PROCEEDINGS PAPERS OF

1st INTERNATIONAL CONFERENCE ON CHEMISTRY, PHARMACY AND MEDICAL SCIENCES (ICCPM)

Theme: Advanced Research Development Base on Local Resources

Bengkulu, 27 – 28 November 2018

Editor: Deni Agus Triawan, S.Si., M.Sc

Penerbit: Unib press

Sponsored by
Proceedings Papers

1st International Conference on Chemistry, Pharmacy and Medical Sciences (ICCPM)

Theme: Advanced Research Development Base on Local Resources

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Publisher : UNIB PRESS
Address : LPPM UNIB,
Gedung B, Jalan W.R. Supratman, Kandang Limun, Kota Bengkulu 38371

Proceedings Papers of 1st International Conference on Chemistry, Pharmacy and Medical Sciences (ICCPM, Santika Hotel, 27-28 November 2018/ Editor Deni Agus Triawan, S.Si., M.Sc

ISBN 978-602-5A30-0L-8

http://iccpm.fmipa.unib.ac.id/
FOREWORD

Assalamu’alaikum warahmatullahi wabarakaatuh and greetings.

This proceeding contains selected papers of 1st International Conference on Chemistry, Pharmacy, and Medical Sciences (ICCPM) which held on November 26-27, 2018, Santika Hotel, Bengkulu-Indonesia. The conference which was organized by the Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Bengkulu.

The ICCPM 2018 is attended by more than 100 participants. In terms of origin, the participants of this ICCPM are coming from 6 countries i.e. Indonesia, Japan, US, Malaysia, Thailand, and India. The conference is the first international conference organized by the Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Bengkulu and is expected to be held continuously every three years.

The conference particularly encouraged the interaction of research students and developing academics with the more established academic community in an informal setting to present and to discuss new and current work. Their contributions helped to make the conference as outstanding. The papers contributed the most recent scientific knowledge known in the field of Organic Chemistry, Material Chemistry, Pharmacy, Agricultural Chemistry, and Miscellaneous topic related to chemistry.

Our deep gratitude is strongly forwarded to all individuals who took part in the conference, especially the keynote speakers, invited speakers, all the presenters and participants as well as all students and staffs who have been involved in the preparation and execution of the conference and the publication of the proceedings. Our deep gratitude also forwarded for all reviewers the manuscript for this proceedings.

These Proceedings will furnish the scientists with a good reference book. I trust also that this will be an impetus to stimulate further study and research in all these areas.

Bengkulu, 30 November 2018
General Chair of ICCPM
Prof. Dr. Morina Adfa, M.Si
Committee

1st International Conference on Chemistry, Pharmacy and Medical Sciences (ICCPM, Theme: Advanced Research Development Base on Local Resources

Santika Hotel, 27-28 November 2018

Organized by Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Bengkulu

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4. Assoc. Prof. Dr. Sirikantjana Thongmee (Kasetsart University, THAILAND)
5. Assoc. Prof. Dr. Mohammad Abrar Alam (United State of America, USA)

Invited Speaker

1. Assoc. Prof. Dr. Mohamad Rafi (Bogor Agricultural University, INDONESIA)
2. Assoc. Prof. Dr. Noor Haida Mohd Kaus (Universiti Sains Malaysia (USM), MALAYSIA)
3. Assoc. Prof. Dr. Akhmad Sabarudin, D.Sc. (Brawijaya University, INDONESIA)
4. Assoc. Prof. Dr. Oman Zuas (Research Center for Metrology - LIPI, INDONESIA)
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The Effect of Ethanol Extract of Mangosteen (Garcinia mangostana L.) Rind to LDL Level on NIDDM Type Rats

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Abstract. Increased level of LDL (Low Density Lipoprotein) is one of the causes of coronary heart disease due to food consumption habits. Diabetes mellitus type II also mostly begins with obesity due to overeating. As compensation, pancreatic β cells respond by secreting more insulin so that insulin levels increased. In diabetes conditions, level of plasma cholesterol usually increased. This can be an important role in the occurrence of vascular arteriosclerosis due to long-term conditions of diabetes mellitus. Focus of this research was to determine the effect of mangosteen rind extract to level of LDL in (non Insulin Dependent Diabetes mellitus) NIDDM-type rats. Extraction method used in this research is maceration. The test was use experimental animals that was conditioned in diabetes mellitus with streptozotosin NA for determination of glucose levels using GOD PAP and LDL levels with CHOD PAP. The results showed that ethanol extract of mangosteen rind can reduce level of LDL in NIDDM type rats with the lowest results at a dose of 100 mg.

