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RESEARCH ARTICLE

α-Mangosteen from Garcinia Mangostana Linn and its Effect in Blood Insulin and Sugar Levels in Hyperglycemic Rat

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ABSTRACT

Introduction: Hyperglycemic triggers various complications, some organs that damage can occur due to the oxidation by oxidant of proteins both structural and non-structural, such as eyes, kidneys, heart, nerves and blood vessels. α-mangosteen as antioxidant can suppress cell damage so that blood sugar can be transported back into the cell and be found in Garcinia *mangostana* Linn. The purpose of this study was to explains the effect of α-mangosteen in increasing blood insulin and reducing blood sugar levels in hyperglycemic rat.

Method: This study uses 9 rat treatment groups. Group I as control, group II as negative control (hyperglycemic), group III as positive control (hyperglycemia + Glybenclamide), group IV-VI treated with extract mangosteen in ethanol rind (EEMR) and group VII-IX treated with isolate α-mangosteen rind (IAMR). After 28 days peripheral blood was taken and measurements the insulin and glucose blood serum level.

Results: Mean insulin control is 19.08μU/mL, after administration of STZ-NA is 6.18μU/mL, after administration with Glibenclamide is 11.58μU/m, after administration with EEMR is 18.69μU/mL. and after administration with IAMR is 17.81μU/mL. Mean glycemic control is 99.90mg/dl, after administration of STZ-NA is 259.90 mg/dl, after administration with Glibenclamide is 123.39 mg/dl, after administration with EEMR is 108.87mg/dl. and after administration with IAMR is 92.52 mg/dl. Showed an increase in insulin serum levels after administration with extract mangosteen and isolate α-mangosteen. Anova Test, showed there was a very significant difference between control and treatment in insulin levels (p=0.001).

Conclusion: α-mangosteen can increasing blood insulin and reduce blood sugar levels in hyperglycemic rat.

Keywords: Hypeglycemic, oxidant, α-mangostin, insulin, glucose, blood serum

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INTRODUCTION

Hyperglycemia in DM triggers various complications, long-term damage. Some organs that can be damaged due to chronic hyperglycemic such as eyes, kidneys, heart, nerves and blood vessels. Hyperglycemia is often associated with Diabetes Mellitus. Diabetes mellitus is a typical syndrome characterized by chronic hyperglycemia and disorders of carbohydrate, fat and protein metabolism associated with insulin deficiency both relative and absolute and impaired insulin action [1]. Cells that suffer from lack of oxygen will try to increase oxygen intake through blood vessel compensation (spasmus). If the spasmus process lasts long and continuous, the blood vessels will be easily damaged [2]. Hyperglycemia condition will trigger ROS (reactive oxygen species) as oxidative stress which will trigger various cells damage [3].

Increased accumulation of ROS in the body that can result in cell death needs to be given powerful antioxidants to reduce free radicals. Fruit that contains strong antioxidants, one of which is Garcinia mangostana Linn., family Clusiaceae (Guttiferae) [4]. The content of xanthones is

commonly found in mangosteen peel which has various biological activities such as antioxidant, anti-bacterial, antifungal, anti-tumor, anti-platelet aggregation and anti-thrombotic.

Garcinia mangostana Linn. (mangosteen), is a functional plant because most of its parts can be used as medicine. Not only the fruit flesh which is consumed and believed to be beneficial for health, but according to the research of mangosteen peel there is also a number of chemicals that are very beneficial for health [6]. G. mangostana Linn., Especially its peel has aroused interest for researchers to conduct intensive studies on the content of the compounds it contains. Mangosteen fruit peels are known to contain xanthone compounds which have the potential to be drug candidates. Xanthones are known to have antioxidants, anti-inflammatory activities [7,8], antifungals [9], chemopreventions [7,10], treatment of abdominal pain, diarrhea, dysentery, infection, pus, and chronic ulcers [11], anticancer [12,13], antitumor [14], antimalarials [15], antiacne [16], antituberculosis [10], neuroprotective [17], antiproliferation [18], antimicrobial [19], cytoprotective [20,21], anti-inflammatory [8]. Besides that, it also acts as an antioxidant [17,19,20,21].

α-mangosteen is the xanthone compound with the second most content after α-mangosteen found in mangosteen, where the two compounds have the most role in biological activity (0,00082%). α-mangosteen has anti-cancer activities [22], antiviral influenza [23] antioxidants [24] and has strong activity against early stage lung cancer cells (NCIH187) [25]. Antioxidants are molecules that are able to slow down or prevent the oxidation process of other molecules. Oxidation is a chemical reaction that can produce radicals free, thus triggering a chain reaction that can damage cells. Antioxidants such as thiols or ascorbic acid (vitamin C) end this chain reaction. [26].

Based on this description can be the basis of research to determine the effect of the extract and isolate of mangosteen (Garcia mangostana Linn.) on insulin and glucose blood levels in hyperglycemic rat.

