

EVALUATION OF ANTI-HYPERGLYCAEMIC EFFECT OF *Alstonia angustiloba*  
LEAF IN NORMAL AND STZ-INDUCED  
DIABETIC RATS

TING PHOOI CHEE

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WITH HONOURS

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Alstonia angustiloba LEAF IN NORMAL AND STZ-INDUCED

DIABETIC RATS.  
 IJAZAH: BACHELOR DEGREE OF CONSERVATION BIOLOGY WITH  
HONOURS

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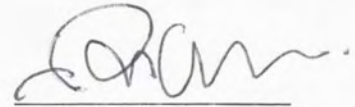
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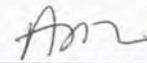
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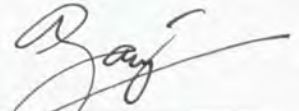

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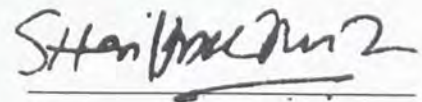
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## ABSTRAK

Kesan anti-hiperglisemik ekstrak daun *Alstonia angustiloba* ke atas aras glukosa darah dan berat badan tikus normal dan tikus diabetik yang diaruh STZ selepas suapan oral yang berulang selama 14 hari dinilai. Ekstrak daun *A. angustiloba* menunjukkan penurunan aras glukosa darah yang signifikan ( $P < 0.05$ ) dalam tikus diabetik yang dirawat dengannya. Walaubagaimanapun, ekstrak daun *A. angustiloba* tidak menunjukkan sebarang kesan ke atas aras glukosa darah dalam tikus normal. Selain itu, tidak terdapat perbezaan yang signifikan ( $P > 0.05$ ) pada berat badan dalam kedua-dua kumpulan tikus normal. Keputusan juga mendapati bahawa ekstrak daun *A. angustiloba* tidak mampu menghalang penurunan berat badan yang disebabkan oleh suntikan STZ di dalam tikus diabetik. Dalam kajian yang lain, ekstrak daun *A. angustiloba* telah ditentukan mengandungi aktiviti antioksida dan jumlah fenolik yang tinggi. Jumlah kandungan fenoliknya adalah  $213.33 \pm 0.03$  mg/g per sampel. Manakala, ekstrak daun *A. angustiloba* menunjukkan nilai aktiviti antioksida yang paling tinggi ( $62.42 \pm 1.08$  %) pada kepekatan  $100 \mu\text{g/ml}$ . Nilai  $\text{EC}_{50}$  ekstrak daun *A. angustiloba* pula adalah  $16.00 \pm 0.71$  %. Keputusan tersebut menunjukkan bahawa ekstrak daun *A. angustiloba* mempunyai keupayaan merendahkan aras glukosa darah secara efektif dalam tikus diabetik. Ini mungkin disebabkan oleh aktiviti antioksida dan kandungan fenolik yang tinggi di dalam ekstrak daun *A. angustiloba*. Penyelidikan selanjutnya dicadangkan kerana *A. angustiloba* adalah sumber yang berpotensi untuk penemuan ubat alternatif diabetes mellitus yang berasaskan tumbuhan.



## ABSTRACT

The anti-hyperglycaemic effect of *Alstonia angustiloba* leaf extract on blood glucose level and body weight in normal rats and streptozotocin (or STZ) - induced diabetic rats after repeated oral administration for 14 days were evaluated. The *A. angustiloba* leaf extract exhibits a significant reduction ( $P < 0.05$ ) of blood glucose in diabetic rats. However, the *A. angustiloba* leaf extract did not exhibit any effect on blood glucose level in normal rats. On the other hand, there was no significant different ( $P > 0.05$ ) on body weight in normal rats. The results also found that the *A. angustiloba* leaf extract could not prevent the reduction of body weight caused by STZ injection in diabetic rats. In another study, *A. angustiloba* leaf extract was determined that it contain high antioxidant activity and total phenolic content. The total phenolic content of *A. angustiloba* leaf extract was  $213.33 \pm 0.03$  mg/g per sample. Meanwhile, *A. angustiloba* leaf extract exhibit the highest value ( $62.42 \pm 1.08$  %) of antioxidant activity at the concentration of  $100 \mu\text{g/ml}$  while the  $\text{EC}_{50}$  value was  $16.00 \pm 0.71 \mu\text{g/ml}$ . These findings indicate that the *A. angustiloba* leaf extract possesses effective blood glucose lowering capability in diabetes rats. This may be due to the high antioxidant activity and phenolic content in *A. angustiloba* leaf. Further investigation is recommended since *A. angustiloba* is a potential source for discovery of plant-based alternative medicines for diabetes mellitus.

