UNIVERSITI PUTRA MALAYSIA

APHRODISIAC POTENTIAL OF THE AQUEOUS EXTRACT OF *MELICOPE PTELEIFOLIA* (CHAMP EX BENTH) T. G. HARTLEY IN SPRAGUE DAWLEY RATS

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By

NAZIZARINI BINTI MOHD NAJIB

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Chair : Tengku Azam Shah Bin Tengku Mohamad, PhD
Faculty : Medicine and Health Sciences

Infertility is the inability of a sexually active spouse that does not possess any contraceptives to achieve pregnancy within a year. Reduced sperm quality and sperm count are among contributing factors that can cause infertility in male. This study aims to investigate the beneficial effects of *Melicope pteleifolia* aqueous extract (MPAE) consumption on aphrodisiac effect in adult male Sprague-Dawley rats. A total of 30 male Sprague Dawley rats were divided equally into five different groups. MPAE was given by orally gavage for 28 days at a dose of 100mg/kg, 200 mg/kg and 500 mg/kg body weight to the animals of group II (n=6), III (n=6) and IV (n=6), respectively. The animals of group I (negative control, n=6) had distilled water and group (positive control, n=6) had sildenafil citrate. Results were analysed using one-way ANOVA test and the data were significant at $p<0.05$. Acute toxicity study, male sexual behaviours, penile erection index, sperm parameters, testosterone level, anabolic effects and histology of testes were evaluated. The result shows no mortality and signs of toxicity recorded in behaviour changes, abnormalities in clinical appearances and body weight changes for a duration of 28 days. It is concluded the Lethal Dose at 50 percent is more than 5000 mg/kg of MPAE. In this present study, rats treated with MPAE appeared to be more sexually active in male sexual behaviours compared to control negative. Interestingly, 500 mg/kg of MPAE showed a significant difference when compared to control negative for penile erection index. Positive increment can also be seen in the sperm count and sperm viability in sperm parameters. Additionally, after 4 weeks of treatment, MPAE treated rats showed an increment in testosterone level. 500 mg/kg of MPAE group showed a significant difference compared to negative control group. Overall, this study demonstrates the potential use of *Melicope pteleifolia* for aphrodisiac potential to help suppress infertility problem.

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

POTENSI AFRODISIAK EKSTRAK AKUEUS *MELICOPE PTELEIFOLIA* (CHAMP EX BENTH) T. G. HARTLEY TERHADAP TIKUS SPRAGUE DAWLEY

Oleh

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Kemandulan ialah ketidakmampuan pasangan yang aktif secara seksual yang tidak mengambil langkah kontraseptif untuk mencapai kehamilan dalam tempoh satu tahun. Kualiti sperma dan kiraan sperma yang rendah merupakan antara faktor yang boleh menyebabkan kemandulan di kalangan lelaki. Kajian ini bertujuan untuk menyiasat kesan penggunaan ekstrak akueus *Melicope pteleifolia* (MPAE) terhadap kesan afrodisiak terhadap tikus jantan dewasa Sprague-Dawley. Sejumlah 30 tikus dewasa jantan Sprague Dawley dibahagikan sama rata kepada lima kumpulan yang berbeza. MPAE diberikan secara gavage oral selama 28 hari berturut-turut pada dos 100 mg/kg, 200 mg/kg dan 500 mg/kg mengikut berat badan haiwan daripada Kumpulan II (n = 6), III (n = 6) dan IV (n = 6), masing-masing. Haiwan daripada Kumpulan I menerima (kawalan, n = 6) air suling dan Kumpulan V menerima sildenafil sitrat. Keputusan analisa menggunakan ujian ANOVA sehala dan data adalah signifikan pada $p < 0.05$. Ujian ketoksikan akut, ujian kesan anabolik, ujian tingkah-laku seksual lelaki, ujian indeks ketegangan penis, ujian parameter sperma, ujian tahap testosteron dan histologi testis juga diuji. Keputusan menunjukkan tiada kematian dan tanda-tanda ketoksikan yang direkodkan dalam perubahan tingkah laku, kesan keabnormalan terhadap tubuh badan dan perubahan berat badan selama 28 hari. Kajian ketoksikan akut merumuskan Dos Maut 50 peratus ialah lebih daripada 5000 mg/kg MPAE. Dalam kajian ini, tikus yang dirawat dengan MPAE dilihat lebih bermotivasi dalam tingkah-laku seksual jantan berbanding kawalan negatif. Menariknya, 500 mg/kg MPAE menunjukkan terdapat perbezaan yang signifikan berbanding kawalan negatif bagi indeks ketegangan penis. Peningkatan yg positif juga dapat dilihat dalam kiraan sperma dan daya maju sperma dalam parameter sperma. Selain itu, selepas rawatan MPAE selama 4 minggu rawatan, tikus yg dirawat dengan MPAE mempamerkan keputusan tahap testosterone yang lebih tinggi. Kumpulan rawatan 500 mg/kg MPAE menunjukkan terdapat perbezaan yang signifikan berbanding dengan kumpulan kawalan negatif. Secara keseluruhannya, kajian ini menunjukkan potensi penggunaan MPAE berpotensi untuk merangsang afrodisiak dalam membantu menyekat masalah kemandulan**.**

