Chinese Herbal Medicine for the treatment of Dysmenorrhea: a Community-based Qualitative Study

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GLOSSARY OF ABBREVIATIONS

ANCP*:* A Newly Compiled Practical English-Chinese Library of Traditional Chinese Medicine (Zuo 2003)

CHM: Chinese herbal medicine

CM: Conventional medicine

DRF: Daily rating form

DSRS: Daily symptom rating scale

E2: Estradiol

FSH: follicle-stimulating hormone

Ha: Experimental hypothesis

H_1: Working or research hypothesis

H_0: Null hypothesis

HPOA: hypothalamus–pituitary–ovary axis

ICC: Intraclass correlation coefficient

IUD: intrauterine device

Kid: Kidney

LH: luteinizing hormone

Liv: Liver

MDQ: The menstrual distress questionnaire

MSQ: The menstrual symptom questionnaire

NRS: Numerical rating scale

NSAIDs: Nonsteroidal anti-inflammatory drugs

OMS: Organización Mundial de la Salud

PD: Primary dysmenorrhea

PG: Prostaglandins

PRL: Prolactin

SD: Systematic desensibilization

SPSS: Statistical package for the social sciences

TCM: Traditional Chinese Medicine

TENS: Transcutaneous electrical nerve stimulation

VAS: Visual analogue pain scale

WHO: World Health Organization

0. ABSTRACT

Background
Dysmenorrhea is a common condition suffered by between 52% and 90% of women and can be severe enough to cause absence from work in about 2% of women. Primary dysmenorrhea (PD) refers to severe pain with no identifiable pelvic pathology that can account for painful menstruation. Evidence of efficacy supports use of pharmacological agents such as NSAIDs, or the use of oral contraceptives to alleviate menstrual pain. However, despite this wide range of treatments, pain relief may be inadequate for some women, or side effects may not be well tolerated and given that conventional treatment for primary dysmenorrhoea has a failure rate of 20% to 25%, Chinese Herbal Medicine (CHM) may be a suitable alternative.

Methodology
A prospective, uncontrolled naturalistic study was carried out in which 10 participants received treatment with a modified Traditional Chinese Herbal formula Xiao Yao Wan during three menstrual periods. Participants were followed for four menstrual cycles; the first one was without treatment and was considered as a baseline.
Modified questionnaires for the assessment of menstrual pain were used for data collection in different phases of the study: a retrospective questionnaire at the beginning of the study, a daily questionnaire during 4 menstrual periods, to be filled out on the days with menstruation, and a final questionnaire.

Results and conclusions
This study assesses the efficacy of treatment of menstrual pain with modified Xiao Yao Wan with a sample of 10 women. For assessing the evolution of menstrual pain, of premenstrual pain, the number of days with pain, the number of days of use of analgesia and the number of days of abandonment of activities due to pain the SPSS programme was used to apply the Student's t-test for related samples. As well, since the study sample number is small, in order to confirm the results the Wilcoxon test was also used, which makes no assumption as to the normal distribution of the frequency of the variables.
The analysis of the study data shows improvement in all menstrual characteristics, with some of these being statistically significant and others not.
The analysis of the results partially confirms the working hypothesis, showing that Xiao Yao Wan is significantly effective ($p \leq 0.05$) for treatment of maximum menstrual pain and reduces the number of days with pain and the number of days of use of analgesia in primary dysmenorrhea.
The results of the study seem to show the effectiveness of treatment of menstrual and premenstrual discomfort in PD with the modified Xiao Yao Wan formula, especially when the predominant disharmony patterns are Qi stagnation, Qi/Xue vacuity and/or el Xue stasis. The study seems to show these as the main TCM disharmony patterns causing dysmenorrhea. There also seems to be a relationship between the characteristics of the menstrual bleeding and the intensity and duration of both menstrual and premenstrual pain.

Keywords
Primary dysmenorrhea, Dysmenorrhoea, Menstrual Pain, Painful menstruation, Tradicitonal Chinese Herbal Medicine, Tradicitonal Chinese Medicine

SECTION 1 – INTRODUCTION

1. INTRODUCTION

1.1 Background and context

Dysmenorrhea is a common condition suffered by between 52% and 90% of women (Weissman et al., 2004) and can be severe enough to cause absence from work in about 2% of women. (Weissman et al., 2004). Primary dysmenorrhea (PD) refers to severe pain with no identifiable pelvic pathology that can account for painful menstruation (Howard, 2000) (Smith et al., 2010)

A study conducted in the Autonomous Community of Madrid, Spain (Larroy C, et al., 2001) showed that **61.9% of women suffer menstrual pain**, said percentage decreasing with age. The study concluded that pain severity depends on age, as well as on the number of children and there was high and significant correlation between pain severity and frequency. 80.7% of women in the sample women reported the location of the pain in the abdominal region, 45% in the lumbar region, 38.9% in the breasts and 7.5% in the thighs. (Larroy C, et al., 2001).

Dysmenorrhea represents a significant health problem on both a personal and public level, being a common complaint in both adolescent and adult women. In the United States, work absenteeism due to dysmenorrhea is estimated at 600 million work hours per year, and the economic consequences are estimated at 2 billion dollars per year (Howard, 2000).

There are **three conventional approaches to the management of primary dysmenorrhea**: pharmacological, nonpharmacological and surgical. Conventional treatments include nonsteroidal anti-inflammatory drugs (NSAIDs), oral contraceptives, danazol, gonadotropin-releasing hormone agonists, medroxyprogesterone acetate, presacral neurectomy, uterosacral neurectomy and trascutaneous electrical nerve stimulation (Howard, 2000).

Evidence of efficacy supports use of pharmacological agents such as NSAIDs (Wong et al., 2009), or the use of oral contraceptives (Sundell et al., 1990) to alleviate menstrual pain. However, despite this wide range of treatments, pain relief may **be inadequate for some women, or side effects may not be well tolerated**. Given that conventional treatment for primary dysmenorrhoea has a failure rate of 20% to 25% and may be

contraindicated or not tolerated by some women (Xiaoshu Zhu et al., 2010), **Chinese Herbal Medicine (CHM) may be a suitable alternative**.

Traditional Chinese Medicine (TCM) throughout its history has treated dysmenorrhea from its own perspective. It is believed that the **first reference to dysmenorrhea in a TCM text dates back to the Han Dynasty (25-220)** (Maciocia, 1998)**,** and is found in the classic text Jin Gui Yao Lue Fang Lun (Synopsis of prescriptions of the Golden chamber) (Zhang, 1987).

Now, Zuo et al. (Zuo Yanfu et al., 2006) consider that dysmenorrhea is usually caused by emotional factors, invasion of six exogenous pathogenic factors and Qi and Blood Stagnation; or by retention of Blood in the Uterus due to Liver Depression and Qi Stagnation resulting from emotional upsets; or by Cold-dampness attacking the Lower Energizer and lodging in the Uterus due to walking in water during menstruation or sitting on damp ground; or by constitutional Qi and blood vacuity, or depletion of Qi and Blood due to serious disease and prolonged illness; or by congenital defect or impairment of the Liver and Kidney, consumption of Blood and malnutrition of the Uterus due to multiparity and excessive sexual activity.

Cochrane recently published a review (Xiaoshu Zhu et al., 2010) where they found promising evidence for the use of CHM in reducing menstrual pain in the treatment of primary dysmenorrhea, compared to both conventional medication such as NSAIDs and the oral contraceptive pill and acupuncture and heat compression. All available measures of effectiveness confirmed the overall superiority of CHM to placebo, no treatment, NSAIDs, OCPs, acupuncture and heat compression. No significant adverse effects were identified in the review. However, the small number and the low quality of included studies did not allow any definite conclusion for their use in clinical practice

1.2 Research question

Can primary dysmenorrhea be effectively treated with modified CHM Xiao Yao San (Xiao Yao Wan)?

1.3 Summary of the research

This research attempts to assess treatment of menstrual pain of PD with CHM. For this purpose the issues that came up were dealt with from four different perspectives; three theoretical and one practical:

- **Theoretical perspective on PD in Conventional Medicine (CM)**: as defined by CM texts on PD, its etiopathogenesis and therapeutic approach
- **Theoretical perspective on PD in TCM:** how TCM texts on PD are considered, its etiology and therapeutic approach
- **Recent research studies:** looking at which research studies have been carried out recently in this area and the conclusions that can be drawn.

The information obtained from this literature review was used to define the study design used:

- **Practical application:** a prospective, uncontrolled naturalistic study carried out in Barcelona between May and September of 2011, in which 14 participants received treatment with Chinese herbs based on the traditional formula Xiao Yao Wan during three menstrual periods.

The data obtained from these three approaches were analysed in order to resolve issues within the research.

