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UNIVERSITAS HASANUDDIN
FAKULTAS KEDOKTERAN
KOMISI ETIK PENELITIAN KESEHATAN
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REKOMENDASI PERSETUJUAN ETIK

Nomor : 0134 /H4.8.4.5.31/PP36-KOMETIK/2014

Komisi Etik Penelitian Kesehatan Fakultas Kedokteran Universitas Hasanuddin, setelah melalui pembahasan dan penilaian, pada rapat tertanggal **2 Januari 2014**, telah memutuskan, protokol penelitian berjudul:

Pengaruh Polifenol Klika Ongkea (Mezzetia parviflora Becc) Terhadap Sel β Pankreas, Kadar Insulin dan Kadar Glukosa darah tikus Wistar yang Diinduksi Streptozotocin

dengan Peneliti Utama: **Jangga.,SSi, MKes, Apt**

No. Register

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yang diterima pada tanggal: **2 Desember 2013**

Perbaikan diterima tanggal: **24 Januari 2014**

dapat disetujui untuk dilaksanakan di **Laboratorium Hewan Fakultas Kedokteran Universitas Hasanuddin dan Rumah Sakit Pendidikan Makassar.**
Persetujuan Etik ini berlaku sejak tanggal ditetapkan sampai dengan batas waktu pelaksanaan penelitian.

Pada akhir penelitian, **laporan pelaksanaan penelitian** harus diserahkan kepada KEPK Fakultas Kedokteran Unhas. Jika ada perubahan protokol dan /atau perpanjangan penelitian, harus mengajukan kembali permohonan kajian etik penelitian (amandemen protokol).

Makassar, 28 Januari 2014

Komisi Etik Penelitian Kesehatan Fak. Kedokteran Unhas

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Effect Of Polyphenols Klika Ongkea (Mezzetia Parviflora Becc) Against Blood Glucose Wistar Rats Induced By Streptozotocin

Jangga, Rosdiana Natsir, Suryani As'ad , Agussalim Bukhari

Abstract: When this has been developed medicines from natural ingredients to control diabetes mellitus, most of these materials have been studied and shown to be effective as an alternative therapy. This study aimed to determine the effect of polyphenols Klika ongkea (Mezzetia parviflora Becc.) To decrease blood glucose levels induced streptozotosin wistar rats (STZ) and to determine the concentration of how the effect is not significantly different from the control group of drugs. In this study used Wistar rats were 120 tails are divided into six treatment groups, the first group of healthy controls were given Na. CMC 1%, group II were given pain control STZ 40 mg / kg body weight of mice, group III was given the drug control galvus (vildagliptin), group IV, V and VI are given polyphenols Klika ongkea each 100mg / kg and 300mg / kg for 21 day. The results showed that administration of polyphenols Klika ongkea 300mg / kg body weight of rats and 300 mg / kg body weight of mice as a protective effect on the decreased levels of blood glucose Wistar rats induced by STZ and giving polyphenols Klika ongkea 300mg / kg body weight of rats and 300 mg / kg rat as protective effect was not significantly different the effect of galvus (vildagliptin) 0.9 mg / 200 gBW mice.

Keywords: blood glucose, polyphenols, streptozotocin.

1. INTRODUCTION

When this has been developed medicines from natural ingredients to control diabetes mellitus (DM), a portion of these materials has been studied and shown to be effective as an alternative therapy (Ali, R. et al. 2009). Antioxidants are found in vegetables and fruits. Components that are antioxidants in vegetables and fruits include vitamin C, vitamin E, carotene, polyphenols, flavonoids, flavones, anthocyanins, catechins, and isokatekin [1], and lipoic acid [2]. This phytochemical compounds help protect cells from oxidative damage caused by free radicals. Damage to the beta cells of the pancreas can be caused by many factors. Among the factors to genetic factors, infection by bacteria, nutritional factors, diabetogenic substances, and free radicals (oxidative stress). Streptocotozin compound is one of the diabetogenic substances that are toxic, especially against pancreatic beta cells, and when administered to experimental animals such as rats can cause rats became diabetic. Pancreatic beta cell damage causes the body can not produce insulin, causing blood glucose levels to rise (a state of hyperglycemia). Conditions of hyperglycemia by [3] can result in the formation of reactive oxygen species (ROS = reactive oxygen species).

