

OBSERVATIONAL STUDY OF "CHAI HU JIA LONG GU MU LI TANG"

(BUPLEURUM AND DRAGON BONE)

ON MENOPAUSAL SYNDROME

BY

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JULY 2015

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Name: Elsie Teo Sin May
Faculty/Centre: Centre of Traditional Chinese Medicine
Date: 9th July 2015

Dear Elsie Teo Sin May,

REF: Decision of Project Title by University Ethics Committee

Thank you for your submission of application to conduct research involving human participation. The University Ethics Committee has met and deliberated over your project. The committee supports your research project entitled "**Clinical Research of Chai Hu Long Gu Mu Li Tang (Bupleurum and Dragon Bone) on Menopause Syndrome**".

There are a few requirements that need to be met during the conduct of research. The Project Leader of the research project is required to distribute Informed Consent Form (Form No: ORD/10/Form/3) to each participant of the research project. Participants are required to fill in the form and return it to Project Leader or designated member of the research project. At the end of the research project, the Project Leader of the research project is required to send a copy of the filled Informed Consent Form of each participant of the research project to ORD for documentation purposes. The Informed Consent Form is attached for your kind action.

The Committee wishes you every success with your project.

Yours sincerely,

Dr Simranjeet Kaur Judge Charanjeet, Chair
University Ethics Committee

Cc:

1. Dr Yong Kian Fui, Director of Centre of Traditional Chinese Medicine
2. Prof Dr saw Soh Heoh, Pro Vice Chancellor of Research

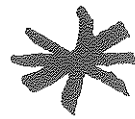
ACCEPTANCE OF DECISION FROM UNIVERSITY ETHICS COMMITTEE

Copy of this acknowledgement receipt must be forwarded to the Office for Research, Development and Consultancy latest by 15th July 2015.

I, the undersigned, am aware of and agree to the decision made by the University Ethics Committee.

Signature:
Name: Elsie Teo Sin May

Date: 15/7/15

**INTI**

LAUREATE INTERNATIONAL UNIVERSITIES

Name: Elsie Teo Sin May
Faculty/Centre: Centre of Traditional Chinese Medicine
Date: 9th July 2015

Dear Elsie Teo Sin May,

REF: Decision of Project Title by Research Approval Committee

Thank you for your submission of application to conduct research involving INTI IU as a Research Subject. The Research Approval Committee has met and deliberated over your project. The committee supports your research project entitled "**Clinical Research of Chai Hu Long Gu Mu Li Tang (Bupleurum and Dragon Bone) on Menopause Syndrome**".

There are a few requirements that need to be met during the conduct of research. The Project Leader of the research project is required to distribute Informed Consent Form (Form No: ORD/10/Form/3) to each participant of the research project. Participants are required to fill in the form and return it to Project Leader or designated member of the research project. At the end of the research project, the Project Leader of the research project is required to send a copy of the filled Informed Consent Form of each participant of the research project to ORD for documentation purposes. The Informed Consent Form is attached for your kind action.

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1. Dr Yong Kian Fui, Director of Centre of Traditional Chinese Medicine
2. Prof Dr saw Soh Heoh, Pro Vice Chancellor of Research

ACCEPTANCE OF DECISION FROM RESEARCH APPROVAL COMMITTEE

Copy of this acknowledgement receipt must be forwarded to the Office for Research, Development and Consultancy latest by 15th July 2015.

I, the undersigned, am aware of and agree to the decision made by the Research Approval Committee.

Signature:
Name: Elsie Teo Sin May

Date: 15/7/15

Acknowledgement

I'm taking this opportunity to convey my deepest gratitude to those that have assist and guiding me in completing this Final Year Project. I felt very grateful and thankful for the thoughtful guidance and constructive criticism that helped in completing this project.

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A special thanks is extended to Dr Yong Kian Fui and Miss Ooi Lay Kuan for their unending dedication and contribution in guiding our faculty in terms of academic and management since its founding.

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Last but not least, to all the volunteers that participate in this study, thanks for all the commitment and trust you put on me, without your cooperation, this project may not have succeed.

Abstract

Introduction. “Menopause” denotes the final cessation of menstruation, resulting from loss of ovarian follicular function, usually due to aging. Symptoms that have been shown to be associated with estrogen deficiency after the menopause are hot flushes and night sweats, insomnia and vaginal dryness. Vasomotor episodes with hot flashes and night sweating are the most prevalent complaints related to menopause. Hormone therapy with estrogen is considered as the most effective treatment in treating symptoms of menopause. However, recent research show that long term use of estrogen increases the risk of serious adverse effects, so, prompting sufferers to seek other therapies.

Aims. The main objective for this research is to investigate the effectiveness of Chai Hu Jia Long Gu Mu Li Tang (Bupleurum and Dragon Bone) in treating menopause syndrome. The specific objectives are to study the effectiveness of herbal formula Chai Hu Jia Long Gu Mu Li Tang (Bupleurum and Dragon Bone) in treating physical and psychological health problems of woman aged between 45 to 55, and to investigate the administration of herbal formula Chai Hu Jia Long Gu Mu Li Tang (Bupleurum and Dragon Bone) would result in the participants in the study achieving lower scores on the Menopause Rating Scale compared with baseline scores reported before the administration of herbal formula.