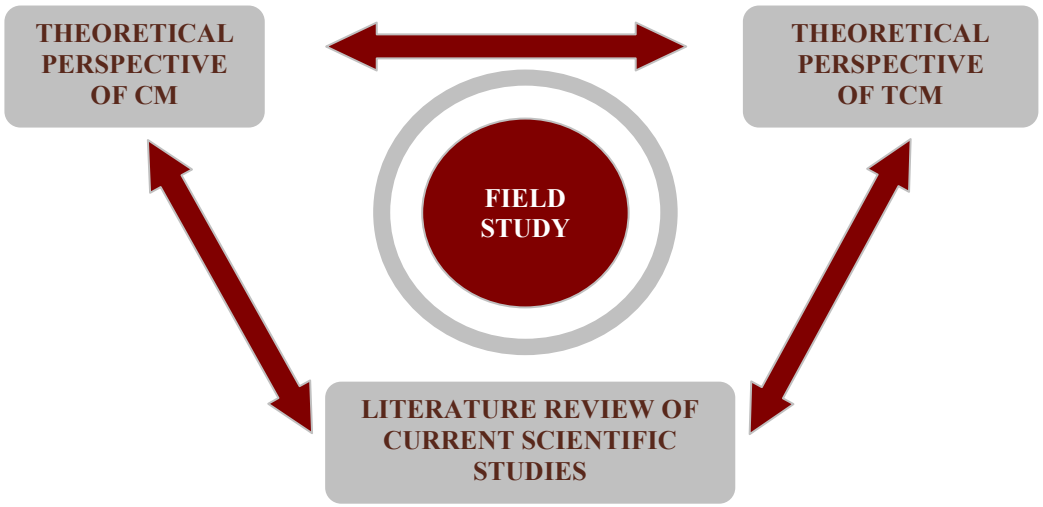


Chart 1.1 Summary of the research

1.4 Hypothesis and variables

1.4.1 Hypothesis

Working hypothesis: Xiao Yao Wan is significantly effective ($p \leq 0.05$) for treatment of menstrual pain in primary dysmenorrhea

Null Hypothesis: Xiao Yao Wan is not significantly effective ($p > 0.05$) for treatment of menstrual pain in primary dysmenorrhea

1.4.2 Variables

Dependent variable: menstrual pain

Independent variable: Xiao Yan Wan

1.5 Relevance of the study

This study:

- Will assess the efficacy of treatment of menstrual pain in PD with Xiao Yan Wan in women that live in Barcelona
- Will offer an alternative treatment for menstrual pain in PD without adverse effects
- Will serve as a base for future research in CHM for treatment of PD
- Will provide knowledge about PD from the perspective of TCM
- Will help promote knowledge of TCM and CHM in Spain
- Will promote the use of TCM and CHM in Spain

1.6 Aims and objectives of the research

- Aims
    - To determine the effectiveness of Xiao Yao Wan in the treatment of pain in primary dysmenorrhea.
    - To create a questionnaire tailored to TCM for assessing menstrual pain
- Objectives

- To determine a differentiation of TCM disharmony patterns in PD
- To review the main pain assessment questionnaires and to assess the possibility of adapting one of them to the specific needs of TCM
- Create a questionnaire tailored to TCM for assessing menstrual pain
- To determine an adequate formula for treatment of menstrual pain in PD for each disharmony pattern
- To determine evolution of the colour of menstrual blood in function of the degree of pain
- To determine the relation between the degree of pain and the presence of clots in menstrual blood
- To determine the relation between the degree of efficacy of the formula de Xiao Yao Wan and the diagnosis of other disharmony patterns, different to Qi/Xue stagnation
- To determine the relation the degree of efficacy of the formula Xiao Yao Wan and pain onset

1.7 Summary

This research attempts to assess the efficacy of the CHM formula Xiao Yao Wan for treatment of menstrual pain in PD.

SECTION 2 – LITERATURE REVIEW

2. LITERATURE REVIEW

2.1 Introduction

2.1.1 PD according to CM

Dysmenorrhea, uterine pain associated with menstrual cycles (Proctor & Cynthia Farquhar, 2006), is one of the most common gynecological disorders and is suffered from by between 52% and 90% of all women of reproductive age (Weissman et al., 2004).

Normally **dysmenorrhea is classified into two types, primary and secondary.** Primary dysmenorrhea is the pain associated to ovulation cycles, without demonstrable lesions that affect the reproductive organs. Secondary dysmenorrhea is the pain associated with ovulatory cycles caused by a demonstrable pathology (Beers et al., 1999). Secondary dysmenorrhea is frequently caused by endometriosis, myomas, adenomyosis, pelvic inflammatory disease or the use of the intrauterine device, among others. (Proctor & Cynthia Farquhar, 2006)

PD usually has its onset near the menarche, normally after 6 to 12 months. Typically the pain lasts between 8 and 72 hours, is associated with the start of the menstrual period, although can begin before, (Martínez & López, 2004), and usually disappears as menstruation tapers off. (Michelle L Proctor and Cynthia M Farquhar, 2006)

Over the years different theories have been brought forward on the **etiopathogenesis of PD**, some of which are now obsolete, for example such as the allergic theory (Palacios, 2000). In spite of the numerous studies carried out the cause is not clear, although in general it is considered that PD is caused by the **excessive production of prostaglandins** (PG) as a consequence of the decreased levels of ovarian hormones that precede the menstrual period (Palacios, 2000). The PG provoke an excessive uterine contractility, which reduces the blood supply to the uterine blood vessels and causes ischemic pain (Dmitrovic et al., 2003; Proctor & Cynthia Farquhar, 2006).

Table 2.1 is a summary of available evidence on the possible role of PG in the etiopathogenesis of PD (Palacios, 2000):

- **The dysmenorrhoeic symptoms can be reproduced by the administration of PG**
- **There are higher levels of PG in the menstrual flow of dysmenorrhoeic women**
- **There is higher plasma concentration of PG metabolites in dysmenorrhoeic women**
- **In anovulatory cycles the concentrations of PG are barely 20% of those in ovulatory cycles**
- **Pharmacological inhibitors of PG are effective in treatment of PD**

Table 2.1 Evidence of the role of PG in the etiopathogenesis of PD

The main **clinical manifestation** of PD is spasmodic pain at the midline of the inferior hemiabdomen, frequently accompanied by nausea, diarrhoea, vomiting, headache and syncope, among others (R. P. Smith, 2004).

Table 2.2 shows current factorisation of dysmenorrhea [(Stephenson et al., 1983) named in (Larroy C et al., 2001)]:

Menstrual pain	Spasms and contractions of the uterine and vaginal muscles. Localised in the abdomen and inner thighs.
Negative premenstrual psychological states	Irritability, dysphoric feelings, fatigue, loss of appetite.
Premenstrual fluid retention	Abdominal pain, inflammation, edema.
Premenstrual general malaise	Dull and diffuse pain, localised in the back (lower back and neck) and headache.
Menstrual back pain	Tensional pain in the lumbar region - is a continuation of the abdominal pain.
Gastric disorders	Constipation or diarrhoea, dizziness, nausea and vomiting.

Table 2.2 Current factorisation of the symptoms of dysmenorrhea

The **diagnosis of PD** is usually made by: (Howard, 2000; Prieto, 2007)

- Anamnesis, investigating the characteristics of the pain and verifying their cyclical nature.
- Gynecological exploration to rule out pelvic pathology
- Rectal examination

There are three conventional approaches to the **management of primary dysmenorrhea**: pharmacological, non-pharmacological and surgical. Conventional treatments include non-steroidal anti-inflammatory drugs (NSAIDs), oral contraceptives, danazol, gonadotherpin-releasing hormone agonists, medroxyprogesterone acetate, presacral neurectomy, uterosacral neurectomy and transcutaneous electrical nerve stimulation (Howard, 2000), local application of heat (R. P. Smith, 2004) and psychological treatment (Palacios, 2000) (see table 2.3). Interestingly some conventional medicine books include acupuncture as treatment for pelvic pain (Howard, 2000).

CONVENTIONAL THERAPY APPROACHES FOR THE TREATMENT OF PD	
PHARMACOLOGICAL	Nonsteroidal anti-inflammatory drugs (NSAIDs), oral contraceptives, danazol, gonadotherpin-releasing hormone agonists, medroxyprogesterone
NON PHARMACOLOGICAL	Local application of heat (R. P. Smith, 2004), Trascutaneous electrical nerve stimulation (TENS)1
SURGICAL	Presacral neurectomy, uterosacral neurectomy
OTHERS	Psychological treatment (Palacios, 2000)

Table 2.3 Conventional therapeutic approaches for the treatment of PD

2.1.2 PD according to TCM

2.1.2.1 Differentiation of disharmony patterns

It is frequent that when consulting the differentiation of disharmony patterns of a pathology or of a symptom TCM texts that we detect differences between different

[1] Nerve Stimulation: "(Treatment for chronic pain that consists of a) *phenomenon of depolarisation of the nervous system, produced by passing an electric current in such a way that the effect can either be stimulation (facilitation) or inhibition, at the same time local or distal*." (Villoria, 2007)

authors. To determine a differentiation of disharmony patterns of dysmenorrhea for application to this study several TCM gynecological texts were consulted. Following is a table with the summary of the different differentiations of disharmony patterns from Maciocia (1998), Flaws (1997), Zuo (2003) [A Newly Compiled Practical English-Chinese Library of Traditional Chinese Medicine encyclopaedia de Shanghai (ANCP)], Riley (2003) and Peilin (2002).

WORK	DIFFERENTIATION OF DISHARMONY PATTERNS
MACIOCIA	Qi stagnation Xue stasis Cold stagnation Heat- dampness Liver Qi stagnation that is converted into Fire Qi/Xue vacuity Yang and Xue vacuity Liv/Kid vacuity
ANCP	Qi stagnation and Xue stasis Cold- dampness that freezes and stagnates Qi/Xue vacuity Liv/Kid vacuity
FLAWS	Qi stagnation and Xue stasis Cold- dampness that freezes and stagnates Stasis de heat- dampness Liver Qi stagnation that is converted into Fire Qi/Xue vacuity Cold internal due to vacuity in the uterus Liv/Kid vacuity Heat due to vacuity
RILEY	Qi stagnation and Xue stasis Internal Cold due to vacuity Cold and dampness that freeze Heat- dampness that descends Qi/Xue vacuity Liv/Kid vacuity
PEILIN	Qi stagnation Xue stasis Accumulation of Cold- dampness Descent of Heat- dampness Qi/Xue vacuity Liv/Kid Yin vacuity Kid Yang vacuity

Table 2.4 Differentiations of disharmony patterns for dysmenorrhea according to traditional TCM texts

As often occurs, differences between the classifications were detected. In order to determine a differentiation of disharmony patterns for this study, a comparative study of these differentiations of disharmony patterns was carried out. It was found that:

- All of the authors consider Qi stagnation to be a disharmony pattern that causes dysmenorrhea. Maciocia and Flaws also take Qi stagnation that is

converted into Fire into consideration. Maciocia and Peilin also consider Xue stasis.

- All of the authors consider the accumulation of Cold-dampness as a cause of dysmenorrhea, except Maciocia who only considers Cold
- All of the authors, except ANCP, consider Yang vacuity as a cause of dysmenorrhea. Maciocia also considers that this is usually accompanied by Xue vacuity
- All of the authors, except ANCP, contemplate Heat- dampness as a cause of dysmenorrhea
- All of the authors contemplate Qi/Xue vacuity as a cause of dysmenorrhea
- All of the authors consider Liver/Kidney (Liv/Kid) vacuity as a cause of dysmenorrhea. Peilin also specifies Liv/Kid Yin vacuity, and Flaws adds Heat due to vacuity.

