EFFECTS OF *STROBLANTHES CRISPUS* CRUDE AND TEA EXTRACTS IN STREPTOZOTOCIN-INDUCED HYPERGLYCEMIC RATS

MOHD FADZELLY ABU BAKAR

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MASTER OF SCIENCE
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By

MOHD FADZELLY ABU BAKAR

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirement for the Degree of Master Science

September 2005
To my beloved mom and dad, for their outstanding support and patience
To my lovely siblings; Adik, Ina and Ain
To diabetics and their families, clinicians and researchers
Who are at war fighting this disease

fadjelly
Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of
the requirement for the degree of Master of Science

EFFECTS OF STROBLANTHES CRISPUS CRUDE AND TEA EXTRACTS IN
STERPTOZOTOCIN-INDUCED HYPERGLYCEMIC RATS.

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September 2005

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Strobilanthes crispus leaf has been used ethnomedically to treat diabetes mellitus and
related disorders in Asia. The first part of this study is to develop a tea from leaves of S.
crispus and investigate its antioxidant properties in vitro. Fermented and unfermented
teas from young and old leaves of S. crispus were developed according to Camellia
sinensis and Camellia theifera preparations for black and green tea, respectively. Three
methods were used to determine the antioxidant activities i.e 1) β-carotene bleaching
method 2) DPPH free radical scavenging assay 3) Ferric reducing/antioxidant power
(FRAP) assay. The total phenolic content was also estimated using Folin-Ciocalteu
method. The result showed that unfermented S. crispus tea displayed a higher
antioxidant activity compared to fermented S. crispus tea. Tea developed from old or
matured leaves possessed higher antioxidant activity compared to young leaves.
However, commercial green (Sencha, UK) and black (Boh, Malaysia) tea that were
developed from leaves of C. sinensis exhibited higher antioxidant activity among all
teas tested. The second part of this study was aimed at determining the effect of *S. crispus* crude extract on STZ-induced hyperglycemic rats. *S. crispus* (young and old leaves) were extracted with distilled water and given to normal and hyperglycemic rats at concentrations of 2.5, 5.0 and 7.5% for 21 days. Plasma glucose, lipid profile (total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol), total antioxidant status and serum potassium and magnesium contents were determined on baseline (day 0), day 7 and day 21. The results showed that *S. crispus* crude extract at concentrations of 2.5, 5.0 and 7.5% from old or matured leaves reduced glucose level significantly in hyperglycemic rats (p<0.05). Third part of this study evaluated the effect of *S. crispus* fermented and unfermented tea in STZ-induced hyperglycemic rats at a concentration of 2% for 21 days. Plasma glucose, lipid profile (total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol), total antioxidant status and serum potassium and magnesium contents were determined during baseline (day 0), day 7 and day 21. The results showed that both fermented and unfermented *S. crispus* tea reduced glucose level in hyperglycemic rats (p<0.05). Fermented and unfermented *S. crispus* tea also improved antioxidant status and lipid profile in hyperglycemic rats by lowering the total cholesterol, triglyceride, and LDL-cholesterol. Total antioxidant status and HDL-cholesterol also increased in hyperglycemic rats treated with fermented or unfermented tea *S. crispus*. Both fermented or unfermented *S. crispus* tea failed to prevent the reduction of serum magnesium in hyperglycemic rats.
Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains

KESAN EKSTRAK KASAR DAN EKSTRAK TEH DARI DAUN STROBILANTHES CRISPUS PADA TIKUS YANG DIARUH HIPERGLISEMIA MENGGUNAKAN STREPTOZOTOCIN