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**LIST OF SYMBOLS**

%	percent
-	minus
°C	degree Celcius
±	plus minus
µg/ml	microgram per milliliter
Abs <sub>518nm</sub>	absorbance at 518 nanometer
Abs <sub>725nm</sub>	absorbance at 725 nanometer
cm	centimeter
g	gram
g/L	gram per liter
IP <sup>DPPH</sup>	DPPH inhibition
kg	kilogram
m	meter
M	molar
mg/g	milligram per gram
mg/ml	milligram per milliliter
ml	milliliter
mM	milli Molar
mmol/L	millimolar per liter
nm	nanometer
S.E.M	standard error mean
SD	standard deviation



## CHAPTER 1

### INTRODUCTION

#### 1.1 Medicinal plants

In recent years, interest on medicinal plants has increased considerably. Medicinal plants are widely used as well as in traditional medicine and in the pharmaceutical industry to investigate and find out the potential properties of medicinal plants in treating various diseases. About 80 % of the world population depends on herbal-based alternative systems of medicine (Daniel, 2006). Herbal medicine is now expanding at an astonishing pace due to the great inputs from ethno-medicinal practices being pooled from all over the world. The medicinal values of plants have assumed an important dimension in the past few decades owing largely to the discovery that extracts from plants contain not only minerals and primary metabolites but also a diverse array of secondary metabolites with medical potential (Arthur & John, 2000).

Medicinal plants have traditionally been used in a variety of local herbal preparations by various ethnic groups in Malaysia (Azah *et al.*, 2000). Medicinal plants are chosen due to its natural effectiveness, less side effect and low cost in comparable to synthetic drugs which causes adverse effects and toxicity. In addition, traditional community depends upon the traditional healers and healing methods because of the availability, accessibility, dependability and utility (WHO, 1992). However, most of the herbal medicine is not scientifically validated and often derived from traditional belief and experience. One of the common problems often faced by local herbal industries is the inadequate standardization and quality control in the preparation of herbal medicines (Azah *et al.*, 2000).

Malaysia is well recognized for its rich biodiversity and biotic resources. It is one of the countries in Southeast Asia which possess high diversity of medicinal value plants with approximately 8000 species (Husain *et al.*, 2000). However, there are only 100 to 150 species are recognized and frequently used in plant-based medicines preparation (Husain *et al.*, 2000). Today, there has been increasing interest in the identification, collection and phytochemical screening of the local flora in looking of their medicinal uses and chemical components. In general, every medicinal plant contains a number of active constituents facilitating its manifold curative activities. A few of these compounds such as reserpine, taxol, vincristine have been isolated or synthesized in a large scale and are used in allopathic systems. Mostly all parts of medicinal plants can be used and extraction can be done onto root, leaf, seed, flower or fruit in order to access the potential properties for various purposes such as nutrition, maintenance, reproduction, healing, defense and offense.



In the present study, it is aimed to assess and find out the plant-based alternative medicine for diabetes mellitus. Thus, the antioxidant activity and total phenolic content of *Alstonia angustiloba* leaf were determined to evaluate their medicinal value. In addition, the effect of *A. angustiloba* leaf on blood glucose levels and body weights in normal rats and streptozotocin(STZ)-induced diabetic rats were evaluated in order to gain an insight into the potential properties for their therapeutic properties and traditional uses.

