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JUDUL: EVALUATION OF ANTI-HYPERGLYCAEMIC EFFECT OF *Leucosyke capitellata* LEAF IN NORMAL AND STREPTOZOTOCIN-INDUCED DIABETIC RATS

IJAZAH: DEGREE OF BACHELOR OF SCIENCE WITH HONOURS IN CONSERVATION BIOLOGY

SAYA LINA LING (HURUF BESAR) SESI PENGAJIAN: 2005-2008

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EVALUATION OF ANTI-HYPERGLYCAEMIC EFFECT OF *Leucosyke capitellata* LEAF IN NORMAL AND STREPTOZOTOCIN - INDUCED DIABETIC RATS

LINA LING

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF BACHELOR OF SCIENCE (HONOURS)

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April 2008

DECLARATION

I declare that this dissertation is my own work product except for narrative and summary that each one has settled its sources and origins.

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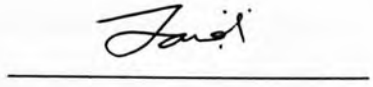

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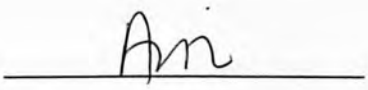

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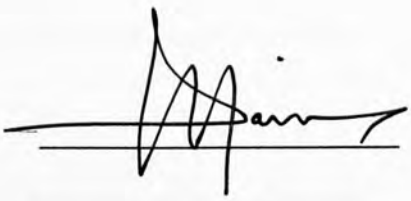

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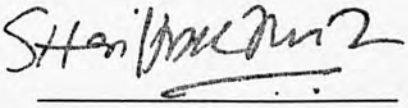

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Abstrak

Leucosyke capitellata (Poir.) Wedd. dipercayai mempunyai potensi untuk merawat penyakit diabetes dan digunakan secara traditional oleh kaum Kadazandusun di Sabah. Terdapat tiga objektif kajian ini iaitu menentukan kandungan fenolik dalam daun *L. capitellata* dengan menggunakan kaedah Folin-Ciocalteu, menentukan aktiviti antioxida dalam daun *L. capitellata* dengan menggunakan cerakin perencatan radical bebas DPPH dan menilai kesan ekstrak daun *L. capitellata* terhadap aras glukosa darah dan berat badan tikus normal dan diabetik yang diaruh streptozotocin (STZ). Dalam kajian ini, ekstrak daun *L. capitellata* menunjukkan nilai jumlah kandungan fenolik yang tinggi iaitu 121.6 ± 4.0 mg/g sampel. Aktiviti antioksida ekstrak daun *L. capitellata* menunjukkan nilai yang tinggi (78.32 ± 1.31 %) pada kepekatan 100 μg/ml. Sementara itu, nilai EC_{50} ekstrak daun *L. capitellata* adalah 16.20 ± 0.51. Dalam kajian haiwan, tidak terdapat perbezaan yang signifikan ($p > 0.05$) pada aras glukosa darah dan berat badan tikus normal yang dirawat dengan ekstrak daun *L. capitellata*. Sebaliknya, terdapat penurunan yang signifikan ($p < 0.05$) pada aras glukosa tikus diabetik yang dirawat dengan ekstrak daun *L. capitellata*. Oleh itu, boleh dikatakan bahawa ekstrak daun *L. capitellata* mempunyai kebolehan untuk menurunkan tekanan oksida dan mempunyai antihiperglisemik ke atas tikus diabetik disebabkan oleh ciri antioksidanya.

Abstract

Leucosyke capitellata (Poir.) Wedd. is believed to has potential to treat diabetes and was traditionally used by Kadazandusun ethnic in Sabah. There were three objectives of this study: determination of total phenolic contents in *L. capitellata* leaves by Folin-Ciocalteu method, determination of antioxidant activity in *L. capitellata* leaves using DPPH free radical scavenging assay and to evaluate the effect of the *L. capitellata* leaves extract on blood glucose levels and body weight in normal and streptozotocin - induced diabetic rats. In this study, *L. capitellata* leaves extract showed a high value of total phenolic content which was 121.6 ± 4.0 mg/g sample. The antioxidant activity of *L. capitellata* leaves extract shows the highest value (78.32 ± 1.31 %) at the concentration of 100 µg/ml. Meanwhile, the EC_{50} value of *L. capitellata* leaves extract was 16.20 ± 0.51. In animal study, there was no significant different ($p > 0.05$) on blood glucose level and body weight in normal rats treated with *L. capitellata* leaves extract. On the other hand, there was a significant reduction ($p < 0.05$) of blood glucose level in diabetic rats treated with *L. capitellata* leaves extract. Thus, it could be suggested that *L. capitellata* leaves extract has the ability to reduce the oxidative stress and possess antihyperglycaemic effect in diabetic rats due to its antioxidant property.