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Strobilanthes crispus telah digunakan terutamanya di Asia dalam perubatan tradisional untuk merawat diabetes mellitus dan penyakit yang berkaitan. Bahagian pertama kajian ini adalah untuk membuat teh dari daun S. crispus dan mengkaji ciri-ciri antioksidan dalam teh tersebut. Teh yang difermentasi dan yang tidak difermentasi dibentuk menggunakan kaedah membuah teh masing-masing dari daun C. sinensis dan C. theifera. Tiga kaedah digunakan untuk menentukan aktiviti antioksidan iaitu 1) Kaedah pelunturan β-karoten 2) Kaedah penghapusan radikal bebas DPPH 3) Kaedah penurunan ferik/kuasa antioksidan (FRAP). Kandungan fenolik keseluruhan juga ditentukan menggunakan kaedah Folin-Ciocalteu. Keputusannya menunjukkan bahawa teh S. crispus yang tidak difermentasi menunjukkan paras aktiviti antioksidan yang lebih tinggi dari yang difermentasi. Teh yang dibentuk dari daun tua menunjukkan aktiviti antioksidan yang lebih tinggi berbanding dengan daun muda. Walaubagaimanapun, teh hijau (Sencha, UK) dan teh hitam (Boh, Malaysia) yang
dibuat dari daun teh (C. sinensis) menunjukkan tahap aktiviti antioksidan yang paling tinggi dalam semua teh yang dikaji. Bahagian kedua kajian ini adalah untuk menentukan kesan ekstrak kasar pada tikus yang diaruh hiperglisemia menggunakan STZ. Ekstrak kasar daun S. crispus (daun muda dan tua) disediakan dengan menggunakan air suling dan diberi pada tikus normal and tikus hiperglisemia pada kepekatan 2.5%, 5.0% dan 7.5% selama 21 hari. Paras glukosa, profil lipid (kolesterol keseluruh, trigliserida, HDL-kolesterol, LDL-kolesterol) plasma, status antioksidan keseluruh dan kalium serta magnesium ditentukan pada hari 0, 7 dan 21. Keputusannya menunjukkan ekstrak kasar daun tua S. crispus pada kepekatan 2.5%, 5.0% dan 7.5% menurunkan paras glukosa secara signifikan pada tikus yang diaruh hiperglisemia (p<0.05). Bahagian ketiga kajian ini adalah untuk menilai kesan pengambilan teh S. crispus (difermentasi atau tidak difermentasi) pada tikus normal and tikus hiperglisemia pada kepekatan 2.0% selama 21 hari. Paras glukosa, profil lipid (kolesterol keseluruh, trigliserida, HDL-kolesterol, LDL-kolesterol) plasma, status antioksidan keseluruh dan kalium serta magnesium ditentukan pada hari 0, 7 dan 21. Keputusannya menunjukkan bahawa ke dua-dua teh S. crispus yang difermentasi atau tidak difermentasi menurunkan secara berkesan paras glukosa plasma pada tikus yang diaruh hiperglisemia (p<0.05). Kedua-dua teh S. crispus yang difermentasi atau yang tidak difermentasi juga mampu membaiki paras antioksidan keseluruh dan juga membaiki profil lipid dalam tikus yang diaruh hiperglisemia dengan menurunkan paras kolesterol keseluruh, trigliserida dan LDL-kolesterol. Status antioksidan keseluruh dan HDL-kolesterol juga meningkat pada tikus hiperglisemia yang dirawat dengan teh S. crispus yang difermentasi atau yang tidak difermentasi. Walaubagaimanapun, ke dua-
dua teh tersebut gagal menghalang penurunan magnesium serum dalam tikus hiperglisemia.
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I certify that an Examination Committee met on 30 September 2005 to conduct the final examination of Mohd Fadzelly Abu Bakar on his Master of Science thesis entitled "The Effects of Strobilanthes crispus crude and tea extracts in streptozotocin-induced hyperglycemic rats" in Accordance with Universiti Pertanian Malaysia (Higher Degree) Act 1980 and Universiti Pertanian Malaysia (Higher Degree) Regulation 1981. The Committee recommends that the candidate be awarded the relevant degree. Members of the Examination committee are as follows:

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Date: 09 MAR 2006
DECLARATION

I hereby declare that the thesis is based on my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously or concurrently submitted for any other degree at UPM or other institutions.

MOHD FADZELLY ABU BAKAR

Date: 15/2/2006
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LIST OF ABBREVIATIONS

AAS = atomic absorption spectrometer
FRAP = ferric reducing ability of plasma or ferric reducing / antioxidant power
HDL-cholesterol = high density lipoprotein cholesterol
LDL-cholesterol = low density lipoprotein cholesterol
VLDL-cholesterol = very low density lipoprotein cholesterol
Min = minute
Hr = hour
Temp = temperature
TBA = thiobarbituric acid
TCA = trichloroacetic acid
DPPH = 1,1-diphenyl-2-picrylhydrazyl
HSDA = N-(2-hydroxy-3-sulfopropyl)-3, 5- dimethoxyaniline
STZ = streptozotocin
GOD = glucose oxidase
POD = peroxidase
TPTZ = 2,4,6-tripyridyl-s-triazine
CHAPTER I

INTRODUCTION

1.1 Background

Prevalence of diabetes in adults worldwide was estimated to be 4.0% in 1995 and this figure was estimated to rise to 5.4% by the year 2025. The prevalence is higher in developed than in developing countries. The number of adults with diabetes in the world will rise from 135 million in 1995 to 300 million in the year 2025. The major part of this numerical increase will occur in developing countries including Malaysia. There will be a 42% increase, from 51 to 72 million, in the developed countries and a 170% increase, from 84 to 228 million, in developing countries. Thus, by the year 2025, more than 75% of people with diabetes will reside in developing countries, as compared with 62% in 1995 (King et al., 1998).