## 1.2 Objectives

The objectives of the study are:

1. To determine antioxidant activity in *A. angustiloba* leaf extract by using 2, 2-diphenyl-1-picrylhydrazyl (DPPH) scavenging assay.
2. To determine total phenolic contents in *A. angustiloba* leaf extract by using Folin-Ciocalteu reagent.
3. To evaluate the anti-hyperglycaemic effects of *A. angustiloba* leaf extract on blood glucose levels and body weights in normal and STZ-induced diabetic rats.

## CHAPTER 2

### LITERATURE REVIEW

#### 2.1 The *Alstonia angustiloba* or Pulai tree

*A. angustiloba* is a tree species under Apocynaceae family. In general, it is a well known medicinal plant in traditional communities. The common name for the species is Devil Tree. Common Australian names are Milkwood, Milk Bean, Milky Pine and White Cheesewood (Hundley, 2005). They are locally named as Pulai or Pulai Daun Merah by Malay village community in Peninsular Malaysia (Werner, 2002) or Tambalit by Murut community in Nebawan Sepulut, area in Sabah. (Fasihuddin & Raji, 2000).

*A. angustiloba* is a tropical tree which grow in tropical rain forest regions and native to Peninsular Malaysia, Sumatera and Borneo (Hundley, 2005). They are commonly found from lowlands to 750 meter above sea level (Hanum *et al.*, 2005). This plant is frequently planted as roadside tree for beautifying and fouling the environment (Singapore National Parks, 2006). It require moderate water and prefer full sunlight.



(Source: Singapore National Parks, 2006)

**Photo 2.1** *Alstonia angustiloba* trees.

### 2.1.1 Taxonomic classification

There are approximately 106 species in this genus (Li *et al.*, 1977). According to Li *et al.* (1977), the taxonomic classification of *A. angustiloba* from the principle level to the species level are:

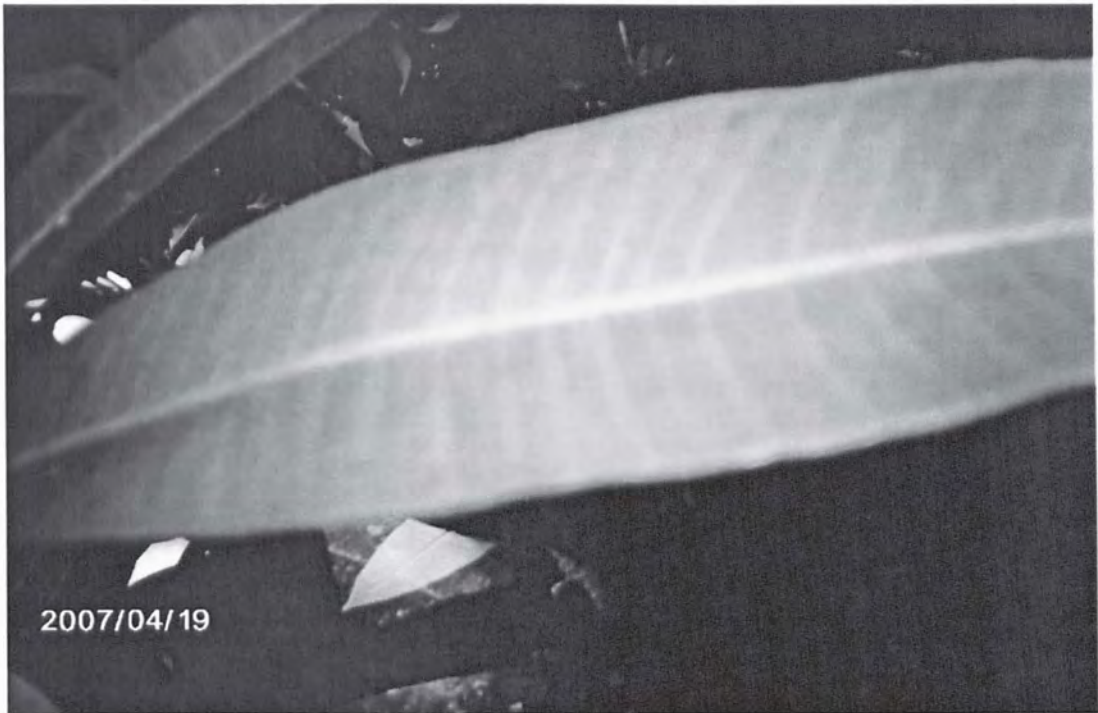
Domain : Eukaryota

Kingdom : Plantae

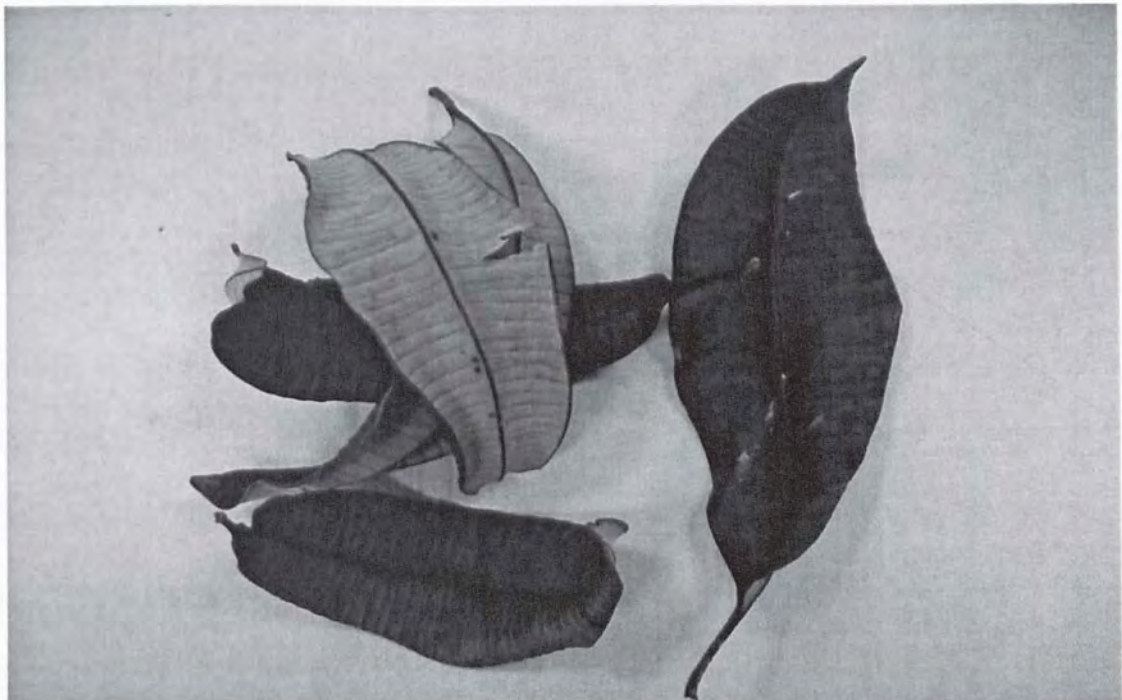
Division : Magnoliophyta  
Class : Magnoliopsida  
Order : Gentianales  
Family : Apocynaceae  
Genus : *Alstonia*  
Species : *Alstonia angustiloba*

### 2.1.2 Morphology characters

According to the morphological description by Hanum *et al.* (2005), *A. angustiloba* is a tall tree with fluted dark grayish to black bole which height up to 10 m and about 1 m in diameter. The injured parts such as twig and bole exude copious white latex. Tree branches which presence in tiers giving the appearance of a pagoda. Leaves are 5 to 8 in whorls, oblong-elliptic, base cuneate to rounded, apex acute with numerous closely arranged parallel secondary veins, palmate compound leaf type, dark green above and glaucous beneath surface, tertiary veins inconspicuous upon drying. Flowers are small, white in colour and with fragrance. Fruits are present in a long woody follicle with many seeds. They are black in colour when dried. It turning into pods filled with small smooth seeds. Photo 2.2 and 2.3 show the fresh *A. angustiloba* leaf and dried *A. angustiloba* leaves, respectively.