	MACIOCIA (Maciocia, 1998)	**ANCP** (Zuo, 2003)	**FLAWS** (Flaws, 1997)	**RILEY** (Riley, 2003)	**PEILIN** (Peilin, 2002)
Qi stagnation	x	x	x	x	x
Xue stasis	x				x
Qi stagnation that is converted into Fire	x		x		
Accumulation of Cold	x				
Accumulation of Cold- dampness		x	x	x	x
Yang vacuity	x (with Xue vacuity)		x	x	x
Heat- dampness	x		x	x	x
Qi/Xue vacuity	x	x	x	x	x
Liv/Kid vacuity	x	x	x	x	x (Yin)
Heat due to vacuity			x		

Table 2.5 Comparative table of the differentiations of disharmony patterns for dysmenorrhea according to traditional TCM texts

On the basis of the comparative study the following differentiation of disharmony patterns for the study were determined:

- **Qi stagnation**: Qi stagnation was included because all of the authors consider this disharmony pattern as a cause of dysmenorrhea
- **Xue stasis**: in spite of only being considered by Maciocia and Peilin all the texts contemplate the possible presence of dark blood or with dark clots. Probably the texts that do not consider Xue stasis as a specific cause is because Qi and Xue are interdependent, they circulate together and Qi stagnation implies, to a certain extent, Xue stasis and vice versa. This would explain that many of the formulas that treat Qi stagnation in dysmenorrhea include one or several of the substances that mobilise Xue. This disharmony pattern was specifically included as it is not infrequent to find many women with dark and often thick menstrual blood, often thick, even sometimes described as 'thick chocolate' or 'with the appearance of faeces'.
- **Cold- dampness**: all of the authors consider Cold as a cause of dysmenorrhea, and all except Maciocia also contemplate Cold- dampness. It was decided to include the Cold- dampness disharmony pattern because the majority include it and because Cold facilitates the accumulation of dampness as it blocks the circulation and obstructs the metabolism of liquids.
- **Yang vacuity**: Yang vacuity was included as the majority of authors, except ANCP, consider it a cause of dysmenorrhea.
- **Heat- dampness:** was included was included as the majority of authors, except ANCP, consider it a cause of dysmenorrhea.
- **Qi/Xue vacuity:** the disharmony pattern Qi/Xue vacuity was included because all of the authors consider it a cause of dysmenorrhea
- **Liv/Kid Yin vacuity**: In spite of the fact that only Flaws specified Liv/Kid vacuity as well as Yin vacuity, it was decided to include the Liv/Kid Yin vacuity disharmony pattern as the only vacuity that Liv and Kid have in common is Yin.

These are the main disharmony patterns contemplated for this study. Fire was also added as a possible disharmony pattern added to Qi stagnation, and Heat as a possible disharmony pattern added to Liv/Kid Yin vacuity.

DISHARMONY PATTERNS	
Qi stagnation	**+ Fire**
Xue stasis	
Cold- dampness	
Yang vacuity	
Heat- dampness	
Qi/Xue vacuity	
Liv/Kid Yin vacuity	**+ Heat**

Table 2.6 Differentiation of disharmony patterns applied to this study

2.1.2.2 Treatments for PD with Traditional Chinese pharmacopoeia

Historically there are a multitude of formulas of traditional Chinese pharmacopoeia for treatment of PD. In order to determine the formulas to use in this study a literature search was carried out and, as with the differentiation of disharmony patterns, treatments specified by the following authors were compared: Maciocia (1998), Flaws (1997), ANCP (Zuo, (2003), Riley (2003) and Peilin (2002).

Following is a table summarising the treatments indicated in the texts mentioned:

WORK	DIFFERENTIATION OF DISHARMONY PATTERNS	FORMULA/S
MACIOCIA	Qi stagnation	Xiao Yao San
	Xue stasis	Tao Hong Si Wu Tang Ge Xia Zhu Yu Tang Tao Hong Yin Nei Yi Fang Hua Yu Ding Tong Tang
	Cold stagnation	Wen Jing Tang Ai Fu Nuan Gong Wan Wen Qi Hua Shi Tang Wen Shen Fu Yang Tang
	Heat- dampness	Qing Re Tiao Xue Tang Er Miao San
	Liver Qi stagnation that is converted into Fire	Xuan Yu Tong Jing Tang Dan Zhi Xiao Yao San
	Qi/Xue vacuity	Sheng Yu Tang Ba Zhen Yi Mu Tang Shi Quan Da Bu Tang
	Yang and Xue vacuity	Dang Gui Jian Zhong Tang Yi Shen Tong Jing Tang Yu Shen Hua Yu Tang
	Liv/Kid vacuity	Tiao Gan Tang Gui Shao Di Huang Tang
ANCP	Qi stagnation and Xue stasis	Xuefu Zhuyu Tang
	Cold- dampness that freezes and stagnates	Shaofu Zhuyu Tang
	Qi/Xue vacuity	Bazhen Tang
	Liv/Kid vacuity	Tiaogan Tang
FLAWS	Qi stagnation and Xue stasis	Ge Xia Zhu Yu Tang Xue Fu Zhu Yu Tang Qing Re Tiao Xue Tang Jia Wei Wu Yao Tang Ba Wu Tang Tao Hong Si Wu Tang Jia Wei Tong Jing Fang Shen Hua Tang Jia Wei Tiao Jing Yin Jia Jian Chai Hu Shu Gan Tang Jia Jian Xiao Yao San
	Cold- dampness that freezes and stagnates	Shao Fu Zhu Yu Tang Wu Zhu Yu Tang Wen Jing Tang Gui Zhi Fu Ling Wan San Jie Fang Dang Gui Si Ni Tang Jia Wei Chu Tong San

Table 2.7 Formulas for treatment of PD used in the traditional TCM texts

In this case more differences were found than in the comparison between the differentiations of disharmony patterns. The number of times a formula was repeated by different authors in the selection of formulas in function of the disharmony pattern was used as criteria.

The following formulas are those that were repeated the most for each disharmony pattern:

- **For Qi stagnation**: Xiao Yao San (3) Xue Fu Zhu Yu Tang (2)
- **For Xue stasis**: Tao Hong Si Wu Tang (3) Ge Xia Zhu Yu Tang (2) Xue Fu Zhu Yu Tang (2)
- **For Cold- dampness**: Wen Jing Tang (2), Shao Fu Zhu Yu Tang (2)
- **For Yang vacuity**: Tong Jing Tang (2)
- **For Heat- dampness**: Er Miao San (2)
- **For Qi/Xue vacuity**: Shi Quan Da Bu Tang (3), Ba Zhen (Yi Mu) Tang (3)
- **For Liv/Kid Yin vacuity**: Tiao Gan Tang (4)

	Maciocia	ANCP	Flaws	Peilin	Most repeated formulas (nº repetitions)
Qi stagnation	**Xiao Yao San**	Xuefu Zhuyu Tang	Jia Jian **Xiao Yao San,** Ge Xia Zhu Yu Tang, Xue Fu Zhu Yu Tang, Qing Re Tiao Xue Tang, Jia Wei Wu Yao Tang Ba Wu Tang, Tao Hong Si Wu Tang Jia Wei, Tong Jing Fang, Shen Hua Tang Jia Wei, Tiao Jing Yin, Jia Jian Chai Hu Shu Gan Tang	**Xiao Yao San**	**Xiao Yao San (3)** Xue Fu Zhu Yu Tang (2)
+ Fire	Xuan Yu Tong Jing Tang, **Dan Zhi Xiao Yao San**		Xuan Yu Tong Jing Tang		
Xue stasis	**Tao Hong Si Wu Tang,** Ge Xia Zhu Yu Tang, Tao Hong Yin, Nei Yi Fang, Hua Yu Ding Tong Tang,	Xuefu Zhuyu Tang	Ge Xia Zhu Yu Tang, Xue Fu Zhu Yu Tang, **Tao Hong Si Wu Tang Jia Wei,** Qing Re Tiao Xue Tang, Jia Wei Wu Yao Tang, Ba Wu Tang, Tong Jing Fang, Shen Hua Tang Jia Wei, Tiao Jing Yin, Jia Jian Chai Hu Shu Gan Tang, Jia Jian Xiao Yao San	**Tao Hong Si Wu Tang** and Shi Xiao San	**Tao Hong Si Wu Tang (3)** Ge Xia Zhu Yu Tang (2) Xue Fu Zhu Yu Tang (2)
Cold- dampness	**Wen Jing Tang,** Ai Fu Nuan Gong Wan, Wen Qi Hua Shi Tang, Wen Shen Fu Yang Tang	**Shaofu Zhuyu Tang**	**Shao Fu Zhu Yu Tang, Wen Jing Tang,** Wu Zhu Yu Tang, Gui Zhi Fu Ling Wan, San Jie Fang, Dang Gui Si Ni Tang Jia Wei, Chu Tong San	Cang Fu Dao Tan Tang	**Wen Jing Tang (2) Shao Fu Zhu Yu Tang (2)**
Yang vacuity	Dang Gui Jian Zhong Tang, Yi Shen **Tong Jing Tang,** Yu Shen Hua Yu Tang	Shaofu Zhuyu Tang	Wen Shen Fu Yang Tang, **Tong Jing** San Hao Fang, Tong Jing Shen Fang	Ba Wei Wan with Wen Jing Tang, You Gui Wan	**Tong Jing Tang (2)**
Heat- dampness	Qing Re Tiao Xue Tang,		Xiao Yao San He Wan Jia Jin,	Long Dan Xie Gan Tang,	**Er Miao San (2)**

Table 2.8 Comparison between the most widely used formulas for treatment of PD in the traditional TCM texts

Therefore the following formulas were those chosen for use in this study:

DISHARMONY PATTERN	FORMULA/S
Qi stagnation	Xiao Yao San
+ Fire	Dan Zhi Xiao Yao San
Xue stasis	Tao Hong Si Wu Tang
Cold- dampness	Wen Jing Tang or Shao Fu Zhu Yu Tang
Yang vacuity	Tong Jing Tang
Heat- dampness	Er Miao San
Qi/Xue vacuity	Shi Quan Da Bu Wan or Ba Zhen Yi Mu Tang
Liv/Kid Yin vacuity	Tiao Gan Tang
+ Heat	Jia Wei Tiao Gan Tang

Table 2.9 Formulas used to treat PD in this study

2.2 Literature review of articles and studies

2.2.1 Introduction

Throughout the history of TCM many forms of CHM have been used for the treatment of menstrual pain. In recent years there have been several studies to verify the effectiveness of these traditional treatments. A literature review of the most relevant TCM current studies in the treatment of menstrual pain with CHM was done to clarify the current status of research in this field.