Method. A small sample, non- randomized cross sectional clinical study design was used in this study. This study was carried out in INTI International University and Negeri Sembilan Chinese Maternity Hospital (NSCMH). Patients were scheduled to receive treatment for 3 consecutive weeks. Each week, patients was given medicinal powder of Chai Hu Jia Long Gu Mu Li Tang. A Menopause Rating Scale (MRS) was then given to the patients to evaluate their conditions and to check if there is any improvement or side effect upon consuming the medication. All results were recorded and analyzed in a table.

Result. After the course of treatment, the average level for each dimension was reduced, the average level of psychological symptoms was reduced up to 53.57 percent, for somatic-vegetative symptoms, it was reduced up to 53.33 percent, while for urogenital symptoms, it was reduced up to 66.76 percent. Overall, it shows an improvement for all the 3 dimensions, especially in urogenital symptoms.

Conclusion. Bupleurum and Dragon Bone (Chai Hu Jia Long Gu Mu Li Tang) is effective in managing menopausal symptoms.

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Chapter One: Introduction

The phenomenon of the menopause was known to the ancient Greeks; Aristotle (384–322 BC) described the cessation of menstruation at the age of 40. In the nineteenth century, the menopause was believed to be directly responsible for madness and even in more modern times it has still been believed to cause certain psychiatric illnesses. (Barlow, 1997) The word ‘menopause’ is derived from *meno* which meant “month or menses” and *pausis* which meant “pause”, and is a direct description of the physiological event in women where menstruation ceases to occur.

As the average woman approaches age 50, her ovaries—the primary source of the female hormone estrogen—gradually cease to function as they have since menarche. As follicle depletion occurs in the ovaries, ovarian hormone production slows, and the menstrual cycle typically becomes irregular and finally ceases. This period in life is called the menopause. (Nelson, 2008) Menopause can be defined as the final menstrual period. It represents the permanent cessation of menses. It usually occurs in woman aged between 45 and 55. In Malaysia, the average age of menopause among Malaysian women had been determined to be 50.7 years. (Ismael, 1994)

Symptoms that have been shown to be associated with estrogen deficiency after the menopause are hot flushes and night sweats, insomnia and vaginal dryness. (Campbell, 1977), (Jaszman, 1976) Vasomotor episodes with hot flashes and night sweating are the most prevalent complaints related to menopause. A hot flash is described as a feeling of intense heat in the face, neck and chest. It lasts on average four minutes, with a range from a few seconds up to 10 minutes or more. Around two thirds of all women experience hot flashes, and 10 – 20 percent of these find the flashes very distressing. (Stearns, 2002)

Many other symptoms and conditions such as irregular menstrual bleeding, osteoporosis, arteriosclerosis, depressed mood, irritability, headache, forgetfulness, dizziness, deterioration in postural balance, palpitations, dry eyes, dry mouth, reduced skin elasticity, restless legs, and muscle and joint pain have also been implicated as associated with the menopause (Brown, 1976) but are not necessarily correlated to estrogen levels. (Rebar, 1987) An overriding issue regarding the biology and symptomatology of the menopause is its relationship to the underlying ageing process.

Hormone therapy with estrogen is the most effective treatment in treating menopause symptoms. However, recent research has shown that long term treatment increases risk of breast-cancer (Beral, 2003) , and estrogen therapy initiated 10-15 years after menopause increases the risk of coronary heart disease and stroke.(Rossouw, 2002) The risks of adverse effects is related to duration of use , dose, formulation and pre-existing morbidity. (Col, Weber, Stiggelbout, Chuo D'Agostino & Corso, 2004) The osteoporosis - preventing effect will manifest after five to 10 years of continuous use. Concerns about the potential adverse effects of estrogen have led to increased interest in non-hormonal therapies for menopausal symptoms, causing them to seek for complementary and alternative medicine (CAM) to help reduce and manage the menopausal symptoms that they are suffering.

Objectives

The main objective of this research is to investigate the effectiveness of Chai Hu Jia Long Gu Mu Li Tang (Bupleurum and Dragon Bone) in treating menopause syndrome.

The specific objectives are to study the effectiveness of herbal formula Chai Hu Jia Long Gu Mu Li Tang (Bupleurum and Dragon Bone) in treating physical and psychological health problems of woman aged between 45 to 55, and to investigate the administration of herbal formula Chai Hu Jia Long Gu Mu Li Tang (Bupleurum and Dragon Bone) would result in the participants in the study achieving lower scores on the Menopause Rating Scale compared with baseline scores reported before the administration of herbal formula.

Research Questions

Does the herbal formula Chai Hu Jia Long Gu Mu Li Tang (Bupleurum and Dragon Bone) effective in reducing symptoms of menopause? What are the functions of individual herbs contained in this herbal formula?

Hypothesis

The administration of herbal formula Chai Hu Jia Long Gu Mu Li Tang (Bupleurum and Dragon Bone) is effective in treating menopause syndrome, and reduce the scores achieved on the 10 items Menopause Rating Scale when compared with baseline scores reported before the administration of herbal formula.