**Photo 2.2** Fresh *A. angustiloba* leaf.



**Photo 2.3** Dried *A. angustiloba* leaves.

Comers (1997) reported that the timber of the Pulai is soft and light, therefore it is not highly valued. The timber is lightweight and used to make plywood, matches and crates. The latex and other parts of the Pulai are used in traditional medicine. The Pulai fast growing but they do not regenerate quickly. Therefore, in most places where they are found, they are only selectively harvested for timber. However, they are not cultivated for their timber.

### 2.1.3 *Alstonia angustiloba* in traditional medicine

*A. angustiloba* has been widely used as alternative herbal remedies in Southeast Asia such as Malaysia, Indian and Borneo (Azah *et al.*, 2000). They are widely used as traditional medicines because it is available locally and commonly prescribed by the traditional medical practitioners who are part of the community in order to make their patients feel comfortable (Ebadi, 2000).

According to Fasihuddin & Raji (2000), *A. angustiloba* is known as folk medicine in Murut community as remedies for hypertensive and antidiabetic. The plant parts used for *A. angustiloba* are leaf and root. This plant is used for internal treatment which the plant parts are boiled in water and taken the water concoction or tea. Table 2.1 give the information on plant used by Murut community, their local names, uses and brief method of preparation.

**Table 2.1** Traditional uses and preparation of *Alstonia angustiloba* done by Murut community in Nebawan Sepulut, Sabah (Fasihuddin & Raji, 2000).

Murut Local Name	Uses	Preparation
Tambalit	Ague	Juice from the drunk for remedy
	Diabetes and lumbago	Roots were boiled and taken as tea

In addition, there was another study regarding to the traditional medicine in Malay village done by Werner (2002) (Table 2.2). According to this study, *A. angustiloba* is traditionally used in remittent fever. It is prepared by smearing coconut oil over the leaves which is then heated and applied hot over the spleen. Besides, *A. angustiloba* can be used in curing the sickness or pains in the bones. It is being prepared in combination with other herbs such as *Delima sarmentosa*, *Micromelum hirstum*, *Fagraea racemosa*, *Peronema canescens*, *Zingiber cassumunar* and *Areca catechu*. The twigs of the herbs combined with *A. angustiloba* and beat the patient's body using the bunch. It is believed that it can exorcise the pains in bones.

**Table 2.2** Traditional medicine uses and preparation of *Alstonia angustiloba* among Malay village community in Peninsular Malaysia (Werner, 2002).

Malay Local Name	Ailment	Preparation
Pulai	Fever	Smearing coconut oil over the leaves, then heat and applies hot over the spleen.
	Pains in the bones	Combination with twigs of other herbs and beating the body using the bunch.

## 2.1.4 Other studies from plants of Apocynaceae Family

### a. *Alstonia scholaris*

*A. scholaris* is a tree species under the same Apocynaceae family with *A. angustiloba*. According to Werner (2002), the vernacular name for *A. scholaris* in Malay village community from peninsular Malaysia is also named Pulai. It has the same name as *A. angustiloba*. However, the Murut community in Nebawan Sepulut called it as Pelai (Fasihuddin & Raji, 2000).

The morphology of *A. scholaris* is almost similar to *A. angustiloba*. According to the description by Vaidyaratnam (1994), *A. scholaris* is a large evergreen tree with height up to 3.0 m in height with a straight often fluted and buttressed bole, about 110 cm in diameter, bark grayish brown, rough lenticellate abounding in bitter, milky latex, leaves 4-7 in a whorl, coriaceous, elliptic-oblong, pale beneath; small flowers, greenish white, numerous in umbellate panicles, corolla tube short, very strongly scented; fruits follicles, 30-60 cm long; seed papillose with brownish hair at each end.

In 1990 and 1995, there were proven scientific studies done on *A. scholaris* for its chemical components and medicinal uses. *A. scholaris* is known as potential medicine in pharmaceutical as antidepressants and antiaging (Marles & Farnworth, 1995). It also can treat beri-beri disease, congestion of liver, dropsy and ulcers (Yamauchi *et al.*, 1990). Table 2.3 give the information on *A. scholaris* for their chemical component and medicinal uses.





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