Keywords: Garcinia mangostana L., Sreptozotosin, reactive oxygen species, LDL, NIDDM

A. Introduction

Diabetes mellitus (DM) is a disease that involves pancreatic endocrine hormones, such as insulin and glucagon. The main manifestations include disorders of lipid metabolism, carbohydrate, and protein so that it will stimulate the condition of hyperglycemia which will evolve into diabetes mellitus with various forms of complications manifestations [1]. The long-term manifestation of diabetes can cause several microvascular and macrovascular complications. Management of diabetes mellitus requires multidisciplinary treatment that includes pharmacological and non-pharmacological therapies given chronic and lifetime. Therefore, effective drugs are needed, low side effects and low prices [2].

Diabetes mellitus can trigger an increase in plasma cholesterol levels, in a long time it will cause constriction and hardening of blood vessel often called arteroclerosis. Arteroclerosis is a cause of coronary heart disease (CHD) characterized by accumulation of lipids and fibrous tissue in the coronary arteries, thus progressively constriction the lumen of blood vessels and accompanied by the occurrence of endothelial disfunction [3]. High LDL cholesterol levels can increase the risk of the body experiencing cardiovascular disorders such as coronary heart disease, peripheral vascular disease, stroke and even death, even in conditions of familial hypercholesterolemia, the body also experiences LDL receptor disorders and effected in increased of LDL levels that can be harmful to the body [4].

Coronary heart disease is the number one cause of death in the world in 2011. World Health Organization (WHO) recorded more than 117 million people died from CHD worldwide in 2002. This numbers is estimated to increase by 11 million people in 2020. In Indonesia, the case of CHD is increasingly found because of the rapid changes in lifestyle, this was stated by WHO according to Riskesdas (2013) [5].

Knowledge of medicinal plants is a national cultural heritage hereditary. Since ancient times, Indonesian people have known and used medicinal plants as an effort to overcome health problems [6]. Mangosteen rind contains xanthone as much as 107.76 mg per 100 g of mangosteen rind. Xanthone is not found in other fruits, therefore the mangosteen is called as the queen of fruits. Mangosteen contains catechins, potassium, calcium,
phosphorus, iron, vitamin B1, vitamin B2, vitamin B6, and vitamin C [7]. The mangosteen rind also contains prenylated xanthone compounds, alpha mangostin, gamma-mangostin and garsinone B [6]. Mangosteen rind contains mangostenol, mangostinon A, mangostenon B, trapezifolixanthone, tovofillin B, beta mangostin, mangostanol, flavonoids, epicatechin, gartanin and garsin E which have the potential to be anti-oxidants [8]. Xanthone compounds also act as a very strong antioxidant when compared to vitamin C and vitamin E in counteracting free radicals and preventing cell damage, also inhibiting cell degeneration [9].

Diabetes is caused by depletion of the cellular antioxidant defense system and increased of "Reactive Oxygen Species (ROS)". The new concept that oxidative stress is the originator of the beginning and evolve of diabetes can be a new choice of therapy for the treatment of disease and its complications by using antioxidants or nutrients that contain high antioxidants [10]. Mangosteen rind containing xanthone can be used as an antioxidant so that this research aims to determine the effect of ethanol extract of mangosteen rind (Garcinia mangostana L.) to decreased of LDL cholesterol levels in serum of NIDDM type rats.

B. Results and Discussion

The results of the research and calculation of LDL levels and fasting blood glucose levels of NIDDM type white rats before and after giving of mangosteen rind extract on days 1, 3 and 28 can be seen in the Table 1.

Table 1. Blood glucose levels and LDL levels in experimental animals.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Measurement Time</th>
<th>Blood Glucose Level mg/dL</th>
<th>LDL Level mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T0</td>
<td>T1</td>
<td>T2</td>
</tr>
<tr>
<td>Normal Control</td>
<td>71.418</td>
<td>72.782</td>
<td>73.452</td>
</tr>
<tr>
<td>Negative Control</td>
<td>71.894</td>
<td>258.872</td>
<td>259.54</td>
</tr>
<tr>
<td>Positive Control</td>
<td>73.446</td>
<td>268.572</td>
<td>101.070</td>
</tr>
<tr>
<td>Extract Dose 25 mg/Kg Body Weight (BW)</td>
<td>67.568</td>
<td>265.94</td>
<td>168.116</td>
</tr>
<tr>
<td>Extract Dose 50 mg/Kg Body Weight (BW)</td>
<td>71.96</td>
<td>262.06</td>
<td>132.04</td>
</tr>
<tr>
<td>Extract Dose 100 mg/Kg Body Weight (BW)</td>
<td>72.62</td>
<td>262.182</td>
<td>110.534</td>
</tr>
</tbody>
</table>