Diabetes is a costly disease and is associated with major long-term implications, not only for the health and well being of the affected individuals, but also for the government. WHO (2002) reported that the direct health costs of treating diabetic patients range from 2.5% to 15% of annual budget, depending on local diabetes prevalence and effectiveness of the treatment available. WHO estimated that there are over 171 million people worldwide who are afflicted with diabetes mellitus (WHO, 2004). These complications contribute to the enormous cost, both economic and
personal, that are associated with this disease. Generally, symptoms of diabetes complications develop years after this disease has occurred (Foster, 1991).

In Malaysia, the high demand for herbs has caused some herbs to be imported from other countries in high quantities. Based on estimated by the Director of Pusat Sumber Genetik Tumbuhan, Institut Biosains, UPM, Dr. Mohd Saad found that value of imported medicinal plants in Malaysia has increased from RM 167 million (1990) to RM 401 million (1997). Meanwhile, the value of medicinal plants exports have also increased from RM 17 million in 1990 to 58 million in 1997. In Berita Minggu Newspaper (1998), he also said that research from their institute found that 80% of the world’s population still depend on traditional medicine, including herb. World Health Organization (WHO), as reported in the Berita Minggu Newspaper estimated that approximately 75 to 95% of world population still depend on traditional medicine for health care.

Malaysia is a country blessed with many kinds of herbs or plants which is frequently used in traditional medicine. In Malaysia, over 15 000 species of higher plants were found and about 1200 of these plant species have been reported to have potential pharmaceutical value some of which are being used as herbal medicine (Soepadmo, 1991). Furthermore, throughout the development of human culture, the use of natural products (especially from medicinal plants) has had magical-religious significance and different points of view regarding the concepts of health and disease existed within each culture (Rates, 2001)
One of the herbs that have great potential and is believed to have health-giving properties is “pecah beling” or *Strobilanthes crispus* (Figure 1.1). It is commonly known as “daun pecah beling” in Jakarta or “enyoh kilo”, “kecibeling” or “kejibeling” in Java (Sunarto, 1977). It is also locally known as “pecah kaca” or “jin batu”.

Figure 1.1: *Strobilanthes crispus* ZII 109 (L) Bremek or *Saricocalix crispus* ZII 109 (L) Bremek (Acanthaceae)
Traditionally, the leaves of pecah beling are boiled with water and the filtrates used in traditional medicine in Malaysia and Indonesia as antidiabetic, diuretic, antilytic and laxative agents. This plant has many cystoliths of calcium carbonate and an infusion is mildly alkaline (Perry & Metzger, 1980). A recent study indicated that the water extract of *S. crispus* contained compounds that inhibits the proliferation of retrovirus; an agent in viral disease such as acquired immune deficiency syndrome (AIDS) and adult T-cell Leukemia (Kusumoto *et al.*, 1992). This plant also possesses antimicrobial properties (Soediro *et al.*, 1983), high antioxidant activity (Ismail *et al.*, 2000), anticancer properties (Endrini, 2003) and antihepatocarcinogenesis (Jaksa *et al.*, 2004).

1.2 Problem statement

Until today, there is no treatment that can completely cure diabetes mellitus. Presently, insulin is used to treat diabetes mellitus type 1. On the other hand, the pharmacological agents currently used for the treatment of type 2 diabetes include sulphonylureas, biguanide, thiazolidinedione and acarbose. These agents however have restricted usage due to several undesirable side effects and failure to significantly alter the course of diabetic complications. Current insulin regimens (in type 1 diabetes mellitus) are problematic in maintaining physiological blood glucose profile (Groop *et al.*, 1985). Hypoglycemic agent such as glibenclamide can cause acidosis and impair cardiac function (Legtenberg *et al.*, 2002) and is not effective in long-term treatment (Gerich *et al.*, 1985). In addition, hypoglycemic drug such as sulphonylurea, leads to a higher risk