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Excessive ROS can cause oxidative stress and can exacerbate the damage pancreatic beta cells [3]. Diabetes mellitus (DM) is a clinical syndrome characterized by polyuria, polidipsi, and polyphagia, accompanied by an increase in blood glucose levels or hyperglycemia (fasting glucose ≥ 126 mg / dL or postprandial ≥ 200 mg / dL or when glucose ≥ 200 mg / dL) . When diabetes mellitus is not addressed will be interference with the metabolism of fats and proteins, and the risk of microvascular and macrovascular impaired increased [4]. Polyphenols are the focus of this study because it has an effect on health, which is anti-atherogenic, antitrombolik, antiinflammatory, antihiperglikemia, can modulate immune, antimicrobial, analgesic, anti-cancer and may prevent cardiovascular disease [5]. Some plants contain compounds called polyphenols, and is often used as a diabetes drug by the public, among others; Ongkea (Mezzetia palviflora Becc.), Mangosteen (Gracinia mangostana Linn.), Aloe Vera (Aloe vera Linn.), Brotowali (Tinospora crispa Linn.) And Noni (Morinda citrifolia Linn.) With a polyphenol content of 20.24% respectively [6], 16.21% [7], 5.62%, 4.34%, and 1.5% [8]. One plant containing the polyphenol compounds that Ongkea, empirically bark decoction is used by the community Bau-Bau Buton as cholesterol-lowering drugs, slimming, diabetes mellitus drug and tumor drug. The effect is caused by antioxidants in high enough quantities therein. Beneficial antioxidant activity to protect cells from a variety of physiological and pathological circumstances. Ongkea phytochemical testing showed a 20.24% polyphenol compounds, flavonoids and tannins 1.76% 26.46% and free radical activity test in vitro showed that the extract Klika ongkea able catch free radical DPPH [6]. This study was conducted in animals (rats) given animal studies, differences in genetic factors can be controlled and ambiguous influence of the environment can be minimized, so Pato mechanism disease can be better explored than human studies. Wistar strain male rats will be used in this study because this mouse strain is more sensitive to the induction of STZ, easier in handling and quieter behavior, as well as selected male rats to eliminate the influence of hormonal [9].

2. METHODOLOGY

Material

Klika ongkea, Wistar strain male rats, FeCl3, Aqua Brom, indofenol, distilled water, aqua pro injection (Otsuka), methanol (E. Merck), alcohol (E. Merck), acetone (E. Merck), n-hexane (E. Merck), diethyl ether (E. Merck), Na.CMC, Galvus, STZ ALX-350-010 from ALEXIS Corporation, fodder (HG II-B) with a composition of 13% water content, protein 21-23% , carbohydrates 45.5 to 47.5%, 5% fat, fiber 5%, 7% ash, 0.9% calcium and 0.6% phosphorus.

Tool

Glucometer, analytical Balance (Sartorius), micropipette (Eppendorf), a set of maceration, a set of tools rotary evaporator (Buchi), animal scales, syringes, needles oral, and rat cage.

Design of Experiments

This research uses experimental methods to design modifications pretest posttest randomized controlled group design. Two research groups: control group (group I; healthy controls, group II; control pain and group III; drug control) and experimental group (group III, IV, and V), where the experimental group were given treatment control group was given no treatment. Rats that met the inclusion criteria of 120 mice, on day 0 taken randomly and then inserted into 6 groups. Each group consisted of 20 birds and caged separately, given the standard feed and drink. Furthermore, each group was given treatment as follows:

Group I, day 1 were fasted beforehand and observed 4 tails, then given a colloidal solution of Na. CMC 1% orally every day for 28 days as healthy controls, on day 7, to 14, to 21 and to 28 fasted beforehand and then observed each 4 tails.

Group II, day 1 were fasted prior and observed 4 tails, then induced STZ, 40 mg / kg single dose in mice ip as pain control, on day 7, to 14, to 21 and to 28 fasted beforehand and then observed each the 4 tail.