2.2.2 Methodology - search strategy

The databases used were:

- Medline
- Cochrane Library Plus

- Informa Healthcare
- JSTOR
- Google Scholars [http://scholar.google.es/]
- ScienceDirect – SciVErse
- SpringerLink
- EBSCOhost
- SCIRUS
- WILEY Online Library
- World Scientific

The search keywords used were:

- Traditional Chinese Medicine
- Traditional Chinese Herbal Medicine
- Dysmenorrhea
- Dysmenorrhoea
- Menstrual Pain
- Painful menstruation

The selection of studies was based on the following criteria:

- Types of studies: This review included RCTs and systematic reviews
- Types of participants: Studies with primary dysmenorrhea participants were included. Studies with secondary dysmenorrhea participants or participants with dysmenorrhea caused by use of an intra-uterine device were excluded
- Types of intervention: Studies that used CHM were included
- Types of targets: Studies that aimed relieve menstrual pain and discomfort associated with primary dysmenorrhea were included

Finally 6 RCTs and a systematic review were found consistent with the detailed criteria.

Non-inclusion of articles in Chinese and the omission of searches on Chinese databases should be considered as a limitation of this review.

2.2.3 Evaluation of papers

2.2.3.1 Description of studies

Six RCTs and a systematic review were selected. The systematic review will be discussed later in point 2.2.4. The studies selected were:

Cheng, J.-F. et al., 2008. 'A traditional Chinese herbal medicine used to treat dysmenorrhoea among Taiwanese women'. *Journal of Clinical Nursing,*17(19), pp.2588-2595. Available at: http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2702.2008.02382.x/full [Accessed October 31, 2010].

Geng, S.S. et al., 2010. 'Effect of Wujijing Oral Liquid on menstrual disturbance of women'. *Journal of Ethnopharmacology*, 128(3), pp.649-653. Available at: http://www.sciencedirect.com/science/article/B6T8D-4Y34V41-6/2/3f282428b22d5608536e540ede488c6c.

Jang, J.-B. et al., 2009. 'Therapeutic effects of Chiljehyangbuhwan on primary dysmenorrhea: A randomized, double blind, placebo-controlled study.' *Complementary Therapies in Medicine*, 17(3), pp.123-130. Available at: http://www.sciencedirect.com/science/article/B6WCS-4TKXD61-1/2/e05378c907e4ea8ce99211d7087575f3.

Kennedy, S. et al., 2006. 'Randomized controlled trial assessing a traditional Chinese medicine remedy in the treatment of primary dysmenorrhea'. *Fertility and Sterility*, 86(3), pp.762-764. Available at: http://www.fertstert.org/article/S0015-0282(06)00957-5/abstract [Accessed October 31, 2010].

Tseng, Y.-F., Chen, C.-H. & Yang, Y.-H., 2005. 'Rose Tea for Relief of Primary Dysmenorrhea in Adolescents: A Randomized Controlled Trial in Taiwan'. *Journal of Midwifery & Women's Health*, 50(5), pp.e51-e57. Available at: http://www.sciencedirect.com/science/article/B6W6R-4H2F7JB-1C/2/8f9a7b0cb082c32cb4588e51f80b2914.

Yeh, L.L.L. et al., 2007. 'A Randomised Placebo-Controlled Trial of a Traditional Chinese Herbal Formula in the Treatment of Primary Dysmenorrhoea'. *PLoS ONE*, 2(8), p.e719. Available at: http://dx.doi.org/10.1371/journal.pone.0000719 [Accessed October 31, 2010].

All selected studies evaluated the effectiveness of treatment of primary dysmenorrhea with one or more TCM remedy. One of them was developed in continental China in Nanjing, 3 in Taiwan, one in Korea and one in Netherlands.

In the studies of Cheng et al. and Yeh et al., Si Wu Tang formula was used, Tseng et al. used Rose tea, Geng et al. used Wujijing, Jang et al. used Chiljehyangbuhwan and Kennedy et al. used a TCM formula consisting of three ingredients (Angelica sinensis root, Paeonia lactiflora root and Corydalis yanhusuo rhizome).

Study	Treatment methods	Country
	Si Wu Tang	China (Taiwan)
(Yeh et al., 2007)	Si Wu Tang	China (Taiwan)
(Tseng, C.-H. Chen & Yang, 2005)	Rose tea.	China (Taiwan)
(Geng et al., 2010)	Wujijing	China (Nanjing)
(Jang et al., 2009)	Chiljehyangbuhwan	Korea
(Kennedy et al., 2006)	TCM formula consisting of three ingredients (Angelica Sinensis root, Paeonia lactiflora root and Corydalis yanhusuo rhizome)	Netherlands in collaboration with The University of Oxford

Table 2.10 Treatment methods and Country of the studies reviewed

2.2.3.2 Research question and hypothesis

The studies did not specify the working hypothesis or the null hypothesis, but specified the objectives.

The purposes of the Cheng et al. study were twofold. Firstly, to ascertain the relative effectiveness of the alternative drug, Si-Wu-Tang, for dysmenorrhoea treatment and

secondly to compare two different timings for consumption of SWT in relation to menstrual pain.

The Yeh et al. study assessed the effectiveness and safety of Si Wu Tang for primary dysmenorrhoea and evaluated the compliance and feasibility for a future trial.

The purpose of the Tseng et al. study was to investigate the effects of drinking rose tea for alleviating the pain and psycho-physiological distress experienced by adolescents with primary dysmenorrhea in Taiwan.

The Geng et al. study attempted to evaluate the clinical efficacy and mechanism of action of Wujijing Oral Liquid for menstrual disturbance.

The Jang et al. study was conducted to investigate the efficacy and safety of an oriental herbal medicine native to Korea, Chiljehyangbuhwan, in treating primary dysmenorrhea.

The Kenedy et al. study assessed the safety and efficacy of a TCM formula as treatment for primary dysmenorrhea; however it showed no statistically significant results over placebo.

2.2.3.3 Design

All studies were controlled and randomized. Participants in studies control group in the Yeh et al., Geng et al., Jang et al. and Kennedy et al. studies received a placebo with a similar appearance to the treatment, however those of the Cheng et al. study received the same treatment as the experimental group but on different days of the menstrual period, and in the Yeh et al. study the control group received no intervention, which could cause serious bias.

Study	Intervention
(Cheng, Lu, Su, Chiang & R.-Y. Wang, 2008)	Two cycles of treatment during which the experimental group (n = 24) was provided with Si Wu Tang for seven consecutive days commencing at the completion of menstruation, while the comparison group (n = 25) was provided with Si Wu Tang on the first day of menstrual bleeding for seven consecutive days
(Yeh et al., 2007)	Three cycles of treatment during which the experimental group (n = 37) was provided with Si Wu Tang for five days from the onset of bleeding or pain, while the comparison group (n = 39) was provided with **placebo** during the same period
(Tseng, C.-H. Chen & Yang, 2005)	Six cycles of treatment during which the experimental group (n=70) was treated with rose tea from 1 week before their menstrual period to the fifth menstrual day, for 12 days every month. The participants drank 2 teacups of rose tea. Participants in the control group (n=60) **did not receive any intervention**
(Geng et al., 2010)	Two menstrual cycles during which the experimental group received Wujijing 10mL twice daily (n = 28) and the control group received an identical-looking **placebo** (n = 25) from the 1st day after onset of menstrual flow until 1 day after onset of menstrual flow of the third cycle.
(Jang et al., 2009)	One menstrual cycle during which the experimental group received *Chiljehyangbuhwan* (n = 24) and the control group received a **placebo** (n = 17), starting at the conclusion of one menstrual period and ending al the conclusion of the next. Each group was further split into smaller subsets (indication, non-indication and unspecified group, according to Korean Oriental medical diagnosis.
(Kennedy et al., 2006)	Three cycles of treatment (plus two observation cycles, one before and one after) during which the participants took three tablets twice per day for 7 days, commencing 2 days before the anticipated start of menstruation during three cycles. The intervention group (n = 17) received a TCM formula consisting of three ingredients (Angelica Sinensis root, Paeonia lactiflora root and Corydalis yanhusuo rhizome) and the control group (n = 19) received **placebo** tablets, indistinguishable in appearance.

Table 2.11 Interventions of the studies reviewed

The treatment period of the studies varied between 1 and 6 cycles, and only Cheng et al., Yeh et al. and Kennedy et al. carried out a follow up after the end of the treatment period.

Geng et al. Jang et al. applied daily treatment during the intervention period, whereas the other studies only applied treatment during certain days of each cycle, which could affect the results, since the pharmacological effect of pharmacopoeial formulas is usually cumulative (Kennedy et al. 2006). In addition, treatments carried out throughout

the cycle may be less symptomatic and have a deeper effect in treatment of the disharmony pattern.

With the exception of Cheng et al. and Tseng et al., the studies used double blinding and appropriate randomization, increasing thereby their reliability.

