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LAMPIRAN

Lampiran 1 Dokumentasi Literatur 1

Judul: *Antidiabetic activity of Ethanolic Extract of Kalanchoe pinnata Leaves in Alloxan Induced Hyperglycaemic Rats* (*Yuliani et al*, 2016).

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Research Article

ANTIDIABETIC ACTIVITY OF ETHANOLIC EXTRACT OF *Kalanchoe pinnata* LEAVES IN ALLOXAN INDUCED HYPERGLYCAEMIC RATS

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ABSTRACT

Diabetes remains a major burden in health care both in developed and developing countries. *Kalanchoe pinnata* has been used as a traditional medicine to treat diabetes. The aim of this study to find scientific evidence of antidiabetic activity of *Kalanchoe pinnata* extract (KPE) through hypoglycemic effect using animal model of diabetes mellitus. Hyperglycaemia was developed in rats using alloxan 150mg/kgBW. Three days after alloxan injection, rats having fasting blood glucose (FBG) >200mg/dL were divided into six groups, namely HG (hyperglycaemia), HG+KPE high-dose (hyperglycaemia+ KPE 33.2mg/kg), HG+KPE medium-dose (hyperglycaemia+ KPE 11.6mg/kg), HG+KPE low-dose (hyperglycaemia+ KPE 5.8mg/kg), standard drug 1 (hyperglycaemia+glibenclamide 1.35mg/kg), standard drug 2 (hyperglycaemia+acarbose 13.5mg/kg). Then, FBG was measured every 5 days recorded as t1, t2, and t3 to determine fluctuations in blood glucose. At the end of the study, rats were sacrified, pancreas was collected and number of pancreatic beta cell langerhans was determined. KPE 11.6mg/kg showed best hypoglycemic effect and improvement of the number of pancreatic beta cell langerhans. KPE has hypoglycemic effect through improvement of the number of pancreatic beta cell langerhans but not in dose dependent manner.

Key words: Antidiabetic, *Kalanchoe pinnata*, hyperglycaemic, alloxan, pancreatic

INTRODUCTION

WHO (2015) reported 9% people aged 18+ worldwide suffered from diabetes, while in Indonesia the prevalence was only 1.5% (Kemenkes RI, 2013). It is worth noticing that this disease is a burden of health care in both developed and developing countries (Abdulazeez *et al*, 2013). Diabetes develops from prolong glucose imbalance between intracellular and extracellular resulted in hyperglycaemia state in which blood glucose can not be utilized by living cells. These conditions lead to vascular complication through increasing oxidative stress and inflammation. Vascular complication is the leading cause of death in both diabetes type 1and type 2 patient (Domingueti *et al*, 2015).

Diabetes mellitus (DM) are classified as two major disease: type 1 DM and type 2 DM. Type 1 DM is an autoimmune disease that immune system of the body attack insulin producing pancreatic β cells resulting in low insulin production. This condition leads to insulin dependent DM. In the other hand, type 2 DM was caused by inadequate action of insulin in action site (Hossain *et al*, 2016).

Pharmacotherapy in DM patient does not eliminate the cause of the disease but its targets on the symptom using insulin and hypoglicemic agent such as sulfonylurea and biguanids (Abdulazeez *et al*, 2013; Verma *et al*, 2015). However, sulfonylurea exert several adverse effect such as hypoglicemia and weight gain, in addition to toxic effect on liver and renal, while metformin cause lactic acidosis (Verma *et al*, 2015).

Alloxan is widely used in experimental pharmacology to induce diabetes in rat. The pathological mechanism is by destruction of insulin producing pancreatic β-cells. Alloxan undergo redox reaction resulted in increase increasing of radical species. In this case, pancreatic β-cells is the most sensitive organ

Lampiran 2 Dokumentasi Literatur 2

Judul: Uji Efek Antidiabetes pada Ekstrak Daun dan Batang Cocor Bebek *Kalanchoe pinnata* (Lam) Terhadap Tikus Galur *Sprague dawley* yang di Induksi Aloksan (Hariani, P., 2019)

SEKOLAH TINGGI ILMU KESEHATAN
SITI KHADIJAH PALEMBANG
PROGRAM STUDI S1 FARMASI
SKRIPSI, AGUSTUS 2019

PUSPA HARIANI

Uji Efek Antidiabetes Ekstrak Daun Dan Batang Cocor Bebek *Kalanchoe pinnata (Lam)* Terhadap Tikus Galur Sprague Dawley Yang Diinduksi Aloksan

