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THE HYPOGLYCAEMIC ACTIVITY OF MENGKUDU (*MORINDA CITRIFOLIA*)

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THE HYPOGLYCAEMIC ACTIVITY OF MENGKUDU (*MORINDA CITRIFOLIA*)

By

CHEE BENG JIN

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

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A Work,
Dedicated to…

My parents, brother and my beloved family members,

Relatives and friends,

Brothers and sisters in Christ,

Diabetes research.

Worship the LORD your God,
and his blessings will
be on your food and water.
I will take away sickness from
among you.

Exodus 23:25

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

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Chairman: Associate Professor Hamdan Noor, Ph.D.

Faculty: Science and Environmental Studies

Diabetes mellitus has existed for at least 2000 years and has been treated with materials derived from plants in many cultures of the world. The mengkudu (*Morinda citrifolia*) are known for countless medicinal values and the ripe fruits were being used traditionally in Malaysia for the treatment for diabetes mellitus. This study was carried out to verify the hypoglycaemic property and its possible effect on insulin secretion. Freeze-dried aqueous extracts of various doses of 3mg/kg, 30mg/kg and 300mg/kg were administered to normal rats in an acute effect study and the doses of 3mg/kg, 30mg/kg, 300mg/kg, 600mg/kg, 900mg/kg and 1200mg/kg were administered to streptozotocin induced type 2 diabetic rats in a chronic effect study in an Oral Glucose Tolerance Test (OGTT). Results from the choric effect study showed that the 300mg/kg dose treated rats had an apparent hypoglycaemic effect as evident from the blood glucose level measured as the area under the OGTT curve (AUC: 4370.70 ± 99.13 mg%min) after 6 weeks of oral administration. Hypoglycaemic activity was also observed in the 600mg/kg dose after 5 weeks of oral administration (AUC: 4486.70 ± 35.60 mg%min), the 900mg/kg dose after 4 weeks of oral administration (AUC: 4340.40 ± 72.90 mg%min) and the 1200mg/kg dose after 4 weeks of oral administration (AUC: 4554.00 ± 49.80 mg%min). All the

AUC values were significantly lower compared to control. The aqueous extracts were also able to impede the rate of glucose increase and enhance the glucose clearance. However, the results from the insulin assay did not show any significant change in the insulin release profile as compared to control. As a conclusion, the aqueous extract of mengkudu (*Morinda citrifolia*) fruit preparations in the doses of 300mg/kg, 600mg/kg, 900mg/kg and 1200mg/kg might contain plant compounds that have substantial hypoglycemic property only in the chronic effect study but did not affect the insulin secretion in the type 2 diabetic rats. Future studies should be carried out in order to further discover its mechanisms of action, isolation and identification of the hypoglycaemic components particularly with regard to the healing of diabetes by means of plant resources.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia
sebagai memenuhi keperluan untuk ijazah Master Sains

AKTIVITI HIPOGLISEMIK BUAH MENGKUDU (*MORINDA CITRIFOLIA*)

Oleh

CHEE BENG JIN

November 2001

Pengerusi: **Profesor Madya Hamdan Noor, Ph.D.**

Fakulti: **Sains dan Pengajian Alam Sekitar**

Penyakit diabetes mellitus telah dikesan semenjak 2000 tahun dahulu dan cara rawatannya dengan menggunakan tumbuhan telah dikenalpasti di pelbagai kebudayaan di merata dunia. Mengkudu (*Morinda citrifolia*) amat terkenal dengan pelbagai nilai perubatan dan telah digunakan secara tradisional untuk merawat diabetes mellitus di Malaysia. Objektif eksperimen ini ialah untuk membuktikan kesan hipoglisemik dan kesannya terhadap perembesan hormon insulin. Ekstrak buah berakua yang telah disejukbekukan telah diberikan kepada tikus normal (3mg/kg, 30mg/kg dan 300mg/kg) untuk kajian kesan akut dan tikus diabetik jenis 2 (3mg/kg, 30mg/kg, 300mg/kg, 600mg/kg, 900mg/kg dan 1200mg/kg) untuk kajian kesan kronik di dalam Ujian Toleransi Glukosa. Keputusan kajian kesan kronik menunjukkan bahawa tikus kajian yang diberikan dos 300mg/kg mempunyai aras glukosa darah yang lebih rendah berdasarkan nilai keluasan dibawah graf (AUC: 4370.70 ± 99.13 mg%min) setelah rawatan oral selama 5 minggu. Kesan hipoglisemik juga diperhatikan untuk dos 600mg/kg selepas rawatan 5 minggu (AUC: 4486.70 ± 35.60 mg%min), dos 900mg/kg selepas rawatan 4 minggu (AUC: 4340.40 ± 72.90 mg%min) dan dos 1200mg/kg juga selepas 4 minggu rawatan (AUC: 4554.00 ± 49.80 mg%min). Kesemua nilai keluasan di bawah graf (AUC)

adalah lebih rendah berbanding dengan kumpulan kawalan.. Ekstrak berakua tersebut juga berupaya untuk merendahkan kadar peningkatan glukosa darah dan mempercepatkan kadar penghapusan glukosa darah. Walau bagaimanapun, keputusan ujian aras insulin menunjukkan bahawa ekstrak tersebut tidak mempengaruhi corak perembesan hormon insulin. Sebagai kesimpulan ekstrak berakua buah mengkudu (*Morinda citrifolia*) berdos 300mg/kg, 600mg/kg, 900mg/kg dan 1200mg/kg berupaya untuk merendahkan aras glukosa darah tikus diabetik jenis 2 di dalam kajian kronik sahaja dan tidak mempengaruhi perembesan hormon insulin. Berdasarkan kepada keputusan ini, kajian lanjutan masih perlu dilakukan untuk mengkaji mekanisme tindakannya, pengasingan dan pengenalpastian komponen-komponen hipoglisemik di dalam ekstrak tersebut seiringan dengan kajian untuk rawatan diabetes mellitus dengan menggunakan sumber tumbuhan tempatan.