Group III, day 1 were fasted beforehand and observed 4 tails, then induced STZ, 40 mg / kg single dose mice by ip as the control drug, starting from day 7 given galvus (pildagliptin) 0.9 mg / 200 gBW mice orally every day for 21 days, and before being given galvus on day 7, to 14, to 21 and to 28 fasted prior then observed each 4 tails.

Group IV, day 1 were fasted beforehand and observed 4 tails, then induced STZ, 40 mg / kg body weight as a single dose mice ip Starting day 7 was given a suspension of polyphenols Klika ongkea 100 mg / kg body weight of mice orally every day for 21 days, before being given polyphenols Klika ongkea on day 7, to 14, to 21 and to 28 fasted beforehand and then observed each 4 tail.

Group V, day 1 were fasted beforehand and observed 4 tails, then induced STZ, 40 mg / kg single dose mice by ip Starting day 7 was given a suspension of polyphenols Klika ongkea 300 mg / kg body weight of mice orally every day for 21 days, and before being given polyphenols Klika ongkea on day 7, 14th, 21th and 28th fasted beforehand and then observed each 4 tail.

Group VI, starting today minus 2 was given a suspension of polyphenols Klika ongkea 300 mg / kg body weight of mice orally every day for 30 days, the 1st day of fasting in advance and observed 4 tails, then induced STZ, 40 mg / kg single dose in mice ip Before given polyphenols Klika ongkea on day 7, to 14, to 21 and to 28 fasted beforehand and then observed each 4 tails.

Examination of Blood Glucose Levels

Examination of blood glucose levels is done 5 times, which is 1 times before STZ induced and 4 times after STZ induced, ie day 7, to 14, to 21 and to 28, with taking blood intraorbita 0.5 ml wear and subsequent capillary pipette blood glucose levels were measured using a glucometer [10].

Data Collection and Analysis Techniques

Primary data collected in this study includes the results of Wistar rat blood glucose levels are before and after induced STZ, 40 mg / kg ip in mice a single dose and after administration of polyphenols Klika ongkea 100 mg / kg, 300 mg / kg rat and galvus (vildagliptin) 0.9 mg / 200 gBW mice orally every day for 21 days. Data analysis was performed using one-way ANOVA test followed by Student Newman Keuls range test.

3. RESULTS AND DISCUSSION

After doing research on the effects of polyphenols Klika ongkea (Mezzetia parviflora Becc.) On blood glucose levels streptozotocin-induced Wistar rats obtained the following results:

Table 1. *Results Of Measurement Of The Average Levels Of Blood Glucose Levels Pre (Before STZ Induced), The Initial Blood Glucose Levels (After STZ Induced) And Blood Glucose Levels After Treatment*

Group Treatment	Samples To	Initial Blood Glucose Levels	Glucose Levels Glucose Early	Treatment (Week 3-5)			The Decline In Blood Glucose Levels (%)
				3	4	5	
Group I	1	84	99	99	99	97	4,46
	2	117	130	129	128	127	15,38
	3	76	87	87	86	86	6,09
	4	109	121	120	120	119	8,33
On Average		96,5	109,25	109,75	108,25	107,25	**8,56**
Group Ii	1	98	169	168	158	158	10,80
	2	103	166	164	162	160	6,34
	3	99	168	166	164	164	4,84
	4	110	169	168	166	162	6,22
On Average		102,5	168	166,5	162,5	161	**7,05**
Group Iii	1	102	108	106	104	103	94,93
	2	108	112	111	110	109	94,11
	3	116	128	123	120	119	78,77
	4	92	106	103	101	97	81,07
On Average		104,5	141	110,75	108,75	107	**87,22**
Group Iv	1	90	132	120	117	110	38,90
	2	91	125	109	107	105	52,94
	3	112	130	121	118	116	64,83
	4	98	128	110	106	102	73,33
On Average		97,75	128,75	115	112	108,25	**57,5**
Group V	1	106	145	120	125	118	61,53
	2	100	153	115	113	109	76,73
	3	98	158	130	124	125	52,78
	4	110	160	121	127	119	75,34
On Average		103,5	154	121,5	122,25	117,75	**66,6**
Group VI	1	109	130	113	110	110	90,47
	2	110	135	116	115	113	81,36
	3	113	140	125	120	115	74,07
	4	105	145	135	114	108	65
On Average		109,25	137,5	122.25	114,75	111,5	**77,73**