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Respectfully yours with sincere gratitude,

Nazizarini Binti Mohd Najib
September 2018

I certify that a Thesis Examination Committee has met on 21th September 2018 to conduct the final examination of Nazizarini Binti Mohd Najib on her thesis entitled "**APHRODISIAC POTENTIAL OF THE AQUEOUS EXTRACT OF *MELICOPE PTELEIFOLIA* (CHAMP EX BENTH) T. G. HARTLEY IN SPRAGUE DAWLEY RATS**" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Master of Science.

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This is to confirm that:

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Signature: _____
Name of Member of Supervisory Committee: Prof. Dr. Mohd. Roslan Bin Sulaiman

Signature: _____
Name of Member of Supervisory Committee: Dr. Enoch Kumar A/L Perumal

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LIST OF ABBREVIATIONS

ABP	Androgen binding protein
ANOVA	Analysis of variance
ATP	Adenosine triphosphate
blAMY	Basolateral amygdala
BTB	The blood-testis barrier
BW	Bodyweight
cAMP	Cyclic adenosine monophosphate
CASA	Computed assisted sperm analysis system
CAT	Catalase
cGMP	Penile cyclic guanosine monophosphate
DHEA	Dehydroepiandrosterone
DHT	Dihydrotestosterone
D.P.X	Di-n-butyl Phthalate in Xylene
E	Estradiol
ED	Erectile Dysfunction
EDTA	Ethlene diamine tetra-acetic acid
EL	Ejaculation latency
EMA	European Medicine Agency
et al	And friends
FSH	Follicle-stimulating hormone
g	Gram
GnRH	Gonadotropin- releasing hormone
HPG	Hypothalamic-pituitary-gonadal
HPTC	Hypothalamic-pituitary-testicular complex
H & E	Hematoxylin and eosin
IF	Intromission Frequency
IL	Intromission latency
kg	Kilogram
LH	Luteinizing hormone
mg	Milligram
ML	Mount latency
MPAE	*Melicope pteleifolia* aqueous extract
MSD	Male sexual dysfunction
OECD	Organisation for economic cooperation and development
PDE5	Phosphodiesterase type 5 inhibitors
PE	Penile Erection
PEI	Post-ejaculatory interval
PI	Penile Erection Index
ROS	Excessive reactive oxygen species
ROW	Relative organ weight
SOD	Superoxide dismutase
SPSS	Statistical Package for Social Sciences
S.E.M	Standard Error of Mean
T	Testosterone
µL	Micro Litre
µmol	Micro Mol
U.S	United States
WHO	World Health Organisation

CHAPTER 1

INTRODUCTION

1.1 Background Study

Sexual interactivity often be expressed as emotional need to be accepted, the necessities for assurance in oneself life occasion. Human life nature inclusive of sensual needs as a subjective comfort (Kandeel, 2007). In recent times, these days, reduced in sexual deficiencies are said related to lifestyle changes as tense living condition, various pollutants, drugs intake, unhealthy diet and nutritional inadequacy (Kenneth, 2001).

Sexual complications are predominant and can cause unfavorable health which cause mood swing, body functioning and relationship between people. The root to this problem is linked to sensual impulse and abnormality of male reproductive organ (Shin *et al.,* 2010). Pare (2014) also agreed that male sexual dysfunction will not solely affect the sexual relationship itself but will affect the substantially life condition that inclusive abnormality of male erectile, ejaculation problem, hypogonadism and without exception general health as a whole.

Diversification of simulated medicament such as Alprostadil, Sildenafil, Cyproheptadine, and Buspirone were disclosed widely used to cure male sexual dysfunction. However, these drugs can lead to consequences reaction of serious allergic, memory loss, burning, prolonged erection, seizure, severe or persistent dizziness, insomnia, decrease of hearing and vision). Nonetheless, this drug is sold are at high price and not easily available (Boyarsky and Hirschfeld, 2000). This is also agreed by the study of Vitezic and Pelcic (2002) that allopathy antidote practice in sexual treatments might reduce human comprehensive health and the non-spiritual activity as well. Contradict, in developing countries, high cost of modern medical healthcare triggered patients to search for traditional medical option. This initiative leads to the discover of many plant extracts are traditionally used to improve sexual performances (Carro-Juarez *et al*., 2004). Thus, the hunt for unrefined supplement from medicinal plants is being reinforce doubtless for the minimal side effects, accessibility and cheaper. (Adbillahi and Van Staden, 2012). Of long ago, people consume external agents in the form of food, drinks and self-made preparation to maintain or enhance the sexual power. These external substances possessed pharmacological and psychological action to fortify the sexual or reproductive system. The ideas to shift to herbal therapy with measured research cause more people to accept the ideas and attracted the high society to try for this option as well. As such, the study of herbal plant has been increased from years to years in conjunction to lesser the unfavorable side effects that are known present in synthetic compound (Wani *et al*, 2011).