Note:
T0 : Time before treatment
T1 : Time after steptozotosin induction
T2 : Time after giving mangosteen extract

The effect of mangosteen rind extract on NIDDM type rats obtained that (T0) the average blood glucose level was normal, (T1) blood glucose levels after Streptozotocin (STZ) induction was increased, and (T2) the blood glucose average levels of the group which given mangosteen rind ethanol extract was decreases, which can be seen in Figure 1.

Fig. 1. Results graph of decrease of blood glucose levels of white rats.

The effect of mangosteen rind extract against measuring of LDL levels, showed that the measurements of the average LDL cholesterol levels on experimental animal can be seen in Figure 2, at (T0) LDL levels are still normal, (T1) LDL levels when induced by STZ was increased above normal levels, but at (T2) after giving of mangosteen rind ethanol extract, LDL cholesterol levels was decrease after giving of mangosteen rind ethanol extract, which can be seen in Figure 2.

Fig. 2. Results graph of average of LDL levels.
The glucose level measurements of the fasting blood of NIDDM rat type before the given of mangosteen extract was 259.504 mg/dL and after the given of mangosteen extract was 110.534 mg/dL at a dose of 100 mg. This shows that a decrease in blood glucose levels of rats before and after the mangosteen rind extract as can be seen in Figure 1. The ability of mangosteen rind ethanol extract in reducing blood glucose levels in STZ-induced rats can inhibit the activity of α-glucosidase enzymes in breaking down polysaccharides into glucose by cutting the α-glucoside bonds. The α-glucosidase enzyme works by breaking down the polysaccharide chain at each branching point that cannot be solved by the amylase enzyme. This enzyme plays a role in the degradation of glycogen by hydrolyzing α (1-6) bonds at the branching point of the glycogen chain to produce D-glucose and glucose residues with α (1-4) bonds [11]. Previous research also states that extract of mangosteen rind also has an influence on blood glucose levels of diabetic rats (Mus musculus L.) induced by alloxan [12].

From the results of this research, it is indicate that the condition of LDL levels showed an average result from negative controls 72.418 mg/dL become 33.754 mg/dL after given the mangosteen rind extract at a dose of 100 mg. This happens because the condition of diabetes mellitus is able to stimulate high levels of free fatty acids in the plasma and increased triacil accumulation of glycerol and phospholipids in cells, including cells that are sensitive to insulin. If triacyl glycerol and phospholipid accumulation occurs in cells, the accumulation will lead to phosphorylation of insulin receptor substrate (IRS) on serine residues, and not on tyrosine residues. This condition can interfere the signal for GLUT-4 translocation to the cell surface, resulting in hyperglycemic conditions outside the cell [13].

Based on Table 1, Figure 1 and Figure 2, it can be seen that the condition of diabetes mellitus induced by STZ can cause an increase in LDL levels under hyperglycemic conditions [13]. Increased of blood glucose level at (T1) after STZ induction is influenced by several factors such as showing the improvement of Langerhans β cells which have an impact on the increase in the hormone insulin, so that glucose can be absorbed by muscle cells, and liver cells. In addition to the above conditions, the given of mangosteen rind ethanol extract is the best decrease in the dose of 100 mg with the average LDL levels from a dose of 25 mg has average LDL 53.83 mg/dL, a dose of 50 mg has LDL levels 43.88 mg/dL) variation 25.50 to 100 mg results the decrease of LDL levels were increased due to insulin deficiency that will result in energy sources taken from the catabolism of Free Fatty Acid (FFA) so that FFA continues to increase in the blood. Excessive Free Fatty Acid (FFA) also increases the conversion of some fatty acids to phospholipid and cholesterol in the liver, high cholesterol in the liver will result in decreased process of LDL clearance in the blood and cause an increased of LDL in the blood [16]. Due to the formation of energy from fat and protein, cholesterol levels formed in the chain of protein and fat metabolism are increased in DM patients, the condition of hyperglycemia causes an increase in the production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) due to increased NADPH oxidation in endothelial tissue. Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS) are highly reactive molecules that can directly oxidize and damage the DNA, proteins, and lipids and cause oxidative stress. Oxidative stress occurs when there is an imbalance between the number of highly reactive molecules (ROS and RNS) and existing antioxidants [13].

