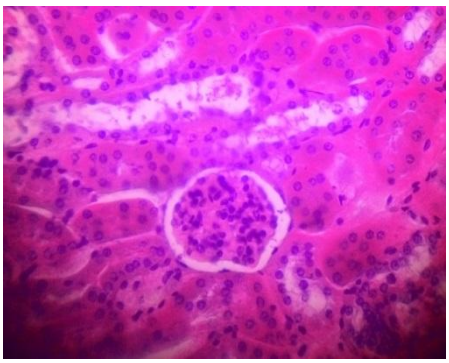

Figure 4. Preparat of histology kidney of control group.

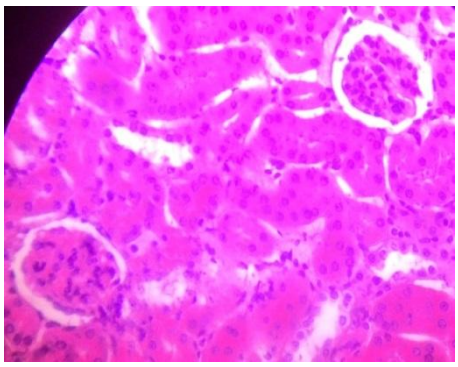

Figure 5. Preparat of histology kidney of control group.

Examination of histological preparations renal glomerular structure found slightly difference between the control group to the treatment group. In Figure 4 is a normal glomerular structure. In Figure 5 seen the widening gap between the glomerulus and Bowman's capsule.

Another thing to consider is the examination of SGOT and SGPT. but found no significant difference in the levels of SGOT and SGPT after statistically tested with t-Tests (Table 3).\

CONCLUSION

Giving a combination of extracts of ginger (*Zingiber officinale* Rosc.) with zinc at a dose (ginger extract 30mg / 20g BW mice and Zn 0.4 mg / 20gBW mice) for 75 days. based on the observation of body weight. liver and kidney histopathology. and examination of the value of SGOT and SGPT did not show any toxic effects and damage to vital organs. such as liver and kidney.

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