Study	(Cheng, Lu, Su, Chiang & R.-Y. Wang, 2008)	(Yeh et al., 2007)	(Tseng, C.-H. Chen & Yang, 2005)	(Geng et al., 2010)	(Jang et al., 2009)	(Kennedy et al., 2006)
Randomisation	Not specified	Computer-generated randomization list	Unclear randomisation	Computer-generated randomization list	Random number table	Computer-generated randomization list
Blinding	No	Double-blind	No	Double-blind	Double-blind	Double-blind
Length of intervention	2 cycles	3 cycles	6 cycles	2 cycles	1 cycle	3 cycles
Follow-up	2 cycles	2 cycles	0 cycles	0 cycle	0 cycle	1 cycle

Table 2.12 Design of the studies reviewed

Cheng et al. and Tseng et al. did not use a placebo for treatment of the control group, which gives less validity to their results. **In the studies using placebo in the control group, those that found significant differences in the level of pain between the experimental and control group at the end of the study were those that applied the treatment throughout the study period - Geng et al. and Jang et al.** On the other hand those that applied the treatment only on certain days of the menstrual cycle during the study period, Yeh et al. and Kennedy et al., found no significant differences.

Generally the studies with the most appropriate methodological designs were Geng et al. and Jang et al., although they did not monitor the evolution of menstrual pain after the study. Jang et al. was the only study that used TCM differentiation of disharmony patterns for choice of treatment.

2.2.3.4 Data collection technique

The data collection techniques were similar in Cheng et al., Yeh et al., Jang et al. and Kennedy et al. who used the Visual Analogue Scale (VAS) for pain assessment, along

with other additional parameters such as duration of pain or intake of NSAIDs. Tseng et al. used specific questionnaires (Short-form McGill Pain Questionnaire and The Short form of the Menstrual Distress Questionnaire) as well as scales for the assessment of stress. Geng et al. used a non specific questionnaire about the intensity of the primary symptoms of menstruation (menstrual blood loss) and menstruation-related symptoms (dysmenorrhea, breast pain, dizziness, fatigue, insomnia) from 0 (none) to 3 (severe), and an assessment of sex hormone profiles included the levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL), estradiol (E2), progesterone (PG) and testosterone.

As discussed below, the VAS is generally considered the most suitable, since its validity and reliability has been widely studied (M. S. Serrano - Atero, 2002). We will also see later that the Menstrual Distress Questionnaire used by Tseng et al. is one of the most criticised, mainly because it is retrospective (Norvell et al.,1987) (Terry et al., 2008). The questionnaire reliability, as well as its validity, are questioned because the factors originally considered by Moos (the author of the questionnaire) as constituents of premenstrual syndrome, have not been later verified (Norvell et al. 1987) (Terry et al. 2008).

In general, all of the studies used appropriate data collection techniques, except Tseng et al. which used questionnaires that currently are of questionable validity and reliability.

Study	Data collection methods
(Cheng, Lu, Su, Chiang & R.-Y. Wang, 2008)	1. **Visual analogue scale** 2. Duration of the pain 3. Frequency of use of NSAIDs
(Yeh et al., 2007)	1.**Visual analogue scale** 2. Four-point pain scale 3. Confounders: Data regarding the type and frequency of the intake of all drugs and the use of other remedies as possible confounders was collected along with the VAS pain intensity in an electronic diary. 4. Adverse reactions or events
(Tseng, C.-H. Chen & Yang, 2005)	1. Short-form McGill Pain Questionnaire 2. The Menstrual Distress Questionnaire Short Form 3. Visual Analogue Scales for Anxiety 4. Perceived Stress Scale 5. The Psycho-physiological Life Adaptation Scale
(Geng et al., 2010)	1. Questionnaire (non specific) on primary symptoms of menstruation (menstrual blood loss) and menstruation-related symptoms (dysmenorrhea, breast pain, dizziness, fatigue, insomnia) from 0 (none) to 3 (severe) 2. Assessment of sex hormone profiles
(Jang et al., 2009)	1. **Visual analogue scale** 2. Verbal Rating Scale 3. Multidimensional Verbal Rating Scale
(Kennedy et al., 2006)	1. **Visual analogue scale** 2. Duration of dysmenorrhea 3. The amount of rescue medication used 4. Global assessment of treatment

Table 2.13 Data collection methods of the studies reviewed

2.2.3.5 Participants

The studies included between 41 and 130 participants with the sum total of 393 participants in all studies.

Yeh et al. and Kennedy et al. used age, duration of the cycles, and absence of associated gynecological pathology as inclusion criteria. Yeh et al. also specified the required number of painful cycles in recent months, however for Kennedy et al. inclusion criteria included menstrual cycles that 'usually' required and obtained relief from analgesia and/or participants whose daily functioning was significantly impaired, which may have caused significant bias.

Cheng et al. and Jang et al. used less specific inclusion criteria limiting it only to age and secondary dysmenorrhea.

Tseng et al. and Geng et al. did not specify the inclusion criteria, which could lead to possible bias, in addition to affecting the reliability of the study.

Cheng et al. and Tseng et al. limited the age range of participants which means that the results are not applicable to the general (El Centro Nacional de la Medicina Complementaria y Alternativa, s.f.).

Study	Subjects	Inclusion criteria
(Cheng, Lu, Su, Chiang & R.-Y. Wang, 2008)	49	Women between 20 and 30 years of age and who, reportedly, had suffered from dysmenorrhoea for a period of more than one year.
(Yeh et al., 2007)	76	Women 18 years or older, with cycles lasting 21 to 35 days, with the actual menstrual periods lasting three to seven days, and that experienced at least 4 consecutive painful periods in the six months prior to the study, with pain starting one day before or on the day of onset of bleeding. The women were not taking oral contraceptive pills and agreed to refrain from sexual activity during the study due to any possible confounding effect on pain and/or early withdrawal due to pregnancy, and they had no prior severe gastrointestinal, gynaecological or autoimmune diseases, or gynaecological surgery, including pregnancy
(Tseng, C.-H. Chen & Yang, 2005)	130	**Not specified (nursing students)**
(Geng et al., 2010)	53	**Not specified** Exclusion criteria: Patients with any prior diagnosis of cardiovascular disease, digestive system diseases, tuberculosis, tumors, hypersensitivity and diseases of the nervous system were excluded. Patients with adenomyosis, endometriosis, or gynaecologic cancer were also excluded.
(Jang et al., 2009)	41	Women over 14 and under 45 years of age and more than 2-3 years past menarche Cyclic, periodic manifestations of dysmenorrhea symptoms No underlying conditions leading to secondary dysmenorrhea Not related to conditions causing pelvic pain outside the uterus Not related to drug interactions (contraceptives, hormonal drugs, analgesics, etc.)
(Kennedy et al., 2006)	44	Women between 18 and 45 years of age, with menstrual cycles occurring every 21 to 42 days and with dysmenorrhea, who usually required and obtained relief from analgesia and/or whose daily functioning was significantly impaired Exclusion criteria: -known to have pathology associated with dysmenorrhea -concurrent use of any other TCM, alternative therapy or herbal remedy for dysmenorrhea -likely to take analgesics, sedatives or muscle relaxants within the 48 hours before menstruation -use of mood-altering medication -not willing to use reliable contraception if sexually active
Total	393	

Table 2.14 Inclusion criteria and subjects of the studies reviewed

All of the studies were approved by an ethics committee, and all, except Jang et al. and Kennedy et al., obtained a signed informed consent from the participants or their parents,

a necessary aspect designed to ensure protection for participants (National Center for Complementary and Alternative Medicine, nd) (Zaslawski, 2010).

Only Jang et al., Yeh et al. and Geng et al. conducted an evaluation of adverse-effects. These three studies and Kennedy et al. performed ultrasound, haematological and biochemical screening tests to evaluate the safety of interventions used.

In the Yeh et al. study no blood chemistry levels changed, except for an increase in heavy metals at the end of treatment. This slight increase occurred not only in the FAD group but also in the placebo group.

In the Geng et al. study 1 patient from the intervention group reported adverse. There were no reports of severe adverse reactions. Level of hepatic and renal function and hemogram parameters were without change.

In the Jang et al. study adverse reactions were recorded on observation charts, and 8 participants in the intervention group reported various forms of discomfort, but none of the subjects chose to leave the trial for these reasons. The 2 subjects who eventually chose to discontinue were all from the placebo group.

Study	(Cheng, Lu, Su, Chiang & R.-Y. Wang, 2008)	(Yeh et al., 2007)	(Tseng, C.-H. Chen & Yang, 2005)	(Geng et al., 2010)	(Jang et al., 2009)	(Kennedy et al., 2006)
Ethical approval	China Medical University, Taiwan	Human Ethics Committee of National Health Research Institutes of Taiwan	Research Ethical Committee of the participating institution	Department of Obstetrics and Gynecology of Nanjing General Hospital firstly	Kyung Hee University Korean Oriental Medicine Hospital Institutional Review Board of Clinical Trials	University of Oxford and The Netherlands by TNO Quality of Life
Evaluation of adverse effects and safety	Not specified	Possible adverse reactions to TCM were annotated. Safety was assessed by using standard haematological and biochemical tests and pelvic ultrasound.	Not specified	At each visit, patients were asked whether there were any adverse effects or not. Safety was assessed by using standard haematological and biochemical tests.	Adverse reactions were recorded on observation charts Safety was assessed by using standard haematological and biochemical tests and pelvic ultrasound.	Evaluation of adverse effects not specified. Safety was assessed by using standard haematological and biochemical tests.
Informed consent	Yes	Yes	Yes	Yes	Not specified	Not specified

Table 2.15 Summary of ethical concerns of the studies reviewed

2.2.3.6 Analysis

Cheng et al. used the SAS program (for Windows) although the study did not specify the kind of statistical test used to analyze the results. The results indicated that the decrease of menstrual pain levels and the duration of pain between the experimental group and the comparison group was not significant. However, the decrease in menstrual pain over the five menstrual cycles within the experimental group and within the comparison group was significant.

Yeh et al. used the SAS program and t-test for statistical testing. They found that at the end of the treatment, both overall-pain and peak-pain decreased in the intervention group and increased in the placebo group; however, the difference between the two groups was not statistically significant.

Tseng et al. also used the SAS program and applied Dunn's method. The results showed that the experimental group, in comparison with the control group, perceived less menstrual pain, distress, and anxiety and showed greater psycho-physiological well-being over time, at 1, 3, and 6 months after the interventions.