V Bab + 68 Halaman + 15 Tabel

ABSTRAK

Diabetes mellitus adalah kelainan yang ditandai dengan glukosa darah yang melebihi normal (Hiperglikemia), *Kalanchoe pinnata (Lam)* secara tradisional digunakan diseluruh dunia sebagai tanaman obat, termasuk untuk mengobati diabetes. Penelitian ini merupakan penelitian experimental dengan metode *pre* dan *post control group design*. Tikus jantan sebanyak 32 ekor dibagi menjadi 8 kelompok perlakuan, tikus diberi aloksan sebanyak 75 mg untukl 1 tikus selama 3 hari untuk meningkatan glukosa darah. Kelompok 1 (kontrol negatif) diberi aquades, kelompok 2 (kontrol positif) diberi glibenklamid, kelompok 3, 4, dan 5 diberi ekstrak daun cocor bebek dengan dosis 16,6mg/100grBB, 5,8mg/100grBB Dan 2,9mg/100grBB. dan kelompok 6,7 da 8 diberi ekstrak batang cocor bebek dengan dosis 16,6mg/100grBB, 5,8mg/100grBB dan 2,9mg/100grBB diberi ekstrak selama 7 hari, hasil penelitian menunujukan dosis daun kelompok 3 dapat menurunkan glukosa darah pada hari ke 3, dengan persen penurunan sebesar 52,59 % untuk kelompok 4 dan 5 dapat menurunkan glukosa darah pada hari ke 7, dengan persen penurunan sebesar sebesar 45,25 %, 53,00 %, untuk dosis batang kelompok 6 dapat menurunkan glukosa darah pada hari ke 3 dengan persen penurunan sebesar 51, 27 %. kelompok 7 dan 8 dapat menurunkan glukosa darah pada hari ke 7 dengan persen penurunan sebesar 46.11%, dan 46.32%, dan data yang diperoleh dianalisa secara statistik menggunakan ove way ANOVA dan persamaan linear didapatkan nilai signa sesudah induksi nilai *P (P-value)* = 0,192, H3 nilai *P (P-value)* = 0,742, dan H7 nilai *P (P-value)* = 0,943 dengan *(P-value)* = 0,05, maka dapat disimpulkan bahwa ada pengaruh ekstrak daun dan ekstrak batang cocor bebek sebagai antidsabetes pada tikus putih galur *Sprague dawley*.

Kata kunci : Daun dan Batang cocor bebek, *Kalanchoe pinna (Lam).*, Antidiabetes

Lampiran 3 Dokumentasi Literatur 3

Judul: *Antidiabetic Activity of Kalanchoe pinnata in Alloxan-Induced Diabetic Rats* (Ophelia, *G.L et al*., 2019).

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Research Article

ANTIDIABETIC ACTIVITY OF *KALANCHOE PINNATA* IN ALLOXAN-INDUCED DIABETIC RATS

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ABSTRACT

Objective: The main purpose of the present study was to analyze the antidiabetic activity of methanolic extract of the leaf of *Kalanchoe pinnata* in alloxan-induced diabetic rats.

Methods: Diabetes mellitus (DM) is a chronic metabolic and endocrine disease regarded as a serious global public health problem. Albino Wistar rats were divided into four groups. Group I (normal) received drinking water throughout the course till 20 days. Groups II-IV received alloxan (120 mg/kg b.w) i.p on the 1st day of the study period. Group III animals received glibenclamide (10 mg/kg p.o) and Group IV received *K. pinnata* (200 mg/kg b.w p.o) for 20 days. The body weight, blood glucose level, serum urea, blood urea nitrogen (BUN), creatinine, cholesterol, total protein (TP), uric acid, and tissue (liver) antioxidant parameters: Malondialdehyde (MDA) and glutathione (GSH) were measured.

Results: *K. pinnata* treated rats showed the percentage increase in the body weight, decrease in the blood sugar level, creatinine, TP level, urea, uric acid, and BUN, MDA, and GSH when compared to alloxan-induced diabetic mellitus control rats. Thus, *K. pinnata* could be possibly employed to treat DM.

Conclusion: This preliminary analysis tested the most promising profile. It seems that methanolic extract of the leaf of *K. pinnata* improved general, blood serum, and liver antidiabetic agent. However, further studies confirming its potential is certainly warranted.

Keywords: *Kalanchoe pinnata*, Malondialdehyde, Alloxan, Blood urea nitrogen, Cholesterol.