METHODS

Plant material: one thousand g dry powder pericarp *G. mangostana* Linn. was collected at Somongari Village, Kaligesing District, Purworejo Regency, Central Java. Alcohol 70%, methanol (technical), acetone (technical), ethyl acetate (technical), *n*-hexane (technical), dichloromethane (technical), chloroform pa (*E. Merck*), *silica* gel 60 GF_{254} (*E. Merck*), silica gel 60 (0.2-0.5mm) (*E. Merck*), silica gel 60 PF_{254} *containing gypsum* (*E. Merck*), distilled water, cerium sulfate ($CeSO_4$), sulfuric acid (H_2SO_4). All solvents were distilled before being used, except chloroform. TLC was carried out using silica gel $60F_{254}$ (E. Merck) and visualized under UV light short and long (254 and 366nm). Vacuum liquid chromatography was performed on silica gel 60 GF_{254} (E. Merck), the extract is impregnated with silica gel 60 (0.2-0.5mm) (E. Merck), and radial chromatography was performed on silica gel 60 PF_{254} containing gypsum (E. Merck).

A set of distillation apparatus (*Duran-Germany*), a set of vacuum liquid chromatography (VLC), radial chromatography (RC), vacuum rotary evaporator (*Buchi*), oven (*Gallenkamp Civilab-Australia*), analytical scales (*Explorer Ohaus*), UV lamps (*Srahlen Germany*). Melting points were measured on a Sybron Thermolyne Melting Point Apparatus MP-12615 and are uncorrected. FT-IR Spectra was on Perkin Elmer FT-IR Frontier. ^1H and ^{13}C-NMR spectra were recorded with an Agilent DD2 system (Agilent Technologies, Santa Clara, CA, USA) operating at 400 (^1H) and 400 (^{13}C) MHz using residual. Unless otherwise indicated, vacuum liquid chromatography, radial chromatography and TLC were carried out using Merck silica gel 60 GF254, silica gel 60 (finer than 0.2-0.5mm) and precoated silica gel 60 PF_{254} containing gypsum plates, respectively. Spots on TLC were visualized under UV light and by spraying with cerium (IV) sulfate reagent followed by heating.

Five thousand gram *G. mangostana* Linn. pericarp powder macerated with 70% alcohol (5L) then filtered. The collected filtrate is concentrated by using a vacuum rotary evaporator until is obtained a thick brown extract (250g), then TLC eluent optimization was carried out in order to determine the mobile phase to be used during separation and purification. 250g of pericarp mangosteen ethanol extract (GME) was separated by using vacuum liquid chromatography (VLC) 10 times (adsorbent silica column 300g while the ratio of sample weight and silica impregnation was 1: 2 (25g GME ethanol extract + 50g) silica impregnation) and eluted with gradient polarity solvent steps starting from *n*-hexane, *n*-hexane-EtOAc, EtOAc and MeOH give five fractions (F1, F2, F3, F4 and F5). Based on the compound stain pattern, further separation of fraction 2 is carried out. Because of the large number (F2 50g), the next step is to do the KVC 2 times, then the results of the KVC are combined so that 4 subfractions of F2 (F2.1 (100mg); F2.2 (31.32g); F2.3 (12.94g) and F2.4 (457mg) Subfraction F2.2 was purified by radial chromatography 6 times using plate 2 and the mobile phase used *n*-hexane: EtOAc (8:2). Based on the same stain pattern then the results were combined again, then subfraction F2.3 too Radial chromatography was performed 4 times (same treatment F2.2). The fraction eluted from radial chromatography monitored by TLC and the fraction which gave a similar KLT pattern was combined so that 7 simple subfractions were obtained. Subfraction 4 from the combined results, purified by radial chromatography and obtained compound 2 as much as 1500mg (1,3,5,8-tetrahydroxy-2,4-bis (3,6,8-trihidroksi-2-metoksi-1,7-bis(3-metilbut-2-enil) xanten-9-on or α-mangosteen).