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BW	Body weight
g	Gram
kg	Kilogram
L	Litre
M	Molar
mg	Miligram
mmol	Milimol
ml	Milimetre
nm	Nanometre
No	Number
pH	Potential of hydrogen
%	Percentage
µg	Microgram
^{o}C	Degree celsius

CHAPTER 1

INTRODUCTION

1.1 Introduction

Malaysia, especially its tropical rain forest contains hidden plant treasures and it is one of the most species-rich terrestrial ecosystems in the world. In this forest, there are still many medicinal plants that have not been explored. About 1500 species of medicinal plants have been used traditionally to treat various diseases in Malaysia (Goh & Hamdan, 1999). There are tremendous herbal resources including "pegaga", "tongkat ali", "mengkudu", ginger and aromatic plants in Malaysia (Utusan Malaysia, 2007). However, many of the uses of herbal medicine is not scientifically proven and usually derived from traditional belief and experience.

In Sabah, there is a long tradition of usage and relying on forest resources, not only in cultivation, but also in forest products (Andersen *et al.,* 2003). According to the Minister of Agriculture and Food Industry of Sabah, Datuk Abdul Rahim Ismail,

Sabah has the potential to become the main supplier of organically grown herbs and medicinal plants. He said Sabah could also supply herb and medicinal plant seedlings nationwide if the nurseries could be developed to make the process commercially viable (Utusan Malaysia, 2007).

According to Ministry of Health, about 2.6 million of people in Malaysia suffering from diabetes and the number were expected to be increased to 3.38 million in year 2020 (MDA, 2007). Besides that, World Health Organization (WHO) estimates about 180 million people of the world who suffer from this disease. It also causes 1.1 million deaths at year 2005 with estimation 5 percent death at the whole world every year (MDA, 2007).

The extraction from roots, leaves, seeds, flowers and fruit of medicinal plants have been extensively practiced in treating various disease such as diabetes, cancer, hepatitis, bacterial and parasitic infections. According to World Health Organization, there are estimate 80% people in developing countries using traditional medicines such as plants extracts or active principles originating from part of plants for their primary health care (Farnsworth *et al.*, 1985). For example, several regions in Borneo, *Atropa belladonna* tincture, *Rauvolfia serpentine* roots and *Papaver somniferum* extract or tincture were used as an antispasmodic, hypertension and analgesic respectively (Farnsworth *et al.*, 1985).

According to Babji *et al.* (1999), the presence of synthetic antioxidants can delay oxidation in food but this cause consumer concern due to health hazards when consume the food product. Animal studies showed that butylated hydroxyl anisole (BHA) which is widely used in food processes are carcinogenic. Recently, scientists are looking into the utilization of natural antioxidants such as phenolic compounds from plant extracts due to fewer side effects (Babji *et al.*, 1999).

As the number of people suffering from diabetes is increasing, there has been an increasing interest in the collection, identification and phytochemical screening of medicinal plants for their medical value and chemical components. This is aiming to find the new treatments and drug for diabetes. In this study, *Leucosyke capitellata* (Poir.) Wedd. is studied because of its potential to treat diabetic which traditionally used by Kadazandusun in Sabah. This has not been scientifically proven.

1.2 Study Objectives

There are three objectives of this study:

1) To determine the total phenolic contents in *Leucosyke capitellata* (Poir) Wedd. leaves by Folin-Ciocalteu method.
2) To determine the antioxidant activity of *Leucosyke capitellata* leaves using DPPH scavenging assay.
3) To evaluate the effect of the *Leucosyke capitellata* extract on blood glucose levels and body weight in normal and streptozotocin - induced diabetic rats.