The Geng et al. study does not specify a statistical program but mentioned that the chi-square tests and the Student´s t-test were used to compare clinical and demographic data between the intervention and control groups. Comparisons were made with t-test and Wilcoxon test before and after intervention in each group. They found that the score for pain and related symptoms of the menstruation decreased significantly among patients treated with the Wujijing. Comparing the Wujijing group and the placebo group, the levels of P and T differed significantly after treatment.

Jang et al. used the SPSS statistical program and t-test. They found that in the non-indication group there were no significant differences in VAS, VRS, and MVRS scores and score changes before and after medication between the placebo group and the Chiljehyangbuhwan group. In the indication group there were significant differences in the changes in VAS and MVRS scores between the placebo group and the Chiljehyangbuhwan group.

Kennedy et al. used the SAS program for data analysis, although did not specify the statistical test used. They found that there were no significant differences in any of the measures of efficacy between the TCM formula and the placebo. However, after cycle 3, 53% of women in the TCM group reported less pain than usual compared with the 26% in the placebo group.

2.2.3.7 Findings

Cheng et al. found that the Si Wu Tang formula can be integrated as an alternative therapy within Western medicine.

Yeh et al. concluded that the finding of statistically significant pain-reducing effect in the first follow-up cycle was unexpected and warrants further study, and a larger, similar trial among primary dysmenorrheic young women with a longer treatment phase

and multiple batched study products could determine the definitive efficacy of this historically documented formula.

Tseng et al. concluded that the findings suggest that drinking rose tea is a safe, readily available and simple treatment for dysmenorrhea, which female adolescents may take to suit their individual needs.

Geng et al. concluded that the Wujijing oral liquid could improve menstrual disorder and is generally safe and well tolerated. The possible mechanism could be associated with its effects on strengthening the kidney and regulating the hypothalamus–pituitary–ovary axis (HPOA).

Jang et al. concluded that the results suggest that Chiljehyangbuhwan is effective and safe in treating primary dysmenorrhea when prescribed appropriately under Korean Oriental medical diagnosis.

Kennedy et al. concluded that, although not statistically significant, there could be an indication of a cumulative effect over time, but that the study was inadequately powered to reject or confirm this possibility completely.

2.2.3.8 Implications for practice

The analysis of the clinical studies discussed allows the deduction that the application of treatment throughout the menstrual cycle may be more effective in treating pain than treatment during only a fraction of the menstrual cycle.

2.2.4 Cochrane systematic review

Cochrane recently published a review (Xiaoshu Zhu et al., 2010). Thirty-nine randomised controlled trials involving a total of 3475 women were included in the review. They included any randomised controlled trials involving Chinese herbal medicine versus placebo, no treatment, conventional therapy, heat compression, another type of Chinese herbal medicine, acupuncture or massage. Exclusion criteria were identifiable pelvic pathology and dysmenorrhoea resulting from the use of an intra-uterine contraceptive device.

They found promising evidence for the use of CHM in reducing menstrual pain in the treatment of primary dysmenorrhea, compared to both conventional medication such as NSAIDs and the oral contraceptive pill and acupuncture and heat compression. All available measures of effectiveness confirmed the overall superiority of CHM to placebo, no treatment, NSAIDs, OCPs, acupuncture and heat compression. No significant adverse effects were identified in the review. However, the small number and the low quality of included studies did not allow any definite conclusion for their use in clinical practice

2.2.5 Conclusions

According to the findings of the discussed studies, we can conclude that:

• The application of a continuous treatment during the study instead of applying it for just a few days during the menstrual cycle may be more effective in treatment of menstrual pain, possibly due to a cumulative effect.

• Treatments may be more effective when prescribed according to a TCM diagnosis and differentiation of disharmony patterns

• Pharmacopoeia treatments applied under the right conditions appear to be safe and could be integrated as alternative treatments to CM

• Further trials with more robust methodology are necessary to reach more definitive conclusions

SECTION 3 – FIELD WORK

3. METHODOLOGY FOR THE FIELD WORK

3.1 Introduction

A prospective, uncontrolled naturalistic study was carried out in Barcelona between May and September of 2011, in which 14 participants received treatment with chinese herbs based on the traditional formula Xiao Yao San during three menstrual periods. The mean age of the participants was (6,6), with a range of 22 to 42 years.

The timeline of the study is specified in the following table:

	April				May				June				July				August				September			
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Recruitment																								
Data collection																								
Literature search																								
Analysis of literature																								
Writing of literature review																								
Writing of introduction																								
Writing of methods																								
Data analysis																								
Writing of results and discussion																								
Submission of project																								

Table 3.1 Gantt diagram

3.2 Design of the research

3.2.1 Recruitment of participants

10 women of reproductive age and over the age of 18 participated in the study. The inclusion and exclusion criteria that were established were the following:

- **Inclusion criteria**:
  - menstrual cycles between 21 and 35 days
  - menstruations with between 3 and 7 days duration

- women that experienced pain unrelated to secondary dysmenorrhea during a minimum of 4 consecutive periods in the 6 months prior to study
- not pregnant
- who did not take oral contraceptives and who were in agreement to use non-hormonal contraceptive methods during the study
- and in the case of taking oral contraceptives, that these had been taken for a minimum of 6 months and with the understanding that they should continue to be taken throughout the entire duration of the study.

- **Exclusion criteria**
  - that the women included in the study were not using an intrauterine device (IUD)
  - had not been diagnosed with any serious illness
  - were not receiving other TCM treatment.

The study was publicised by posters in natural health centres and therapies schools in Barcelona (see Appendix I– Poster), and through announcements in social networks and Web pages (see Appendix II– Announcements in social networks and Appendix III– article in Web pages).

56 candidates who responded to these advertisements were interviewed by telephone to evaluate their suitability for the study. To standardise the interviews a telephone script and a questionnaire were used (see Appendix IV– Telephone script for preliminary assessment of candidates and Appendix V– Questionnaire for preliminary assessment of candidates).

Of the 56 candidates, 19 did not comply with the inclusion criteria, it was not possible to contact 9 by telephone, 3 responded that they would have to think about it and 25 decided to participate in the study. 5 of the latter did not attend the initial interview and gave no explanation as to why they had decided to not participate.

Of the **19 candidates that did not meet the requirements**, 4 were receiving TCM treatment, 1 was underage, 3 did not meet the requirements regarding cycle or duration of the menstrual period, 7 suffered from secondary dysmenorrhea, 1 did not meet

requirements regarding pain, 1 was trying to get pregnant and was not prepared to use contraceptive methods, 1 did not meet the requirements regarding oral contraceptives and 1 was excluded because of living far away from the centres where the interviews would be carried out and on her informing that she was not going to be able to travel to any of them.

20 participants were included in the study, 6 of whom abandoned for personal reasons or were excluded because they did not follow the treatment adequately (they did not collect the different formulas on time) and 4 of them was not included in the results as the study would finalise outside the deadline of this work. Therefore the study sample size was 10 participants.

3.2.2 Design

A prospective, uncontrolled naturalistic study was carried out in which participants received treatment with a traditional Chinese herb formula during three menstrual periods.

The study obtained prior approval from the Ethics Committee of the University of East London (www.uel.ac.uk)

The initial design of the study contemplated carrying out a randomized controlled trial but this was not possible due to the time constraints of the deadline for this work. In order to carry out a trial with these characteristics in Spain approval from a Spanish ethics committee is necessary and this takes from six months to a year to process. For this reason it was decided to carry out an uncontrolled naturalistic study, respecting the diagnostical bases of TCM.

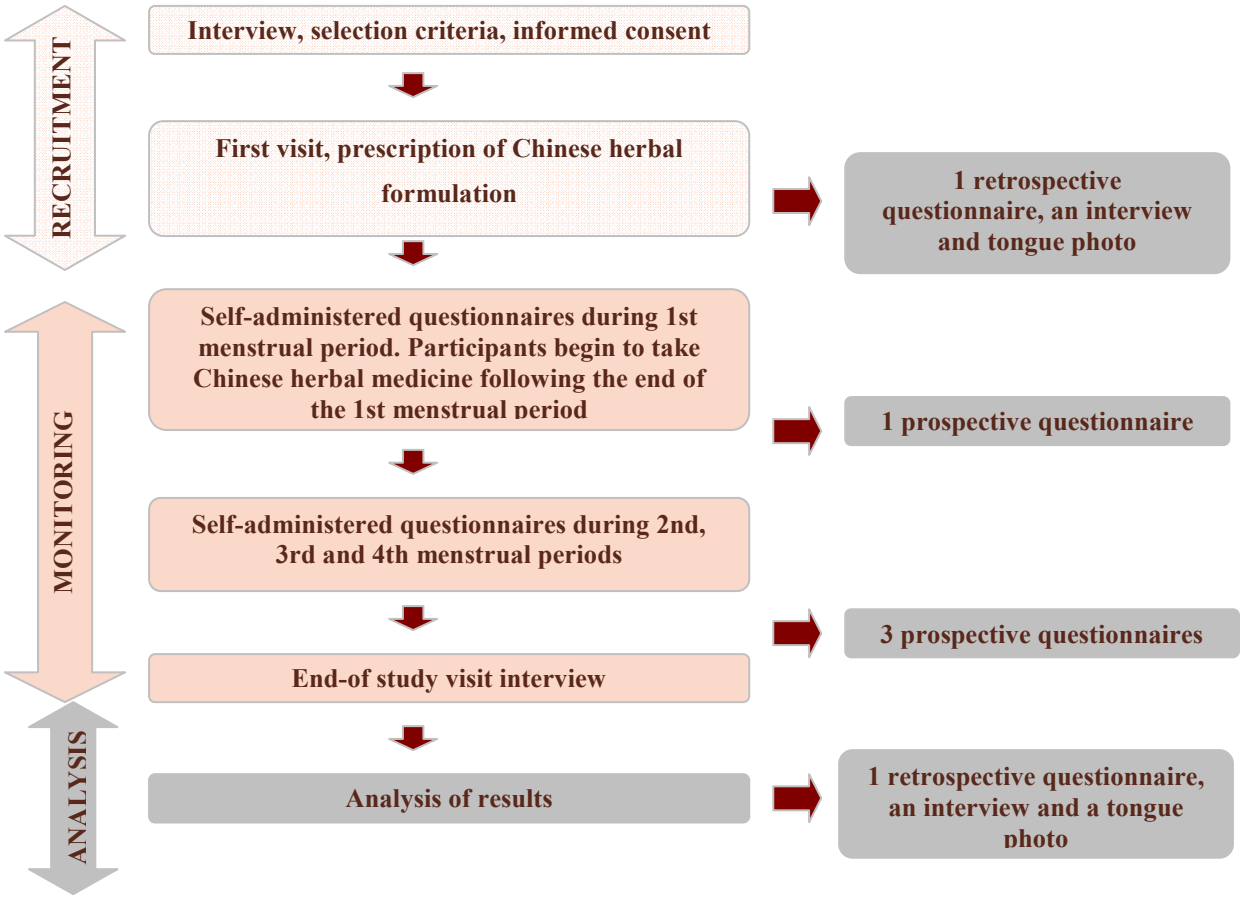


Chart 3.1 Study design

The World Health Organisation (WHO), in its initiative to develop standardisation of evidence based Traditional Chinese Medicine (Chang, 2004) recommends the application of TCM diagnostic criteria. The initial design of the study contemplated personalised choice for the formulation of remedies with traditional Chinese herbs based on the differentiation of disharmony patterns of dysmenorrhea as determined in section 2.1.2:

DISHARMONY PATTERN	FORMULA/S
Qi stagnation	Xiao Yao San
+ fire	Dan Zhi Xiao Yao San
Xue stasis	Tao Hong Si Wu Tang
Cold-Humidity	Wen Jing Tang or Shao Fu Zhu Yu Tang
Yang vacuity	Tong Jing Tang
Heat-Humidity	Er Miao San
Qi/Xue vacuity	Shi Quan Da Bu Wan or Ba Zhen Yi Mu Tang
Liv/Kid Yin vacuity	Tiao Gan Tang
+ heat	Jia Wei Tiao Gan Tang

Table 3.2 – Formulas used depending on disharmony pattern

The design of the study was modified as, when carrying out the initial interviews and determining the diagnosis according to TCM, it was found that all of the participants presented signs and symptoms that coincided with Qi stagnation. For this reason it was decided to prescribe modified Xiao Yao Wan for all cases (See Appendix VI– Composition of the formula used in the study and Appendix VII- Traditional composition of Xiao Yan San) and in this way simplify the final analysis of the study results.

The herbal based formulas used in the study were formulas commercialised by Fitoki (www.fitoki.com). The Fitoki formulas are registered in the European Union and have obtained the necessary health records required by the Spanish Ministry of Health and by the provincial government for their production, commercialisation and distribution as alimentary supplements (see Appendix VIII– Laboratory quality control certificates).

Spanish legislation only permits TCM therapists to prescribe registered products and not personalised formulas and this was another reason for using registered products for the study (see Appendix IX- Precepts of the law "Law 29/2006, of the 26th of July" of guarantees and rational use of medicaments and health care products)

3.3 Data collection and analysis

3.3.1 Material

All participants signed an **informed consent** (see Appendix X– Informed consent) and a document under the **Organic Law on data protection in Spain** (see Appendix XI– Organic Law on Data Protection).

Modified questionnaires for the assessment of menstrual pain were used for data collection (Larroy, C et al.,2001) in different phases of the study:

- A retrospective questionnaire at the beginning of the study (see Appendix XII – initial menstrual pain questionnaire)
- A daily questionnaire during 4 menstrual periods to be filled out on the days with menstruation (see Appendix XIII– daily menstrual pain questionnaire)
- A final questionnaire (see Appendix XIV– final menstrual pain questionnaire)

At the first interview participants were individually informed about the study details and the process, intervention and informed consent were all explained. The participants also received instructions on how to fill out the questionnaires and were free to ask any questions and comment on any doubts that they might have.

The participants were informed that in the case of presenting any unpleasant symptoms that they believed to be related to taking the herbal formula that they could consult someone using the telephone number or email given in the informed consent, as well as being able to consult their doctor if considered necessary. A form was provided for making note of any possible adverse effects from the medication (see Appendix XV– Adverse effects report) where the contact telephone number and email where once again specified.

The participants were informed that they were allowed to take pain killers during the study and they were shown where to annotate this on the daily menstrual pain questionnaire. They should indicate any other medication in the **report of medication taken** (see Appendix XVI– Medication Report)

3.3.1.1 Menstrual pain assessment questionnaire used in the study

There are several different questionnaires for the assessment of pain and specifically menstrual pain. The most commonly used questionnaires for assessment of menstrual pain are:

- The Menstrual Distress Questionnaire (MDQ) (Moos, 1968)
- The Menstrual Symptom Questionnaire (MSQ) (Chesney & Tasto, 1975)
- Daily Symptom Rating Scale (DSRS) (Taylor, 1979)
- Daily Rating Form (DRF) (J Endicott et al., 1986)
- The end of day questionnaire (Choi & Salmon, 1995)
- Menstrual pain questionnaire (Larroy, C et al., 2001)

Sometimes generic pain assessment scales are used, the most important of which are: (Ferreira-Valente et al., 2011) (M. S. Serrano - Atero, 2002) (Price et al.,1983)

- Numerical rating scales (NRS)
- Visual analogue pain scale (VAS)

The **factors that determine whether a questionnaire is adequate for use** are its reliability and its validity. Martín Arribas defines these parameters in the following way: (Martín Arribas, M.C., 2004) us it is explained in Appendix XVII.

Summing up, Martín Arribas (Martín Arribas, M.C., 2004) highlights the following points to clarify what is meant by validity and reliability:

1. What is validated is not the test but the test scores and therefore the question we try to answer is: Are the scores of this test valid for use?
2. Validity cannot be summed up in a single indicator or numerical index, the same as with reliability (reliability coefficient, Cronbach's alpha, etc.)
3. Validation is a continuous and dynamic process and
4. **The theory plays an important role as a guide both for the development of a test and its validation process**.

This last point in particular explains and justifies the need to have a questionnaire for assessment of menstrual pain that is specific to TCM as the very theory of TCM takes into consideration some quite different parameters to those considered in CM.

As there was no pre-existing questionnaire for assessment of menstrual pain specific to TCM, the first step was to draw one up for this study. The process of creation of the questionnaires for the study was the following:

- Selection of a valid questionnaire, adaptable to the necessities of TCM
- Adaptation of the questionnaire to the necessities of the study
- Application of the questionnaire to the study.

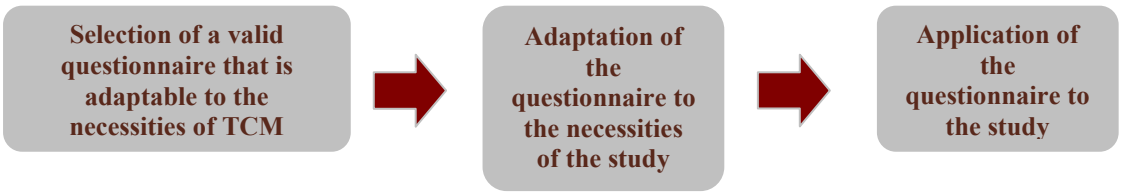


Chart 3.3- Process of creation of the questionnaires for the study

The stages of validation of a questionnaire are: (Morales & Zárate, 2004)

- Selection of the best available instrument for measuring the phenomenon being studied
- Translation into Spanish and afterwards translation back to the original language.
- Pilot test: to assess the points of the questionnaire, their usefulness as well as the format
- Assessment of reliability
- Assessment of validity
- Assessment of the sensitivity to change: it is necessary that the questionnaire be sensitive to even slight clinical variations. To assess the sensitivity to change requires application of the same questionnaire to the same subject on repeated occasions, for example before and after treatment. Some authors have proposed indexes for measuring sensitivity to change, such as the ratio obtained from the division of the average intraindividual score changes, after an effective treatment, by the variability between stable subjects. This index can help in calculating the

sample size necessary for the study of measuring instruments [(DeVellis, 2003) mentioned in (Morales & Zárate, 2004)].

- Revision depending on the previous steps and new application of the instrument.

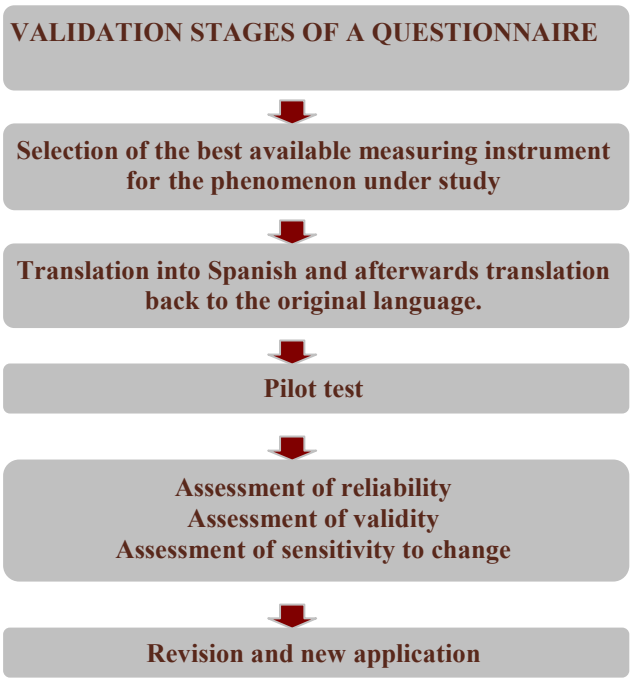


Chart 3.4 Stages of adaptation of a questionnaire

Based on the necessary stages for validation of a questionnaire, as defined by Morales & Zárate, the process of creation of an assessment of menstrual pain questionnaire for the current study was determined.