Null hypothesis

There will be no changes in scores achieved on the 10 items Menopause Rating Scale pre and post administration of the herbal formula Chai Hu Jia Long Gu Mu Li Tang (Bupleurum and Dragon Bone).

Value of Study

This research was carried out is to fill a gap in research regarding the usage and functions of herbal formulas that are commonly used in the clinics and private practices of Chinese medical practitioners. Besides, people nowadays are seeking for complementary and alternative medicine (CAM) instead of hormone therapy due to its potential adverse effects on health. The clinical research of this herbal formula and its effect on managing the symptoms of menopause may provide a safe, effective and with a lesser side effects alternative. This research may inspire further research under controlled and double blinded conditions to hold up to scientific scrutiny and validation.

Definition of Terms

- **Complementary and Alternative Medicine (CAM):**

CAM therapies include a broad range of practices such as acupuncture, herbal remedies, chiropractic care and reiki. They are defined by the National Center for Complementary and Alternative Medicine as a group of diverse medical and healthcare systems, practices, and products not presently considered part of conventional medicine. (NCCAM, 2013)

- **Herbal Formulas**

The Chinese word for formula or prescription is Fang Ji. Fang usually refers to the written prescription itself and Ji refers to the act of administering the prescription. (Scheid, Bensky, Ellis & Barolet, 2009)

- **Menopause Rating Scale (MRS)**

MRS refers to questionnaire that were used as a basis for assessing menopausal symptoms in this study, it has been widely used and validated and have been used in many clinical and epidemiological studies, and in research on the etiology of menopausal symptoms to assess the severity of menopausal symptoms.

(Heinemann LAJ, Potthoff P, Schneider HP, 2003)

- **Qi**
Is the basic for all the phenomena in the universe, it can have the quality of course material form but also manifest as non-material energies. (Macioca, 2005)
- **Yin and Yang**
Is a concept that embraces the duality of all phenomena in the universe and arose from the observation of nature. (Macioca, 2005)
- **Genuine Qi**
It circulates throughout the body and nourishes the organs and provides protection against external pathogens. It consists of two different forms, Nutritive Qi and Defensive Qi. (Macioca, 1989)
- **Qi Mechanism**
Qi Mechanism is a term that includes the ascending-descending and entering-exiting of Qi. The ascending-descending of Qi represents a “vertical” movement of Qi while the entering-exiting represents a “horizontal” movement of Qi. (Macioca, 2014)
“Su Wen” in chapter 68 says: “Without exiting-entering of Qi, there would be no birth, growth, maturity and decline. Without ascending-descending, there would be no birth, growth, transformation, receiving and storage. All organs rely on the ascending-descending and exiting-entering of Qi”.
- **Stages of Reproductive Aging Workshop (STRAW)**
STRAW proposed nomenclature and a staging system for ovarian aging including menstrual and qualitative hormonal criteria to define each stage.
- **Final Menstrual Period (FMP)**
FMP was defined as the initial day of the last menstrual period preceding 12 consecutive months of amenorrhea.

Chapter Two: Literature Review

Overview

The research information gathered for this literature review was obtained from sources such as Google Scholar, Pubmed, Elsevier Ltd, CNKI, Journal of Chinese Medicine, World Health Organization (WHO), textbook by Giovanni Macioca and text from "Discussion of Cold Induced Diseases" (Shang Han Lun). Key search words included: Menopause, Menopausal and Aging, Menopause Rating Scale, Physiology of Menopause, Vasomotor Symptoms and Somatic symptoms of Menopause, Menopausal Syndrome, Pathophysiology of Menopause, Menopause and Emotion, How Menopause affect the Whole Body's Qi Mechanism, and Menopause and Stress in Woman.

This chapter will begin with a brief discussion of menopause in the perspective view of modern medicine, which include the terminologies and pathophysiology of menopause. Follow up by perspective view of menopause in Traditional Chinese Medicine (TCM), etiology and pathogenesis of menopause. Next, there is a section that describes aspects of the Bupleurum constitution and presentation. This chapter proceeds with a discussion of the specific formula used in this research, follow up by discussion of "Shang Han Lun" (Discussion of Cold Induced Diseases) on relationship between external diseases and internal diseases, and lastly precaution of this specific formula.

Terminologies

	Final Menstrual Period (FMP)							
Stages:	-5	-4	-3	-2	-1	0	+1	+2
Terminology:	Reproductive			Menopausal Transition		Postmenopause		
	Early	Peak	Late	Early	Late*	Early*	Late*	
				Perimenopause				
Duration of Stage:	variable			variable		③ 1 yr	④ 4 yrs	until demise
Menstrual Cycles:	variable to regular	regular		variable cycle length (>7 days different from normal)	≥2 skipped cycles and an interval of amenorrhea (≥60 days)	Amen. x 12 mos	none	
Endocrine:	normal FSH		↑ FSH	↑ FSH		↑ FSH		

*Stages most likely to be characterized by vasomotor symptoms.