CHAPTER 2

LITERATURE REVIEW

2.1 Taxonomy of *Leucosyke capitellata*

Kingdom: Plantae

Phylum: Tracheophyta

Class: Magnoliopsida

Order: Urticales

Family: Urticaceae

Tribe: Boehmerieae

Genus: *Leucosyke*

Species: *Leucosyke capitellata* (Poir.) Wedd.

(Wedd., 1869)

2.2 Family Urticaceae

According to Keng (1978), the Urticaceae are fibrous herbs, shrubs or soft-woody trees. The leaves are simple, alternate or opposite and stipulate. The flowers are small,

usually unisexual, cymose or capitate. The perianth is usually four to five lobed. The stamens are four to five, opposite to the perianth-lobes; filaments curved inwards in bud. The ovary is one-carpellate, one-loculate and one- ovulate; one style. The fruit is an achene or drupe and often invested by perianth.

There are about 45 genera and about 11 genera in Malaya. They are classified in tribe Urticeae, tribe Procrideae and tribe Boehmerieae (Keng, 1978). In tribe Urticeae, the plants have stinging hairs while the tribe Procrideae and tribe Boehmerieae are without stinging hairs.

2.3 Introduction of *Leucosyke capitellata*

The synonyms of *Leucosyke capitellata* include *Missiessya capitellata* and *Cypholophus molucanus* sensu (Goh *et al.*, 1995). The vernacular name in Murut is 'Kuliatmato', while in Dusun is 'Mandahasi' (Fasihuddin, 2000). Besides that, *L. capitellata* is also called 'daun semutu', 'teh kampong' or 'sembutu' (Coode *et al.*, 1996) by Iban and 'krangan' or 'serangan' by the Bidayuh. The local name by Malay people is 'balik sumpah' (MIPRBD, 1994).

2.3.1 Morphology

According to MIPRBD (1994), the *L. capitellata* is branched small tree. The leaves are alternate with petiole 1 cm long; lamina dark-green, scurfy above but white and

glabrous below with about 12 cm x 5 cm; leaves are oblong-elliptic with oblique base and narrow acute apex; and serrated margins (Fig. 2.1 and Fig. 2.2). The inflorescence of this species is at the leaf-axil with 1 or 2 heads; each head is about 4-5 mm across and has rounded outline.