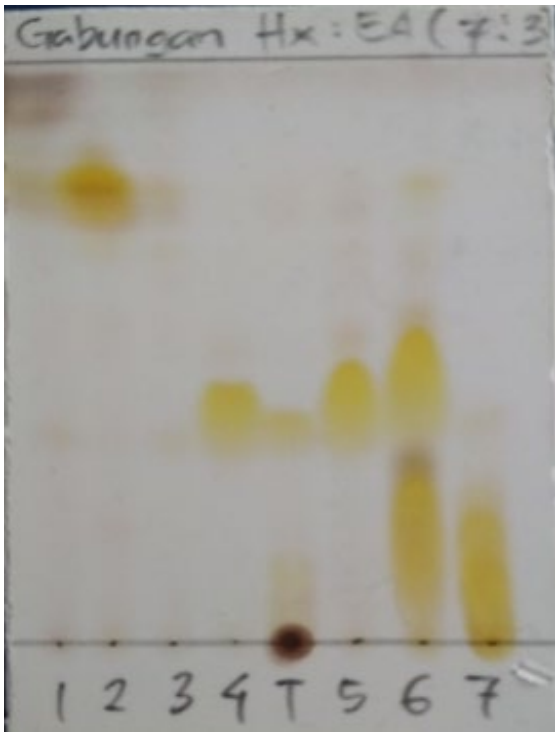

Figure 1. Chromatogram merging the fraction VLC F2.2

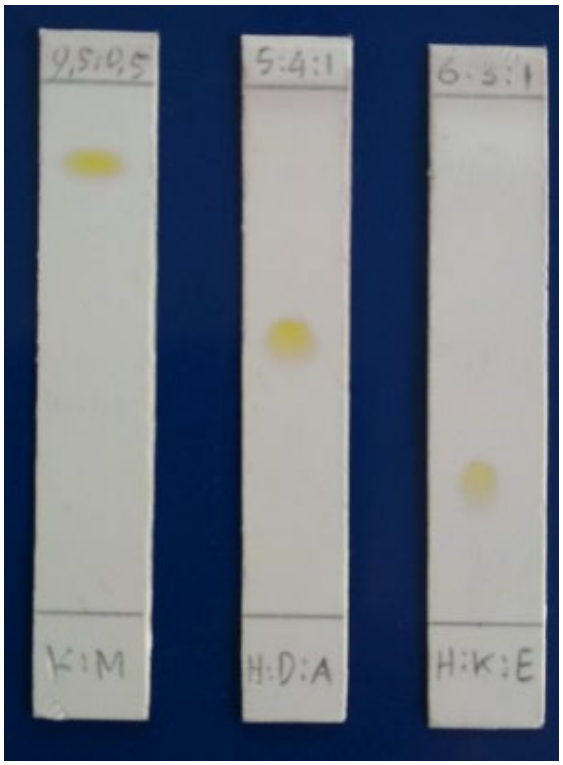

Figure 2. Chromatogram of three eluent system

The pure compounds obtained were measured and collected by using various spectrometry methods, namely FT-IR, 1-D NMR (^{1}H, ^{13}C and DEPT) and 2D NMR (HMBC and HMQC). The data obtained is translated by looking at the literature so that the structure can be known.

This study used 9 treatment groups. Group I as a control; group II as a negative control (STZ-NA); group III as positive control (STZ + glybenclamide); group IV (STZ + mangosteen rind ethanol extract dose 25mg/200g BW rats), group V (mangosteen rind ethanol extract dose 50mg/200g BW rats) and group VI (ethanol extract mangosteen rind dose 100mg/200g BB rats). The group giving α-mangosteen compounds are group VII (α-mangosteen 0.032mg/200g BW rats), group VIII (α-mangosteen 0.064mg/200g BW rats) and group IX (α-mangosteen 0.13mg/200g BB rats) for 28days. Next blood insulin and glucose levels were measured.

RESULT

Isolate Identification

Separation and purification in isolation of chemical compounds was carried out using chromatographic techniques. Chromatography is a way of physical separation with the elements to be separated distributed between two phases, the stationary phase and the mobile phase. The result of the separation can be seen in **Figure 1**. In **Figure 1** shows that there are several fractions with compounds that have a very high Rf value which indicates that the fraction contains very nonpolar compounds. Separation prioritizes the factions that still have the most stains, the results of which are then combined with other factions with fewer stains. Separation by liquid vacuum column chromatography continued until a simpler subfraction was obtained, then purified using radial chromatography to obtain a single stain.

The amount of pure isolates obtained was 1500mg. Testing the purity of isolate 2 was done by TLC using three eluent systems, the stains of these compounds on the 3 types of eluents used can be seen in **Figure 2**. In the chromatogram in **Figure 2** shows that isolate 2 has a single stain on the 3 three of eluent systems used. This shows that the compound has been pure and is supported by the results of the melting point test that has been carried out. The melting point of isolate 2 gave quite sharp results, namely at a temperature of 180-182°C.

Identification of isolates was done by analyzing IR spectroscopy and NMR 1D and 2D spectroscopy. Analysis by IR spectroscopy was carried out to identify functional groups contained in the molecule while NMR analysis aimed to determine the number and type of proton, carbon, DEPT, HMBC and HMQC atoms in isolate molecules.

The spectrum in **Figure 3** shows the absorption of infrared radiation by a molecule measured by an IR spectrophotometer. The frequency of the Csp3-H bond stretch is shown by the absorption of the wave numbers 2920.35 cm^{-1} and 2859.59 cm^{-1}. Csp2-H bond is shown by the absorption of the wave number 3060.20 cm^{-1}. Typical uptake that shows the presence of hydroxyl (OH) groups is shown at wave number 3419,94 cm-1. At wave number 1722.51 cm^{-1} indicates the presence of C = O bonds. The frequency of the bond between C-C is shown by the absorption at the wave number 1232.57 cm^{-1}.