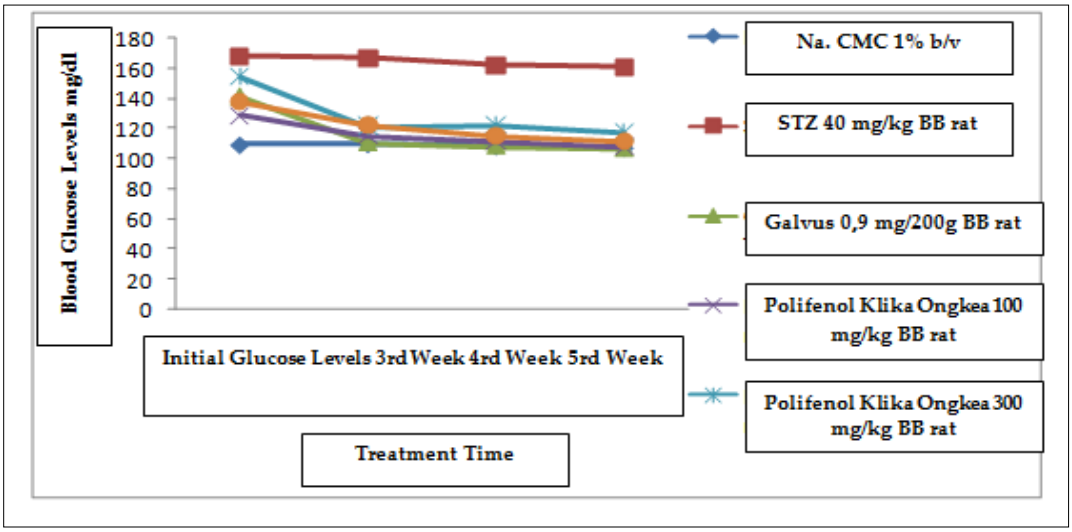

Figure 1. *Graph the average levels of blood glucose vs. time treatment*

Diabetes mellitus is a clinical syndrome characterized by polyuria, and polyphagia polidipsi accompanied by an increase in blood glucose levels or hyperglycemia (fasting glucose ≥ 126 mg / dL or postprandial ≥ 200 mg / dL or when glucose ≥ 200 mg / dL). When diabetes mellitus not addressed will be interference with the metabolism of fats and proteins and the risk of microvascular and macrovascular impaired increased [4]. This research uses experimental animals are often used to study experimental diabetic rats are wistar strain. Wistar rats easily cultivated, can be used as a model of diabetic spontaneously or by induction diabetogenic substance, has a relatively rapid metabolic capabilities making it more sensitive when used in research related to metabolic body [11]. Terms of mice used 1,5 2 months old weighing 150 to 200 grams and before being used in adapted for 2 weeks to adjust to the environment [12]. Given the potential and the high content of polyphenolic compounds in the Klika ongkea, it has done the research to develop herbal extract standardized Klika ongkea be the anti-diabetes effect, assessed by a decrease in blood glucose levels in male rats of wistar strain. Polyphenols Klika ongkea given in the form of a suspension with a dose of 100 mg / kg body weight of rats and 300 mg / kg rat. Determination of the dose is based on the results of the previous orientation. Rats were used as much as 120 tail, before treatment the mice were divided into 6 groups, group I as healthy controls given Na. CMC 1%, group II as pain control given STZ, 40 mg / kg rat, Group III as a control drug was given galvus (vildagliptin) 0.9 mg / 200 gBW mice, group IV as a Klika ongkea polyphenol treatment given 100 mg / kg body weight of mice, V as a given treatment group Klika ongkea polyphenols 300 mg / kg rat and VI as the treatment group was given polyphenols Klika ongkea 300 mg / kg body weight of mice 2 days before given STZ. All groups of rats were fasted in advance to avoid the influence of food at the time of blood glucose measurements, in addition to optimizing drug absorption [12]. This study used a single dose of STZ 40 mg / kg ip in mice, in which the dose STZ induction is used to create a mouse model of diabetes. STZ has nitrosourea group and produces NO (nitric oxide) which can damage the pancreatic β cells, so that the β cells of the pancreas can not produce normal amounts of insulin and cause high blood glucose levels [13,14,15]. Giving STZ 40 mg / kg ip rats cause hyperglycemia in the first week and remained until the fifth week [16,17]). In this study, blood glucose levels at 7 days after STZ induced hyperglycemia show has occurred in all treatment groups, it indicates there has been a pancreatic β cell destruction, the results can be seen in Table 1. The results showed that the average percentage of each group decreased glucose levels are at 8.56% in group I, group II at 7.05%, 87.22% for Group III, Group IV of 57.5%, group V at 66 , 6% and group VI of 77.73%. The percentage decrease in the average lowest glucose levels was Group II which is 7.05% and the average percentage decrease glucose levels were highest in group III which is 87.22%, this can be seen in Table 1. When presented in a graph of the six groups above can be seen in