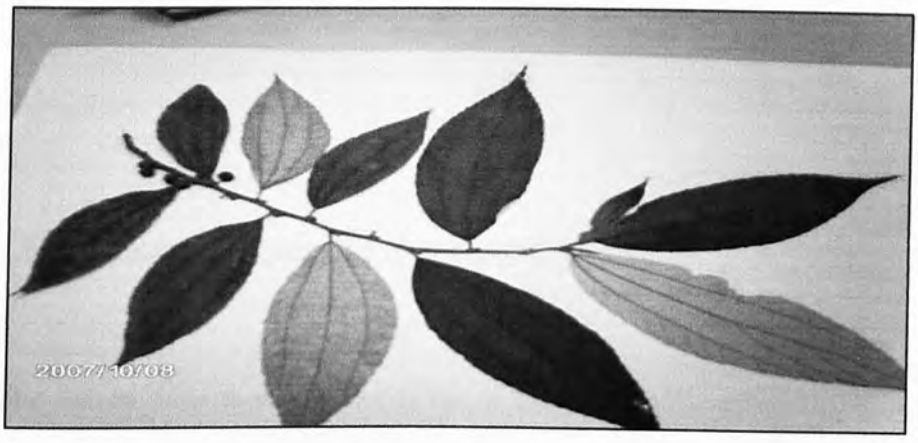

Figure 2.1 Morphology of *Leucosyke capitellata*

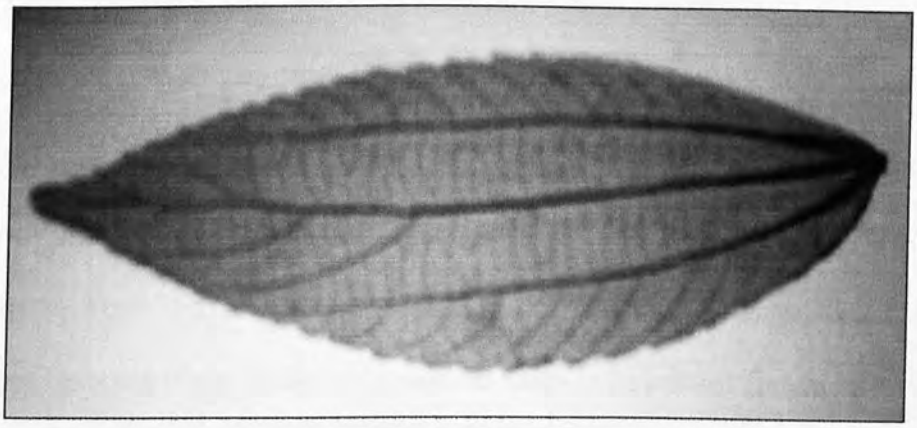

Figure 2.2 Single leaf of *Leucosyke capitellata*

2.3.2 Habitat

L. capitellata is commonly found growing quickly at the edge of secondary forest on clay soil under partial shade or in the open; it coppice readily from the stump. It fruits regularly and can be propagated from stem-cuttings (MIPRBD, 1994). This species is midstorey or subcanopy tree; usually grow at altitude 60-150 m (Coode *et al.*, 1996).

2.3.3 Mineral composition of *Leucosyke capitellata*

The leaves have high concentration of calcium and magnesium, 403 mg/g and 626 mg/g respectively (MIPRBD, 1994). The study of Voon & Kueh (1999) also shows that the leaves are also contain fosforus (35 mg), potasium (310 mg), ferum (3.5 mg), mangan (8 p.p.m.), cuprum (3.1 p.p.m.), zink (3.1 p.p.m.) and vitamin C (6.5 mg) per 100g edible portion.

Calcium (Ca) can helps clotting of blood and function of muscle, control the beating of heart, growth and strengthen the bone and teeth; the blood will not clot without calcium. It is very important to the women who menopause for prevention of osteoporosis (Ong, 2004). Magnesium (Mg) is important for the growth of bone and function of muscle, strengthen teeth and bone, and also important for the excretion process of hormone and enzyme in body (Ong, 2004).

2.3.4 *Leucosyke capitellata* on diseases

On field interview in several villages in Sabah by the Fasihuddin (2000), the leaves of the plant, *L. capitellata* is decoction as tea to treat diabetes, hypertension and gastric. The villagers of Kuyongon, Sabah use the plant sap of *L. capitellata* as eye-drops and for pain in ears (Andersen *et al.* 2003). *L. capitellata* is also used for eye diseases especially conjunctivitis and cancer of the cornea, called 'lantok' in Dusun (Guntavid, 1982). The sap of individual plant is allowed to drip into the eyes so that it can gently washes the eyes (Guntavid, 1982).

The plant also contains anti-tuberculotic property (MIPRBD, 1994). The decoction of roots can be used to cure pulmonary tuberculosis, cough, headaches and gastralgia (pain in the stomach) according to ASEAN centre for biodiversity in the Checklist of Medicinal Plants in Southeast Asia (2004). The twigs are traditionally boiled in combination with 8-10 other herbs and the resultant decoction has been used as an herbal bath for the mother after childbirth (MIPRBD, 1994). This can help mothers to regain her health and strength and to prevent certain post-natal depression (MIPRBD, 1994).

According to Guntavid (1982), *L. capitellata* is thought to have a powerful affect against high fever when composed with six different species of plants such as *Clausena excavate* Burm., (Rutaceae) "Lango-langot" (Dusun), *Nephrolepis falcate* (Cav.) C. Chr., (Asclepediaceae) "Monompuru" (Dusun), *Erythrina varicgata* L., (Leguminosae) "Dadap" (Bajau) and another two leguminous plants. These plants are

pounded together and made into a poultice. The prescribed colour of the poultice is blood-red.

2.4 Phenols

'Phenolics' circumscribes all the compounds which possess an aromatic ring bearing a hydroxyl group or its substituents and most of the phenols are derived from 5-dehydroquinic acid (Daniel, 2006).