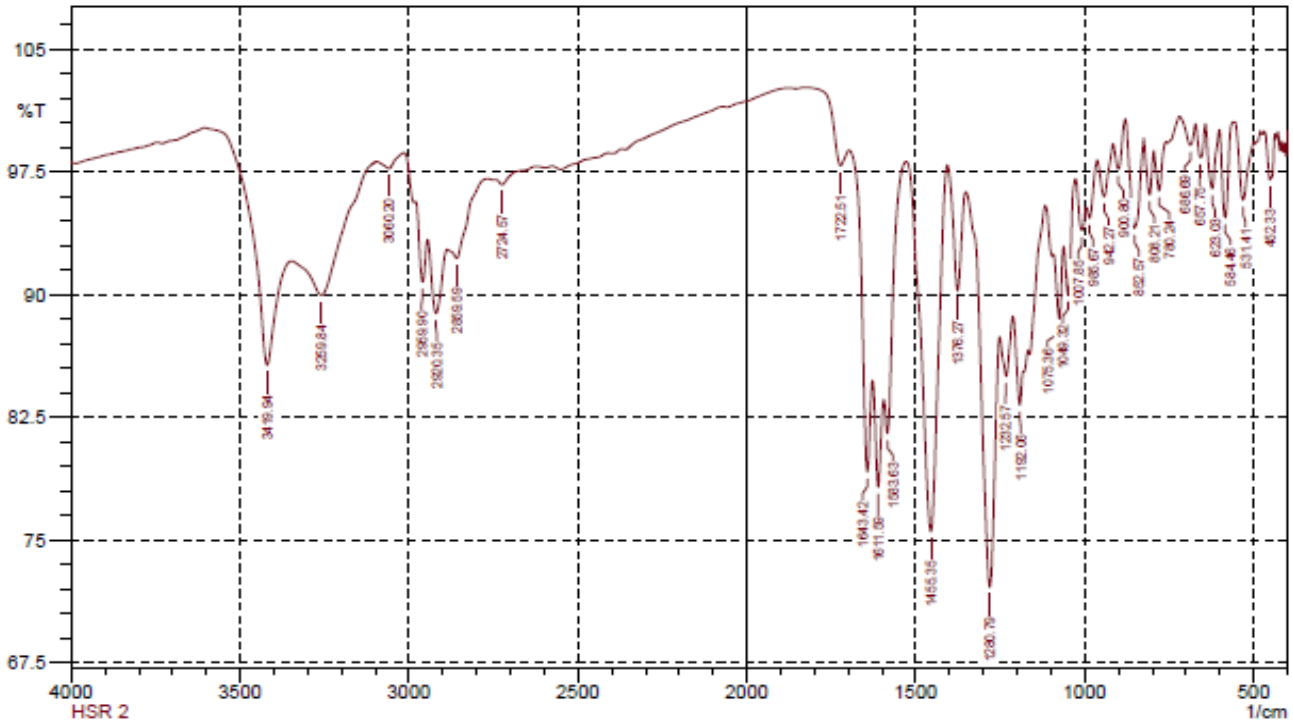

Figure 3. IR Spectrum of isolate compound 2

The ^{13}C NMR spectrum provides clues about carbon atoms in organic molecules. Whereas the ^{1}H-NMR spectrum provides structural information about hydrogen atoms in an organic molecule. From the ^{13}C-NMR spectra of isolate 2, there was carbon sp^2 indicated by the carbon atom signal which appeared on a relatively large chemical shift of 182.1; 161.6; 160,6; 155.8; 155.1; 154.6; 142,6; 137.1; 135.7; 132.2; 123.2 and 121.5 which are estimated to be Csp^2. The carbon atom signal on chemical shift 182.1 is thought to be Csp^2 on carbonyl (C=O) due to the electronegativity difference factor between carbon and oxygen so that electrons are more attracted to oxygen and make carbon atoms become more unprotected (deshielding) which causes chemical shifts in the carbon becomes large. Whereas in the chemical shift 161.7; 160,6; 155.8; 155.1; 154.6; 142,6; 137.1; 135.7; 132.2; 123.2 and 121.5 are thought to be Csp^2 in alkenes (C=C). In the chemical shift range of 26.6-18.0ppm shows Csp^3 carbon, which is 4 carbon.