Figure 1, the sixth graph of time versus treatment groups showed that administration of polyphenols Klika ongkea 100 mg / kg body weight of mice, 300 mg / kg body weight of mice, 300 mg / kg rat as protection and groups drug control (galvus 0.9 mg / 200 gBW rat) lowers blood glucose levels approaching the healthy control group and a control group of drugs (galvus 0.9 mg / 200 gBW mice) capable of lowering blood glucose levels exceed the healthy control group at week 4 and to 5. While the content of the blood gluksa STZ group given 40 mg / kg rats away from the healthy control group. In the treatment group, a decrease in blood glucose levels caused by polyphenols Klika largest ongkea 300 mg / kg rat as protection, then polyphenols Klika ongkea 300 mg / kg body weight of mice, and the smallest is the polyphenol Klika ongkea 100 mg / kg rat. The most effective treatment to lower blood glucose levels are polyphenols Klika ongkea 300 mg / kg rat as protection. Statistical testing of blood glucose test group animals STZ-induced, performed by the method of one-way ANOVA showed a significant difference between groups ($p < 0.05$). Testing continued with Student Newman Keuls range test to see significant differences between the groups. In Student Newman Keuls range test 5 weeks showed a significant difference ($p < 0.05$) between the control group of healthy, pain control, drug control and treatment groups. This shows that the control group remained in a state of hyperglycemia sick while in the other groups already in the normal state. In the control group the drug showed no significant difference in the treatment group Klika ongkea polyphenol administration of 300 mg / kg body weight of rats and 300 mg / kg rat as protection, which means giving polyphenols Klika ongkea 300 mg / kg body weight of mice can reduce levels of blood gluoksa wistar rats STZ induced. One class of chemical compounds contained in the Klika ongkea (Mezzetia parviflora Becc.) Is a polyphenol. Polyphenols are organic compounds which have aromatic rings containing more than one hydroxyl group, which comprises two groups, namely phenolic acids and flavonoids [18]. Polyphenols have privileges as radical scavenging activity [19]. As antioxidants, polyphenols can capture free radicals by removing the hydrogen atom from the hydroxyl group. Granting this will cause the hydrogen atoms become stable free radicals and stop doing extreme movements, so as not to damage lipids, proteins and DNA target cellular damage [20]. Polyphenols have various pharmacological effects such as anti-obesity [21,22,23]), antidiabetic [24]), anticancer [25]), allergy and is able to regenerate pancreatic β cells [24]). Polyphenols reduce hyperglycemia in peripheral tissues in several ways, namely inhibiting gluconeogenesis [26,27]), the adrenergic stimulation of glucose uptake (Cheng, et al. 2000), stimulation by insulin release pancreatic β cells [28].

4. CONCLUSION

1. Provision of Polyphenols Klika ongkea at 300 mg / kg body weight of rats and 300 mg / kg rat as protective effect on glucose levels Streptozotocin induced Wistar rats.
2. Provision of polyphenols Klika ongkea 300 mg / kg rat and 300 mg / kg rat as protection against a decline in blood glucose levels were not significantly different effects by administering galvus 0.9 mg / 200 gBW mice as a control drug.

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