Phenolics are very effective antioxidants (Daniel, 2006). Phenolics have received considerable attention because of their physiological functions, including antioxidant, antimutagenic and antitumour activities (Othman *et al.*, 2007). Phenolics include simple phenolics, phenolic acids, phenyls propanes, acetophenones, stilbenes, xanthones, flavones, flavonols, catechins, aurones, chalcones, isoflavonoids, flavans, neoflavonoids, tannins (Daniel, 2006) and hydroxycinnamic acid derivatives (Amin *et al.*, 2004c).

The effects of phenolic compounds are shown in cocoa bean (Othman *et al.*, 2007). Study shown that there was 60 % of cocoa bean is flavanol monomers and procyanidin oligomers which can combat free radicals that dangerous to our body (Adamson *et al.*, 1999). Besides that, these compounds shown to have some biological activities such as the ability to scavenge superoxide radicals and hydroxyl radicals,

reduce lipid peroxyl radicals and inhibit lipid peroxidation. Moreover, the utilization of cocoa decreases the risk of cardiovascular disease (Keen, 2001). Cocoa powder and cocoa beans extract were shown to exhibit anti-hyperglycaemic effects on streptozotocin induced diabetic rats (Amin *et al.*, 2004a). Furthermore, Malaysian cocoa liquor in ethanolic extract shows ability in decreasing the severity of hepatocarcinogenesis in rats (Amin *et al.*, 2004b). By the study of Duke (2000), two spoons of cocoa in water could be used as a palliative treatment of Parkinson's disease, mastitis, liver diseases, sexual dysfunction, fever, cystitis, cold, burns, asthma and bronchitis, diabetes and obesity.

According to the study of Wu *et al.* (2007), the total phenolic content of *Laggera pterodonta* especially isochlorogenic acids such as 3, 4-O-dicaffeoylquinic acid, 3, 5-O-dicaffeoylquinic acid and 4,5-O-dicaffeoylquinic acid, may be the major active compounds responsible to treat hepatitis. Besides that, the phenolic acids of the dried root of *Salvia miltiorrhiza* (Danshen) is extensively used to treat coronary heart diseases, cerebrovascular diseases, bone loss, hepatitis, hepatocirrhosis and chronic renal failure, dysmenorrheal and neurasthenic insomnia (Liu *et al.*, 2007).

Furthermore, from epidemiological evidence, *Carica papaya*'s leaves also contain phenolic compounds which can prevent some chronic diseases such as cardiovascular disease, cancer, diabetes, bacterial and parasitic infections. In the tropics, the leaves are cooked as a vegetable and in preparation of teas and infusions (Canini *et al.*, 2007).

2.5 Antioxidant

Antioxidants can scavenge free radicals and protect the human body from oxidative stress, which causes cancers, heart diseases (Sun *et al.*, 2007), ageing, stroke, diabetes and neuron-degenerative disease such as Alzheimer's disease and Parkinsonism (Daniel, 2006). The increased levels of sugars in blood caused by diabetes will leads to the production of free radicals which leading to oxidative stress. Oxidative stress is defined as excess of formation or incomplete removal of highly reactive molecules such as reactive oxygen species (ROS). ROS include free radicals such as superoxide, hydroxyl radical, peroxyl radical as well as nonradical species such as hydrogen peroxide (Ardestani & Yazdanparast, 2007). Oxidative stress is considered playing a prominent causative role in many diseases including liver damage (Wu *et al.*, 2007).

Supplements of antioxidants have shown to decrease oxidative stress and diabetic induced defects in diabetic animals (Daniel, 2006). Food such as fruits, vegetables and grains are reported to contain a wide variety of antioxidant components, including phenolic compounds (Othman *et al.,* 2007). Besides phenolic compounds, other antioxidant components including vitamin C, vitamin E, carotenoids, lycopenes and other phytochemicals (Amin *et al.*, 2006). Asparagus, broccoli (Sun *et al.*, 2007) and *Amaranthus sp.* (bayam) (Amin *et al.*, 2006) are vegetables that contain high antioxidant activity. Studies have shown that big amount of antioxidants in the diet will help to prevent the disease (Daniel, 2006).

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