 DOI: http://dx.doi.org/10.22159/ajpcr.2019.v12i3.30160

INTRODUCTION

Fast-growing socioeconomic development in the past 10 years has revealed a rise in the lifestyle disorders among which diabetes mellitus (DM) is growing rapidly and has turned out to be like an epidemic in many parts of the world. In 2015, DM and its associated complications affected 415 million people globally and resulted in 5 million deaths [1]. The effects of DM include long-term complications such as heart disease, stroke, dysfunction, and failure of various organs [15].

The World Health Organization (WHO) has estimated that diabetes will be one of the world's leading causes of death and disability within the next quarter century [14]. The incidence of DM is markedly increased worldwide due to modern sedentary lifestyle with consumption of junk food. Carbohydrates are the major constituents of the human diet and play an important role in energy supply [11]. DM is a major complex chronic condition that is a major source of ill health worldwide. Cardiovascular diseases, neuropathy, nephropathy, and retinopathy are among the major risks that are associated with diabetes [16]. This metabolic disorder is characterized by hyperglycemia and disturbances in carbohydrate, protein, and fat metabolism. Excessive generation of free radicals on unsaturated fatty acids has been implicated in the pathogenesis of vascular diseases and leads to increased oxidative stress [12]. According to the WHO projections, the prevalence of diabetes is such as to increase to 35% by 2020. At present, there are over 150 million diabetics worldwide and this is likely to increase to 300 million or more by the year 2025. Statistical projection of India suggests that it is speculated to have the highest number of diabetics in the world since the number of diabetics will rise from 15 million in 1995 to 57 million in 2025. Reasons for this rise include an increase in sedentary lifestyle, consumption of energy-rich diet, obesity, and a higher life span [2]. The treatment of DM in clinical practice has been confined to the use of oral hypoglycemic agents and insulin; the former being reported being endowed with characteristic profiles of serious side effects [10]. *Kalanchoe pinnata* is a succulent perennial plant that grows 3–5 feet tall. It commonly known as "air plant," it has tall hollow stems, fleshy dark green leaves that are distinctively scalloped and trimmed in red, and bell-like pendulous flowers. This is employed in folk medicine for the treatment of kidney stones, gastric ulcer, pulmonary infection, rheumatoid arthritis, etc. [3]. Alloxan is toxic glucose analogs that preferentially accumulate in pancreatic beta-cells through the GLUT2 glucose transporter. In the presence of intracellular thiols, especially glutathione (GSH), alloxan generates reactive oxygen species (ROS) in a cyclic redox reaction with its reduction product, dialuric acid. Autooxidation of dialuric acid generates superoxide radicals, hydrogen peruxide, and, in a final iron-catalyzed reaction step, hydroxyl radicals. These hydroxyl radicals are ultimately responsible for the death of the beta-cells [4]. In the present study, the methanolic extract of the leaves of *K. pinnata* was used to evaluate its antidiabetic efficacy in alloxan-induced diabetic rats.

METHODS

Animals

Male albino Wistar rats (180–200 g) were purchased from Adita Biosys Private Limited, Tumakuru-572106. CPCSEA Reg No - 1868/Po/Bt/S/16/CPCEA and were maintained in the animals house of PES College of Pharmacy, Bengaluru. Once procured, animals were acclimatized for 10 days under standard husbandry conditions, the animals were housed in polypropylene cages maintained under controlled temperature at 23°C±2°C, relative humidity 45–55%, and with 12:12 h day/night cycle. Temperature and humidity were recorded daily. The animals had free access to standard rat pellet along with water supplied *ad libitum* under strict hygienic conditions. The experimental protocols were subjected to approval by the Institutional Animal Ethics Committee (IAEC approval No - PESCP/IAEC/63/2018

Lampiran 4 Dokumentasi Literatur 4

Judul: *Antidiabetic potential of ethanol leaf extract of Bryophyllum pinnatum on alloxan-induced diabetic rats and their haematological profiles* (*Casmir et al*., 2017).

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African Journal of Pharmacy and Pharmacology

Full Length Research Paper

Antidiabetic potential of ethanol leaf extract of *Bryophyllum pinnatum* on alloxan-induced diabetic rats and their haematological profiles