In this research it was found that the increase of LDL cholesterol levels in experimental animals resulted in an average of negative control 72.418 mg/dL due to DM conditions where insulin deficiency that also disrupted the metabolism of proteins and fats which caused weight loss. If insulin deficiency occurs, excessive protein in the blood circulation cannot be stored in the network. All aspects of fat metabolism are greatly increased if there is no insulin [15].

The NIDDM type rats on negative control (STZ), LDL levels were increased due to insulin deficiency that will result in energy sources taken from the catabolism of Free Fatty Acid (FFA) so that FFA continues to increase in the blood. Excessive Free Fatty Acid (FFA) also increases the conversion of some fatty acids to phospholipid and cholesterol in the liver, high cholesterol in the liver will result in decreased process of LDL clearance in the blood and cause an increased of LDL in the blood [16]. Due to the formation of energy from fat and protein, cholesterol levels formed in the chain of protein and fat metabolism are increased in DM patients, the condition of hyperglycemia causes an increase in the production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) due to increased NADPH oxidation in endothelial tissue. Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS) are highly reactive molecules that can directly oxidize and damage the DNA, proteins, and lipids and cause oxidative stress. Oxidative stress occurs when there is an imbalance between the number of highly reactive molecules (ROS and RNS) and existing antioxidants [13].

After giving the ethanol extract of mangosteen rind to experimental animals NIDDM type rats with a dose variation 25.50 to 100 mg results the decrease of LDL levels from a dose of 25 mg has average LDL 53.83 mg/dL, a dose of 50 mg has LDL levels 43.88 mg/dL) the best decrease in the dose of 100 mg with the average level of LDL to 33.754 mg/dL. The decrease of LDL in the given of mangosteen rind ethanol extract is influenced by several factors such as showing the improvement of Langerhans β cells which have an impact on the increase in the hormone insulin, so that glucose can be absorbed by muscle cells, and liver cells. If triacyl glycerol and phospholipid accumulation occurs in cells, the accumulation will lead to phosphorylation of insulin receptor substrate (IRS) on serine residues, and not on tyrosine residues. This condition can interfere the signal for GLUT-4 translocation to the cell surface, resulting in hyperglycemic conditions outside the cell [13].

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C. Conclusion

Based on the results of research that has been done, it can be concluded that the mangosteen rind ethanol extract at doses of 25 mg/Kg body weight, 50 mg/Kg body weight and 100 mg/Kg body weight has an effect on reducing the level of blood glucose in male rats and can reduce LDL levels in NIDDM type rats.

D. Experimental Section

The tools used in this research are laboratory glassware, blenders (Philip), desiccators, freeze dryers (Edward), oral sonde, electric ovens, water heaters, rotary evaporators (Heidolph VV-2000).

The materials used in this research include plant material and chemicals, plant materials used are mangosteen rind Kaligesing village, Yogyakarta, while chemicals include ethanol 70% of reagent, analysis of LDL levels that is cholesterol oxidation phenol reagent kit, 4-aminoantipyrin peroxidase, buffer, phosphotungstic acid, MgCl2, STZ. Experimental animals used were male white wistar strain rats (Rattus norvegicus strain wistar) weighing 180-200 g, 2-3 months old.

The research was begun with the making of mangosteen rind ethanol extract obtained by maceration method with 70% ethanol. Because the maceration process experienced diffusion resulting in the osmotic pressure in the cell to be different from the situation outside the cell. So that compounds that have the same polarity as solvents are then pushed out due to differences in osmotic pressure inside the cell and outside the cell. The sample of research consisted of 30 male rats, divided into normal control groups (KN) and diabetics group (induced by STZ). Positive control group into normal control groups (KN) and diabetics group (induced by STZ). Positive control group.

E. Acknowledgement

I express my gratitude and highest appreciation to Prof. Dr. R.A. Oetari, SU., MM., M.Sc., Apt and Dr. Adi Prayitno, drg., M.Kes as the research funders for the Grant Program of the Ministry of Research, Technology and Higher Education, Faculty of Pharmacy Universitas Setia Budi and PAU Universitas Gajah Mada for the convenience provided to us to use the laboratory facilities.

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