^{13}C-NMR with the DEPT (Distrortionless Enhancement by Polarization Transfer) technique was performed to distinguish the types of carbon atoms in isolates such as methyl (CH_3), methylene (CH_2), methylene (CH) and quaternary carbon (C_q) types. These carbon signals can be distinguished by looking at the position of the signal pointing up or down. In the translation of DEPT spectra, methyl and metin are positioned upward, the methylene downward and the quaternary carbon are lost. The results obtained from the ^{13}C-NMR spectrum with the DEPT technique showed that isolate 2 had 4 metin, 2 methylene, 13 quartenerary carbon and 4 methyl.

^{13}C-NMR analysis is also supported by the presence of ^{1}H-NMR signal isolate compound 2. Data obtained from ^{1}H-NMR in the form of chemical shifts, multiplicity, coupling constant and integration. Chemical shift is a comparison between the location of a certain proton resonance with the standard resonant resonance location, multiplicity shows the number of protons in neighboring carbon, the coupling constant shows the value of the pair fixed from each division while the integration shows the number of protons bound to each carbon.

The ^{1}H-NMR spectrum of isolate 2 shows 6 signals representing 26 protons. Some signals are present in a fairly large chemical shift. which indicates that the proton has a very small electron density. This happens because the proton is bound directly to the Csp^2 carbon atom where the carbon atom has a small electron density due to the formation of 2-fold bonds so that the Csp^2 carbon atom is very strong attracting electrons to the proton that are bound directly to the carbon atom. Protons have a signal at a large chemical shift of 13.7ppm. This signal shows that the proton binds to the hydroxy group. Other proton signals have a small chemical shift with a range of 1.8-1.2ppm. This is because the proton is bound to the Csp^3 atom which has a greater electron density compared to the Csp^2 atom. Data ^{1}H and ^{13}C-NMR can provide information on the molecular formula of the isolate compound C24H26O6 with DBE (Double Bond Equivalence)=12, derived from 8 double bonds formed by 2 carbon sp^2 and 1 carbon carbonyl and 3 from bicyclic.

Hydrogen atoms which are bound directly to carbon atoms can be identified using NMR-2D with the HMQC

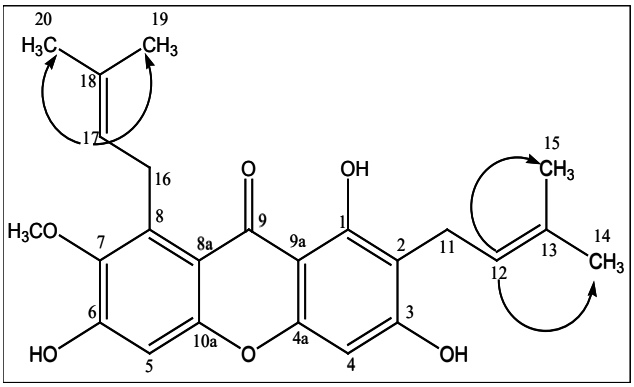

Figure 4. HMBC Strukture isolate compound 2

technique. The HMQC spectrum shows the correlation between the proton signal and the carbon signal which is indicated by the appearance of a contour. The carbon signal at 121.1ppm chemical shift has a correlation with the proton signal with a chemical shift of 5.25ppm which indicates that the carbon atom with the chemical shift binds the hydrogen atom. The carbon signal at a chemical shift of 21.4ppm has a correlation with the proton signal with a chemical shift of 3.45ppm. Carbon at the 160.6ppm chemical shift does not have a correlation with the proton signal indicating that the carbon atom with the chemical shift does not bind to the hydrogen atom. Carbon atoms are included in the type of quaternary carbon atom. The direct correlation between protons and neighboring carbon can be identified using the HMBC spectrum.

The HMBC spectrum states the distance correlation of up to 3 bonds between protons and their neighboring carbon. The determination of the position of carbon atoms in a compound is based on the correlation between the proton signal and the interlocking carbon rival. Carbon carbonyl with a chemical shift of 121.1ppm has a correlation with hydrogen atoms with a chemical shift of 1.76ppm and 1.83ppm which indicates that the carbonyl carbon atom is adjacent to carbon atoms 14 and 15 with chemical shifts of 26.0ppm and 18.1ppm.

The structure of compounds can be seen in **Figure 4** and based on **Table 1**, the similarity between isolate 2 and α-mangosteen is quite significant so it can be said that isolate 2 is α-mangosteen.

Extract and Isolate Trials on Rat

Mean insulin control is 19.08μU/mL. Mean insulin serum after administration of STZ-NA is 6.18μU/mL.Next mean insulin serum after administration with Glibenclamide is 11.58μU/m, after administration with EEMR is 18.69μU/mL. and IAMR is 17.81μU/mL. Mean glycemic control is 99.90μU/mL. Mean glycemic serum after administration of STZ-NA is 259.90μU/mL.Next mean glycemic serum after administration with Glibenclamide is 123.39μU/m, after administration with EEMR is 108.87μU/mL. and IAMR is 92.52μU/mL And showed an increase in insulin and decrease in blood glucose after administration with extract mangosteen and isolate α-mangosteen. For Anova Test, there was a very significant difference between control and treatment in insulin and glucose levels (p=0.001).