Melicope ptelefolia (M. ptelifolia) recognized as “setenggek burung,” by the local

is a type of herbal that have been used traditionally in Peninsular Malaysia and also in several other Asian countries (David, 1995). This herb served by the Malay of Malaysian community as a raw fresh vegetables dish. Different parts of *M. ptelifolia* has been used for centuries as a purpose for natural remedy to cure fever, emmenagogue, stomach ache, inflammation, irritation and wound treatment (Perry and Metzger, 1980). *M. ptelifolia* is proclaimed to lower blood pressure and thus help to prevent premature ejaculation. Unfortunately, these usages are not substantiated by any written document (Abas *et al*., 2006). Hence, this study is being proposed to simultaneously identify *M. ptelifolia* towards its aphrodisiac potential.

1.2 Problem Statement

The repeated incapability to accomplish normal sexual intercourse is known as Male sexual dysfunction (MSD). MSD can be in vary form such as premature ejaculation, erectile dysfunction, arousal difficulties, retrograded, retarded or inhibited ejaculation (lessen libido), irresistible sexual actions, orgasmic chaos and omission of detumescence. Yakubu et.al. (2007), stated that MSD problem is rising because of the elderliness population and etiological factors. MSD as characterized by Malviya *et al* (2013) and Monga (1999) is the failure to achieve or retain an erection of the penis. The reason for MSD to occur can either be physiological or psychological (Bosch *et al*., 1991). This is explained by Kaminetsky (2008) and Burnett (2006) that penile erection involved a complicated process. The process involved psychological and hormones, nerves and muscle neurotransmitter, noncholinergic mechanism.

In Malaysia, it is reported 13% of men have sterility with no possible of treatment, 11% have sterility with possible of treatment conditions and 76% have problems of sperm production. Throughout worldwide, a huge number of plants have been experimented for positive fertility purpose. (Bhatia *et al.*, 2010). As an initiative to create awareness of herbal medicine in Malaysia, local authorities should provide more knowledge for consumers to understand the herbal usage.

Based on these facts, there is a need to monitor medicinal plants presence in Malaysia towards its potential health benefit. Hence, this study is being proposed to simultaneously identify *M. pteleifolia* towards its aphrodisiac potential.

1.3 Research Justification

Malaysia is a country that rich with its flora and fauna and has a great potential to venture in herbal properties. It is reported that there are about 1200 herbal plants can be found in Malaysia which can be discovered for its own benefit from time to time study (Aman, 2006). Even though most of the plants are described as having potential values however only few of the herbal plant have been fully studied and extracted for its active ingredients to use in beauty care and health care products. The research and development (R&D) growth in Malaysia is increasing and Malaysia is expected to become a hub for herbal medicines to

improve human's health in the future (Karim *et al.*, 2011). For example, *M. pteleifolia* have a great potential to export worldwide as a substitute for modern treatment for its aphrodisiac potential as it lowers blood pressure and thus help to suppress premature ejaculation. Even though *M. pteleifolia* is known to for its fertility benefit unfortunately no pharmacological report has been submitted up to this date (Sulaiman *et al.*, 2010). Therefore, this study will simultaneously identify the effects of *M. pteleifolia* towards its aphrodisiac potential. Such a study has not been reported previously.

1.4 Objectives

1.4.1 General Objective

To study the aphrodisiac effects and sexual parameters of male Sprague Dawley rats supplemented with MPAE.

1.4.2 Specific Objectives

To study the acute toxicity of aqueous extract of *M. pteleifolia* on male Sprague-Dawley (SD) rats.

To determine and to compare male sexual behaviors, penile erection index, sperm parameters, testosterone level, anabolic effects and histology of testes between control negative, control positive and *M. pteleifolia* treated groups for 4 weeks' treatment.

1.5 Hypothesis

Treatment of MPAE shows a positive reaction on Aphrodisiac effects and sexual parameters on male Sprague-Dawley (SD) rats.

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The student of this thesis, Nazizarini Binti Mohd Najib was born on 17th October 1991 in Kota Kinabalu, Sabah and graduated from International Islamic University Malaysia in 2015 and was conferred with Bachelor of Science in Biotechnology. She was inspired to continue her study in order to gain knowledge and research insight towards the beneficial and potential role of herbs in prevention of infertility. Therefore, she continued her study in Master of Science Physiology, supervised and guided by Dr. Tengku Azam Shah bin Tengku Mohamad from Department of Biomedical Science, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia. The title for the research was "Aphrodisiac Potential of *Melicope Ptelifolia* Aqueous Extract in Sprague-Dawley rats"

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