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Amen.

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mg%	milligram per 100 milliter
OD	Optical Density
n	number of replicates or individuals
b.w.	body weight
[G]	Blood glucose concentration
[I]	Blood insulin concentration

CHAPTER 1

INTRODUCTION

Diabetes mellitus is currently a major global issue in public health. The occurrence and prevalence of this disease are alarmingly escalating in developing and newly industrialized countries (King, 1993). The prevalence of diabetes worldwide was estimated to be 4% (135 million people) in 1995 and to increase to 5.4% (estimated 300 million people) by the year 2025 (King et al., 1998.)

The World Health Organization (WHO) has recognized 2 major clinical forms of diabetes mellitus, namely Insulin-Dependant Diabetes Mellitus (IDDM) or Type 1 Diabetes Mellitus and Non-Insulin-Dependent Diabetes Mellitus (NIDDM) or Type 2 Diabetes Mellitus. About 90% of all cases of diabetes in developed and developing countries are NIDDM, primarily found in adult of more than 30 years old (WHO Study Group, 1994).

Asia faces the greatest threat of an epidemic of NIDDM. In 1994, over 43 million people in Southern, Southeast and East Asia were estimated to have NIDDM. WHO has recognized that Asia as having a potential increase with 2.5 to 3 times more common diabetes than the situation today. Hence by the year 2010, Asia is estimated to have 138 million diabetic patients (Amos et al., 1997).

In Malaysia, diabetes is a growing concern among the population especially the government and health practitioners. Throughout the six years Healthy Lifestyle Campaign by the Ministry of Health, which started in 1991, diabetes mellitus became the theme for the year 1995. In 1986, the prevalence of the disease in Peninsular Malaysia as reported in the First National Health and Morbidity Survey was 6.3% and in 1995, the Cardiovascular Unit in the Department of Public Health, Ministry of Health reported that the prevalence to at 7.7%. The prevalence seemed to be on the rise. Recognizing diabetes as a growing public health problem in Malaysia, a scope on diabetes was introduced in the Second National Health and Morbidity Survey (NHMS2). It was carried out to provide a comparative picture of the epidemiology of diabetes mellitus in the population of Malaysia within the last ten years since 1986. In 1997, the survey reported that the national prevalence was found to be 8.3% in the population of age 30 years and above. (Ministry of Health, 1999)

The highest occurrence of identified diabetics by ethnicity was amongst Indians (11.5%) and they were considerably higher than other ethnic groups. The prevalence amid Chinese was 6.3% and Malays was 5.2% whilst other Bumiputera had significantly lower prevalence 2.7%. The prevalence of known diabetics by gender showed that males reported to have higher prevalence (5.9%) compared to females (5.8%)(Ministry of Health, 1999).

Undiagnosed diabetes was defined as whole blood capillary glucose level of equal or more that 11.1 mmol/l among those who did not report themselves as known

diabetics. From the survey, the national prevalence of undiagnosed diabetics was 2.5%. By ethnicity, Indians had the highest prevalence of undiagnosed diabetics, which was 3.4% and by gender; females recorded higher prevalence (2.6%) than males (2.5%)(Ministry of Health, 1999).

In Malaysia, a number of reported death cases from the Ministry of Health (1999) were related to heart disease, stroke or chronic renal failure, some of which might be associated to diabetes. It is projected that the number of diabetics will be rising from 418,000 cases in 1994 to 810,000 cases and 1,201,000 estimated cases in year 2000 and 2010 respectively (Ministry of Health, 1999)

The Ministry of Health in Malaysia has reported that in 1994, about 4.3% of diabetic patients seek treatment in private and government hospitals and about 0.9% seeks treatment in traditional medicine practitioner (Ministry of Health, 1995). Even today, the practice of various traditional medicinal systems are still flourishing in different countries and among different ethnic groups and nearly 80% of the rural population still depend on plant based medicines (Sasson, 1996). About 80% of the rural population in many tropical developing countries still depends on traditional practitioners for their health care, which means that the community has to rely on medicinal plants for treatment (Farnsworth, 1983).

The traditional method of treating diabetes is yet to be explored; Malaysia is richly endowed with diverse flora with good potential to be developed into various useful natural products (Soepadmo, 1993). Our country is known to have a large amount of plant species and a number of them have been traditionally used to treat many disease and ailments. Similar to other diseases, diabetes mellitus has been treated traditionally by oral consumption of plant extracts based on folk and traditional cures since ancient times (Ajgoankar, 1979).