Table 1. Comparison of ^{1}H and ^{13}C NMR data for isolate compound 2 with literature

No C	^{1}H- NMR (ΣH, *m, J* in Hz)		^{13}C-NMR		DEPT 135
	Senyawa 2 (a)	Alfa mangostin (b)	(a)	(b)	(a)
1	13,76 (*s*, OH)	13,80 (*s*, OH)	160,7	160,6	Cq
2			108,6	108,4	Cq
3	6,15 (*s*, OH)	6,12 (*br*, OH)	161,7	161,6	Cq
4	6,3 (*s*)	6,27 (*s*)	93,4	93,3	CH
4a			154,6	155,1	Cq
5	6,8 (*s*)	6,81 (*s*)	101,6	101,5	CH
6	6,27 (*s*, OH)	6,27 (*s*, OH)	155,1	154,5	Cq
7			142,6	142,5	Cq
8			137,1	137	Cq
8a			112,2	112,2	Cq
9			182,1	182	Cq
9a			103,7	103,6	Cq
10a			155,8	155,8	Cq
11	3,44 (2H, *d*, J = 7,5 Hz)	3,45 (2H, *d*, J = 7,3 Hz)	21,5	21,4	CH2
12	5,25 (1H, *t*, J = 7 Hz)	5,25 (1H, *t*, J = 7,3 Hz)	121,5	121,4	CH
13			132,3	135,9	Cq
14	1,76 (3H, *s*)	1,75 (*s*)	25,9	25,9	CH3
15	1,83 (3H, *s*)	1,81 (*s*)	18,3	18,2	CH3
16	4,08 (2H, *d*, J = 6,5 Hz)	4,07 (2H, *d*, J = 7,0 Hz)	26,6	26,6	CH2
17	5,27 (2H, *t*, J = 7 Hz)	5,28 (2H, *t*, J = 7,3 Hz)	123,2	123,5	CH
18			135,7	132,2	Cq
19	1,82 (3H, *s*)	1,82 (*s*)	18,01	17,9	CH3
20	1,68 (3H, *s*)	1,68 (*s*)	25,93	25,8	CH3
7-OMe	3,79 (*s*)	3,79 (*s*)	62,13	62,1	

Keterangan:: a = Isolat 2; b = Anggia (2015)

The results of the study after administration of EEMR and IAMR showed an increase in blood insulin levels in the optimum dose (EEMR 50mg/200g BW rats, IAMR 0.064mg/200g BW rats) (showed in **Table 2**).

The results showed in **Table 3** that the control group and α-mangosteen group differ very significantly (p=0.001) was able to increase the insulin levels of test animals at optimum doses (EEMR 50mg/200g BW rats, IAMR 0.064mg/200 g BW rats).

Table 2. Blood insuline level (µU/mL) between controll, after given STZ (Hyperglycemic), Hyperglycemic after given Glybenclamide and DM after being given α mangosteen

	Blood insulin level (µU/mL)								
	Control	Hyperglycemic	Hyperglycemic + Glibenclamide	EEMR			IAMR		
				1	2	3	1	2	3
	I	II	III	IV	V	VI	VII	VIII	IX
1	20.36	5.51	11.45	19.45	18.68	19.61	19.70	17.37	17.65
2	17.68	7.86	10.61	21.61	19.45	19.09	17.65	16.55	16.80
3	18.23	4.43	11.09	16.09	16.62	16.43	16.80	19.67	16.29
4	19.39	7.72	13.90	17.90	20.92	18.92	16.29	20.39	17.38
5	19.77	5.61	10.87	17.87	18.72	19.90	17.38	19.70	17.37
Mean	19.08	6.18	11.58	18.58	18.69	18.79	17.56	18.73	17.09