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Bryophyllum pinnatum **is a known herb found in the tropical region of Africa and other parts of the world. In this study, the ethanol extract of the plant was investigated for possible anti-diabetic effect on alloxan induced hyperglycaemic wistar albino rats. Phytochemical studies revealed that Flavonoids and alkaloids were highly abundant compared to steroids and terpenoids which were slightly present while glycosides and reducing sugar were moderately present. Diabetes was induced via intraperitoneal injection using alloxan monohydrate. Groups 2 to 5 were induced while Groups 1, 6 and 7 were not. Group 1 was negative control group; Group 2 was positive control group, while Group 3 was the standard control. Groups 4 to 7 were the treatment groups. The results of anti-hyperglycaemic effect of the extract showed a significant ($p<0.05$) reduction in the glucose level of alloxan-induced diabetic rats in Groups 4 and 5, respectively treated with 200 and 400 mg/kg body weight of the extract when compared with the positive control. However, there was a significant increase ($p<0.05$) in some haematological parameters such as red blood cell count, haemoglobin count, packed cell volume of groups 4, 5, 6, and 7 when compared with the positive control. There was a significant decrease ($p<0.05$) in the malondialdehyde, low density lipoprotein, triacylglycerol and total cholesterol concentrations of groups 4, 5, 6, and 7 when compared with the positive control. The result of the study showed that the extract of B. pinnatum exhibited anti-hyperglycaemic activities in alloxan-induced diabetic wistar albino rats.**

Key words: *Brohyllum pinnatum*, phytochemistry, Diabetes, haematological parameters.

INTRODUCTION

Tropical forests are biologically lavished with diverse ecosystem of plants whose potential value as natural pharmacy is yet to be discovered (Cohen-Kohler, 2007). The native people have used plants as medicine for

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Lampiran 5 Ethical Clearance

KEMENTERIAN KESEHATAN REPUBLIK INDONESIA
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KEMENKES RI

PERSETUJUAN KEPK TENTANG
PELAKSANAAN PENELITIAN BIDANG KESEHATAN
Nomor:0172/KEPK/POLTEKKES KEMENKES MEDAN 2021

Yang bertanda tangan di bawah ini, Ketua Komisi Etik Penelitian Kesehatan Politeknik Kesehatan Kemenkes Medan, setelah dilaksanakan pembahasan dan penilaian usulan penelitian yang berjudul:

"Studi Literatur Uji Antidiabetes Ekstrak Daun Cocor Bebek (Kalanchoe pinnata Lam) Pada Hewan Percobaan Yang Di Induksi Aloksan."

Yang menggunakan manusia dan hewan sebagai subjek penelitian dengan ketua Pelaksana/ Peneliti Utama : **Vefi Oktaviani Yesa**
Dari Institusi : **Jurusan D-III Farmasi Poltekkes Kemenkes Medan**

Dapat disetujui pelaksanaannya dengan syarat :
Tidak bertentangan dengan nilai – nilai kemanusiaan dan kode etik penelitian kesehatan
Melaporkan jika ada amandemen protokol penelitian.
Melaporkan penyimpangan/ pelanggaran terhadap protokol penelitian.
Melaporkan secara periodik perkembangan penelitian dan laporan akhir.
Melaporkan kejadian yang tidak diinginkan.

Persetujuan ini berlaku sejak tanggal ditetapkan sampai dengan batas waktu pelaksanaan penelitian seperti tertera dalam protokol dengan masa berlaku maksimal selama 1 (satu) tahun.

Medan, April 2021
Komisi Etik Penelitian Kesehatan
Poltekkes Kemenkes Medan

Ketua,

Dr.Ir. Zuraidah Nasution,M.Kes
NIP. 196101101989102001

Lampiran 6 Kartu Bimbingan

POLITEKNIK KESEHATAN
JURUSAN FARMASI
JL. AIRLANGGA NO. 20 MEDAN

KARTU LAPORAN PERTEMUAN BIMBINGAN KTI MAHASISWA TA. 2020/2021

Nama : Vefi Oktaviani Yesa
NIM : P07539018038
Pembimbing : Lavinur, S.T., M.Si.

NO	TGL	PERTEMUAN	PEMBAHASAN	PARAF MAHASISWA	PARAF PEMBIMBING
1	20/01/2021	1	Perkenalan dan arahan		
2	23/01/2021	2	Diskusi dan penentuan judul KTI		
3	25/01/2021	3	ACC judul KTI		
4	12/02/2021	4	Pengumpulan proposal KTI		
5	15/02/2021	5	Bimbingan penulisan KTI		
6	19/02/2021	6	Diskusi proposal KTI		
7	26/02/2021	7	Revisi proposal KTI		
8	27/02/2021	8	ACC proposal KTI		
9	3/05/2021	9	Diskusi bab IV dan V		
10	9/05/2021	10	Revisi KTI		
11	9/06/2021	11	Revisi KTI setelah seminar hasil		
12	17/06/2021	12	ACC KTI		

Ketua

Dra. Masniah, M.Kes.,Apt
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