

**UNIVERSITI TEKNOLOGI MARA**

**INVESTIGATION OF ANTINOCICEPTIVE  
MECHANISM CAUSED BY MITRAGYNINE  
(MAJOR CONSTITUENT OF MITRAGYNA  
SPECIOSA EXTRACT) IN MICE**

**PUTRI NUR NADIAH BT MEGAT MOHD  
GHAZALI**

**Dissertation submitted in partial fulfillment of the requirements for the  
Degree of Bachelor of Pharmacy from the Faculty of Pharmacy, UiTM**

Faculty of Pharmacy

October 2006

## **ACKNOWLEDGEMENTS**

This study was made possible thanks to supervisor, Miss Nur Suraya Adina Suratman, laboratory assistants especially Miss Norliah Saba for their help and support and to a grant Faculty of Pharmacy, Universiti Teknologi MARA (UiTM), for all the facilities and equipments.

TABLE OF CONTENTS

	PAGE
TITLE PAGE	
APPROVAL	
ACKNOWLEDGEMENT	ii
TABLE OF CONTENTS	iii
LIST OF TABLES	
LIST OF FIGURES	
LIST OF ABBREVIATIONS	
ABSTRACT	
CHAPTER1 (INTRODUCTION)	
1.1 BACKGROUND	1
1.2 STATEMENT OF THE PROBLEM	3
1.3 SIGNIFICANCE OF THE PROJECT	4
1.4 OBJECTIVES	4
CHAPTER 2 (LITERATURE REVIEW)	
2.1 INTRODUCTION TO PAIN	5
2.2 OPIOD ANALGESIC	7
2.2.1 MORPHINE	7
2.2.2 <i>MITRAGYNA SPECIOSA</i>	8
2.3 NON-OPIOD ANALGESIC	15

## ABSTRACT

*Mitragyna speciosa* is classified under the family of *Rubiaceae* (Matsumoto et al., 1996). In folk medicine, it can be used to treat diarrhea and alleviate pain from cutting wounds (Kumarnsit et al., 2006). Farmers, laborers, and peasants tend to use the plant for its anti-fatigue effects and used to enhance physical performances (Kumarnsit et al., 2006). Mitragynine is composed of about 66% of the total alkaloids extracted from the young leaves of the plant (Matsumoto et al., 1996, Matsumoto et al., 2005). Its' young leaves contain mitragynine and are chewed, smoked or drank as tea to produce its' opiod-like effects (Matsumoto et al., 1996). Mitragynine was found to act as an agonist at the opiod receptor (Kumarnsit et al., 2006, Matsumoto et al., 2005) and can produce antinociceptive effect (Matsumoto et al., 1996) while the antinociceptive effect of mitragynine administered i.c.v was found to be maximal at about 15 minutes after administration and may last to 45 minutes. This study was done to evaluate the analgesic effect of *Mitragyna speciosa* using the tail-flick test method. From the data collected, the mice treated with MS extract at dose of 15mg/kg, 25mg/kg and 35mg/kg and 35mg/kg administered paracetamol showed significant difference in response ( $P$  value  $< 0.05$ ) compared to mice treated with saline 0.9% 0.01mg/kg that act as a control. This occurred at the minutes of 20<sup>th</sup>, 40<sup>th</sup> and 70<sup>th</sup>. The mean reaction times are higher in MS extract at all doses compared to paracetamol starting from the 20<sup>th</sup> until the 60<sup>th</sup> minutes. The mean reaction time of saline remains the lowest during the study period. This study also showed that at the 10<sup>th</sup> and 20<sup>th</sup> minutes after dose, 25mg/kg MS extract treated mice have the highest mean reaction time followed by the dose of 15mg/kg and 35mg/kg. At the 30<sup>th</sup> until 50<sup>th</sup> minutes, the result was 15mg/kg MS extract has the highest mean reaction time followed by MS extract 35mg/kg, 25mg/kg and paracetamol 35mg/kg. This may suggests that MS extract exerts higher potency than paracetamol in the antinociceptive activity. It is likely to have the potential to replace morphine as an analgesic (Matsumoto et al., 1996, Yamamoto et al., 1999).

# CHAPTER 1

## INTRODUCTION

### 1.1 Background

Botanically, the *Mitragyna speciosa* is a leafy tree, classified under the family of *Rubiaceae* (Matsumoto et al., 1996) as the coffee tree, found in regions of Asia and Africa. The African species are sometimes classed in a separate genus, *Hallea*. The *Mitragyna speciosa* can easily be found in Thailand and is also known as Kratom, Ketum, Kakuam, and Ithang and in southern regions called Thom (Suwanlert, 1975). There are different types of Kratom and the main types are distinguished by the colour of veins in the leaf; the red or green-white colour. The users believed that the green-white veined type is supposed to have stronger effect. It is found that most of the users preferred a mixture of both, followed by red veined and then the green-white veined (Erowid, 2006).

From the past, when opium is unavailable, people often used Kratom as a substitute for opium, or to moderate opium addiction. In folk medicine, it can be used to treat diarrhea, reducing coughing and alleviating pain from cutting wounds (Kumarnsit et al., 2006). Minorities of users use it to prolong sexual intercourse (Erowid, 2006). Farmers, laborers, and peasants tend to use the plant for its anti-fatigue effects and used to enhance physical performances (Kumarnsit et al., 2006), thereby enabling them overcome the burdens of their hard work and meagre existences. Heavy users may chew