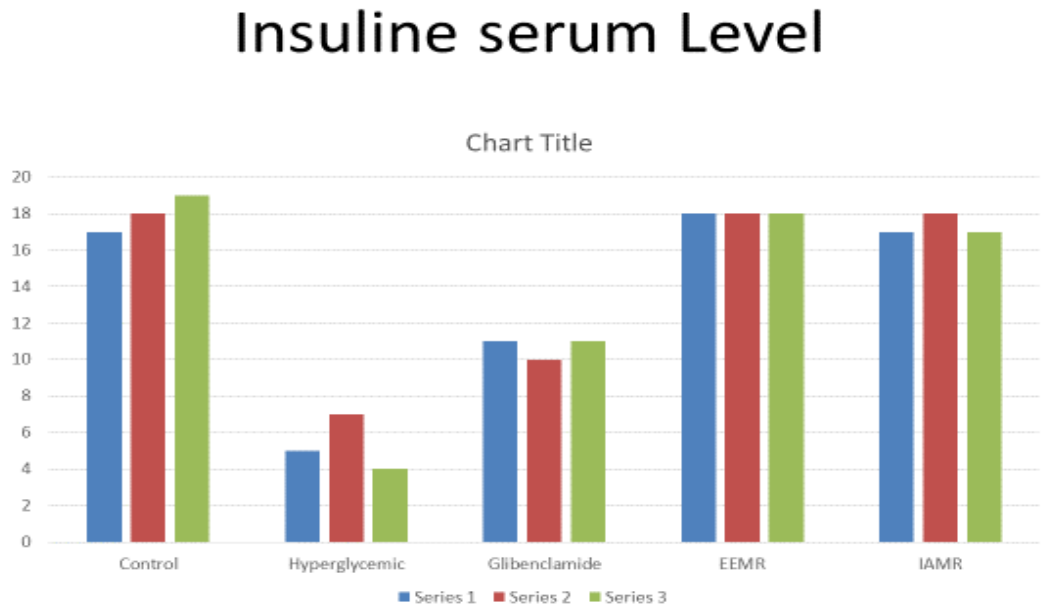

Figure 5. Graph insulin serum level in 5 group (control, hyperglycemic, hyperglycemic treat by glybenclamide, hyperglycemic treat by EEMR, hyperglycemic treat by IAMR)

Table 3. Anova Test for Insulin Significancy

	Insulin Significancy	p
1	Between Hyperglicemic – Hyperglycemic Glibenclamide	0.001
2	Between Hyperglicemic – EEMR	0.001
3	Between Hyperglicemic – IAMR	0.001
4	Total	0.001

The latest results show a decrease in blood glucose levels at a minimum dose (EEMR 25mg/200g BW rats, IAMR 0.032mg/200g BW rats) (showed in **Table 4**) and reduce levels blood glucose at minimum dose (EEMR 25mg/200g BW rats, IAMR 0.032mg/200g BB rats).

DISCUSSION

Oxidant effects on target cells can damage multiple functional pathways inside the cells, as well as give rise to malignant transformation via DNA damage [26]. ROS is considered destructive and this is not always true, because it plays an important role in many physiological reactions, such as oxidation mediated by cytochrome P450, regulation of smooth muscle tension, and killing of microorganisms. Imbalances in antioxidant-antioxidant activity are involved in many pathological events that are mediated by free radicals, for example, ischemic reperfusion and asthma. In an effort to alleviate this pathology antioxidants are used and it should be noted that these compounds are not specific functions as antioxidants only [27]. The occurrence of

Table 4. Blood gukose level (mg / dL) between normal, after being given STZ (DM), DM after being given Glybenclamide and DM after being given α mangosteen

	Blood glucose level (mg/dl)								
	Control	Hyperglycemic	Hyperglycemic + Glibenclamide	EEMR			IAMR		
				1	2	3	1	2	3
	I	II	III	IV	V	VI	VII	VIII	IX
1	98.01	258.01	126.46	122.14	102.14	102.14	101.46	96.46	86.46
2	100.14	260.14	118.73	110.36	104.36	100.36	98.73	98.73	88.73
3	107.30	257.30	121.55	128.58	108.58	108.58	91.55	97.55	85.55
4	93.35	263.35	125.27	113.29	111.29	102.29	95.27	96.27	85.27
5	108.72	258.72	124.96	108.98	104.98	104.98	94.96	84.96	84.96
Mean	99.90	259.50	123.39	116.67	106.27	103.67	96.59	94.79	86.19

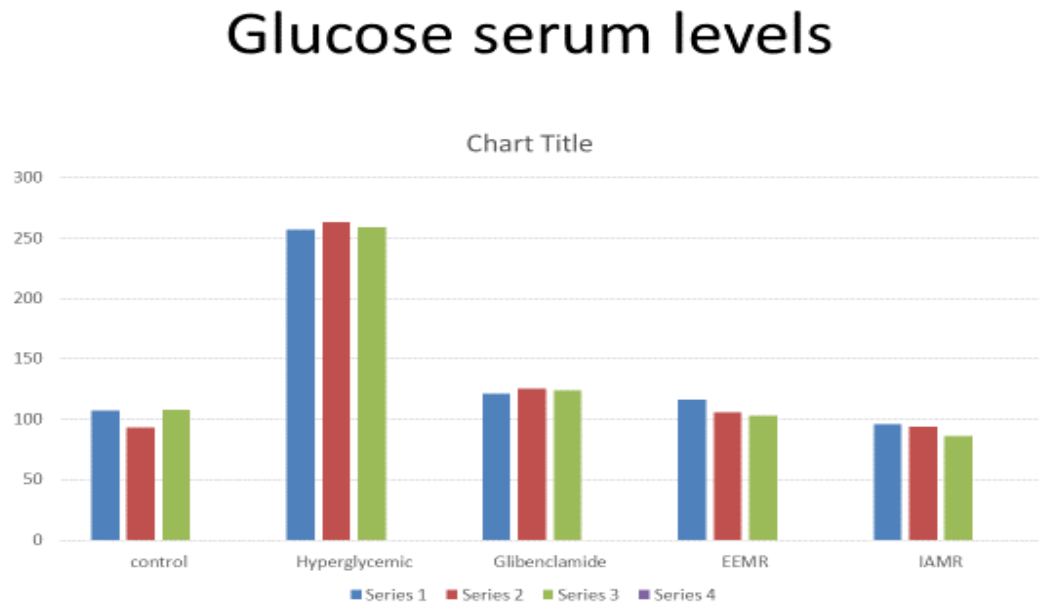

Figure 6. Graph glucose serum level in 5 group (control, hyperglycemic, hyperglycemic treat by glybenclamide, hyperglycemic treat by EEMR, hyperglycemic treat by IAMR)

reactive oxygen species, known as pro-oxidants, is an attribute of normal aerobic life. The formation of pro-oxidants in a balanced state is balanced with the same level of consumption with antioxidants that are enzymatic and / or nonenzymatic. Oxidative stress results from an imbalance in the pro-oxidant-antioxidant balance that supports pro-oxidants. A number of diseases are associated with oxidative stress, which form the basis of antioxidant therapy. Current evidence in clinical research does not show a clear difference between the causal or associative associations of pro-oxidants and the disease process [28].

Free radicals damage cells by damaging cell membranes first by free radicals covalently bind to enzymes or receptors in cell membranes so that they change the activity of cell membrane components. Free radicals covalently with membrane cells so that change the membrane functions, free radicals disrupts the membrane transport system through covalent bonds, oxidizes the thiol group (converts polyunsaturated fatty acids), next free radicals initiate lipid peroxidation directly against polyunsaturated cell wall fatty acids The earliest known mechanism of cell damage caused by free radicals is lipid peroxidation. Lipid peroxidation is most abundant in cell membranes [29,30]. The consequences for molecular oxygen blockages at the molecular level, cell membranes and tissues have implications that provide a better understanding of pathology in almost every major medical condition known to mankind. New advances in free radical chemistry that increase the saturation of carbon-

molecular bonds and spread cross bonds between unsaturated carbon-carbon double carbon bonds (C = C) to improve organization [31] can be applied to basic fluid-mosaic membrane models (F-MMM)) [32, 33]. According to the original F-MMM in 1972 globular intrinsic proteins were thought to be embedded in the phospholipid matrix and had translational mobility [33].

In this study the ability of mangosteen rind extract and α-mangostin was associated with antioxidant activity, which in hyperglycemic antioxidants regenerated damaged extracellular matrix proteins and cell growth due to ROS through glycation of non-enzymatic proteins and auto oxidation [34]. Thus, these antioxidants provide protection and repair of pancreatic beta cells that are damaged by free radicals by preventing the reaction of superoxide into hydrogen superoxide. This antioxidant activity is given by the presence of hydroxyl groups (-OH). Phenol/polyphenol compounds are believed to reduce oxidative stress by preventing the reaction of converting superoxide to hydrogen superoxide by donating hydrogen atoms from the aromatic hydroxyl group (-OH) polyphenol compounds to bind to free radicals and remove them from the body through the excretion system [35]. In cells that have insulin receptors (muscle cells, adipose cells, and liver cells), the binding of free radicals increases insulin signaling in intracellular GLUT-4 translocation to the cell membrane so that it is able to extract glucose from the blood. In addition, phenol compounds in mangosteen peel also have the potential to be anti-insulin. Insulin is an insulin degradation enzyme and the presence of this enzyme can increase insulin availability in mice experiencing hyperglycemia [36]. The mechanism of action of antioxidant mangosteen peel extract through 3 channels, namely superoxide free radical scavenging activity, inhibition of linoleic acid peroxidation and radical scavenging activity. Antioxidant properties in mangosteen peel extract exceeds vitamin E and vitamin C, so xanthone compounds are needed in the body to balance peroxides, and xanthones work to bind ROS in the body by inhibiting the process of damage cell (necrosis) [37,38].

In a state of hyperglycemia damage occurs in pancreatic β cells, consequently the production of insulin in the blood decreases and causes a buildup of glucose in the blood. Damage to pancreatic β cells results in damage to some cells in several organs such as the liver, kidneys, and lymphocytes. Damage in these cells caused by free radicals. Oxidant effects on target cells can damage multiple functional pathways inside the cells, as well as give rise to malignant transformation via DNA damage [27,39].

CONCLUSION

α-mangosteen can increasing blood insulin and reduce blood sugar levels in hyperglycemic rat.

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Consent for publication: Data about herbal is suspected to be lacking especially in the occurrence of diseases of the oral cavity.

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