In the following table are shown the actions taken in each of the stages:

VALIDATION STAGES OF A QUESTIONNAIRE (Morales & Zárate, 2004)	STAGES FOLLOWED IN THE STUDY
Selection of the best available measuring instrument for the phenomenon under study	Selection of the Larroy menstrual pain questionnaire
Translation into Spanish and afterwards translation back to the original language.	Not applicable
Pilot test: to assess the points of the questionnaire, their usefulness as well as the format	In spite of it being advisable to carry out a pilot to test to try out usage, refine technical aspects and improve and correct any deficiencies that might be found (Morales & Zárate 2004), given the limitations of resources and time this was not done and the questionnaire was applied directly to the study. It should be noted that the variations to the original questionnaire are minimal, to be exact 8 questions were added, 2 were excluded, 1 was modified and the 20 remaining questions were maintained. Details of the changes made will be given below. (Section 3.2.1.3)
Assessment of reliability	Larroy & cols. Carrying out of the relevant assessments for the validation of the original questionnaire: (Larroy, C et al. 2001) "The discriminative value of the elements in the questionnaire were put to the test with a Crombach test and the differences in mean point scores for the items, finding that all the relevant elements (items) were able to differentiate between people with and without disorders (i.e. dysmenorrhea) with a level of confidence of 99%." In the current study no assessment of the reliability or validity of the adapted questionnaire was made because of limitations of resources and time. In future researchs it would be recommendable to carry out these steps.
Assessment of validity	
Assessment of sensitivity to change	
Revision depending on the previous steps and new application of the instrument	After application of the questionnaire some slight changes to some of the questions were proposed. Details of these will be given below. (Section 3.2.1.5)

Table 3.4 Stages of questionnaire validation

Finally therefore, the **process of creation of the assessment of menstrual pain questionnaire** used in the study was the following:

- Bibliographical review and selection of the best measuring instrument available for measuring pain in PD for the current study (see page 57)
- Adaptation of the questionnaire to the necessities of the study (see page 61)
- Application of the questionnaire to the study (see page 62)

- Revision of the questionnaire used and proposal for a revised questionnaire for assessment of menstrual pain in PD in TCM (see page 62)

3.3.1.2a Review of questionnaire bibliography

As has already been mentioned there are several menstrual pain questionnaires, the main ones of which are commented on below.

The Menstrual Distress Questionnaire (MDQ) (Moos 1968)

A retrospective questionnaire consisting of 47 items measured on a scale of 6 points, ranging from not experiencing symptoms through to experiencing incapacitating symptoms. Here the participants are asked to assess their premenstrual, menstrual and inter-menstrual symptoms, allowing comparisons to be made between the luteal phase and the follicular phase. Different variations of the questionnaire have been created, some of which are prospective (A. Haywood et al., 2002).

There is no outline of advice specified for interpretation of the data and levels of suffering. Tests of reliability and validity have not been carried out (A. Haywood et al., 2002).

The MDQ is the most widely used questionnaire but is also one of the most criticised, with doubts as to both its reliability and its validity. Furthermore the factors that Moos originally considered constitute premenstrual syndrome have been questioned as they have not been subsequently verified. Along the same lines numerous studies consider it invalid because of being retrospective (Norvell et al., 1987) (Terry et al., 2008), although some studies consider that it can provide valuable information. (Hawes & Oei, 1992) (Ross et al., 2003)

The Menstrual Symptom Questionnaire (MSQ) (Chesney and Tasto 1975)

A prospective questionnaire consisting of 25 items measured on a scale of 5 points, ranging from experiencing no symptoms to experiencing symptoms always. (Buela-Casal, Caballo & Sierra, 1996)

Chesney and Tasto developed the MSQ based on Dalton's theory that differentiates between two types of dysmenorrhea, spasmodic and congestive, caused by opposite

hormonal alterations and which therefore cannot be encountered in the same woman. There are studies that suggest that this theory is incorrect and propose modifications to the questionnaire. (Wildman & White, 1986), (Cox, 1977) and (Webster et al., 1979) concluded that Dalton's theory is not correct as menstrual pain depends on more than 2 factors and that premenstrual and menstrual pain can occur in the same woman.

(Cox, 1977) carried out a study that reproduced Chesney and Tasto's study and concluded that:

(a) the MSQ does not have significant test-retest reliability
(b) the dimension of congestive - spasmodic symptoms of the MSQ is not dichotomous and that
(c) the MSQ does not predict the effectiveness of systematic desensibilization. (SD)[2] (Cox, 1977)

Daily Symptom Rating Scale (DSRS) (Taylor 1979)

A prospective questionnaire consisting of 17 items measured on a scale of 6 points, ranging from not experiencing any symptoms through to experiencing severe symptoms. Each form registers 5 weeks of symptoms. (A. Haywood et al. 2002)

There is no outline of advice specified for interpretation of the data and levels of suffering. Reliability and validity are considered adequate. (A. Haywood et al., 2002) (Taylor, 1979)

Daily Rating Form (DRF) (Endicott et al. 1986)

A prospective questionnaire consisting of 20 items measured on a scale of 6 points, ranging from experiencing no symptoms to experiencing extreme symptoms. Each form registers data from 5 days before the menstrual period until 5 days after menstruation. (A. Haywood et al. 2002)

[2] Systematic desensibilization (SD): "SD is a technique for reducing anxiety that is more complex than the relaxation procedures that are also included in it. It is recommended in those cases where a phobic component or intense fear are an important part of the expression of pain. Its creator was J. Wolpe. It consists of progressively presenting the subject with a series of previously hierarchised aversive stimuli while he/she remains in a relaxed state. It attempts to find the incompatibility between different psychological states (tension vs. relaxation) in order to eliminate the cause of the fear or flight/avoidance mechanism. (Villoria, 2007)

In spite of not assessing the reliability of the questionnaire during the study, this questionnaire has been widely used in different population types. Validity tests were not done. (A. Haywood et al. 2002)

The end of day questionnaire (Choi and Salmon 1995)

A prospective questionnaire consisting of 42 items measured on a scale of 5 points, ranging from not experiencing symptoms to experiencing severe / intolerable symptoms. There is evidence of the internal consistency of this questionnaire; however its validity is seriously questioned. (A. Haywood et al. 2002)

Menstrual pain questionnaire (Larroy, C et al. 2001)

The reliability and consistency were determined with a Crombach test and through the different scoring methods for the items. It was found that all the relevant items were able to differentiate between subjects with or without disorders to a level of confidence of 99%. (Larroy, C et al. 2001)

The questionnaire collects information on different aspects of primary dysmenorrhea and is useful both in prevalence studies and clinical studies. (Larroy C, et al., 2001)

Others

Other questionnaires can be found however those that only assess the premenstrual period were rejected for this study.

3.3.1.2b Selection of the best available measuring instrument for pain assessment in PD for the current study

The Moos (1968) MDQ was ruled out mainly because it is a retrospective questionnaire (Norvell et al., 1987) (Terry et al., 2008) as well as because of the doubts as to its reliability and validity. (A. Haywood et al., 2002) (Hawes & Oei, 1992)

The Chesney and Tasto (1975) MSQ was ruled out because of the multiple evidence found that indicates that the questionnaire is based on an incorrect theory and therefore should be modified. (Webster et al., 1979) (Cox, 1977) (Wildman & White, 1986) (Buela-Casal, Caballo & Sierra, 1996)

The Choi and Salmon (1995) end of day questionnaire was ruled out because of evidence found as to its possible lack of validity. (A. Haywood et al., 2002)

The Endicott et al. (1986) DRF was ruled out because in spite of being widely used no validity tests have been done. (A. Haywood et al., 2002)

The two remaining questionnaires were those considered for use in the study. In spite of the reliability and validity of the DSRS, Taylor (1979), being considered adequate (A. Haywood, P.Slade & H.King, 2002) (Taylor, 1979), the Larroy questionnaire was the one finally selected. One of the main reasons for selecting this questionnaire was that it was created in the same country, which minimises the cultural / regional differences in interpretation of the questions in such a way as to guarantee that in the application of the questionnaire the validity and reliability of the initial interview and inquiry would be maintained. (Morales & Zárate 2004).

The Larroy questionnaire contains "sociodemographic data (age, profession, education); factors that may influence menstrual pain (number of children, number of years since menarche); characteristics of menstrual pain (intensity and localisation of the pain, number of painful menstruations, moment of pain onset); request for professional help because of menstrual pain; symptoms associated with menstrual pain; strategies used for pain relief (taking medication and rest); and other symptoms and disorders" (Larroy, C, Meseguer, C & Crespo, 2001) which allows multidimensional assessment of dysmenorrhea (M. S. Serrano - Atero, 2002). This is interesting given that the different physiopathological changes may be accompanied by other changes such as in behaviour and mood states. (Uriel Halbreich & Jean Endicott, 1985)

The questionnaire also includes a daily / monthly chart (see Appendix XVIII – Larroy menstrual pain questionnaire) which facilitates differentiation between dysmenorrhea and premenstrual syndrome by determining the days on which associated symptoms appear.

The Larroy (Larroy, C and al. 2001) version was used, that uses the NRS for pain assessment instead of the version that uses VAS. Both are the most widely used and are considered the most adequate (M. S. Serrano and Atero 2002) (Ferreira-Valente et al., 2011). The validity and reliability of both has been demonstrated, however the NRS is slightly more sensitive (Ferreira-Valente et al., 2011). Furthermore the NRS has the

advantage of defining equal intervals amongst the different levels (M. S. Serrano - Atero, 2002). Even Larroy, in another study, concluded (Larroy, C, 2002) that the use of the NRS is simpler and more convenient.

In spite of the endorsement by numerous studies of the use of the VAS considering it a simple, solid, sensitive and reproducible instrument (Price et al. 1983) (Rosier et al., 2002), a study carried out by (Yarnitsky et al., 1996) presents the VAS as a useful instrument that reflects the differences in individual response to treatment and placebo, but one that has a low test re-test reliability in determined circumstances such as pain from application of heat.

3.3.1.3 Adaptation of the questionnaire to the necessities of the study

The Larroy questionnaire adapts well to the necessities of the study and it was completed with sections for assessment of aspects of menstruation considered important in TCM.

The structure of the questionnaire was maintained along with the majority of the questions. Only the following modifications where made:

- Question 6: was not included as this was a prerequisite for participation in the study
- Question 21: was simplified, reducing the number of answer possibilities from 6 to 3
- Question 23: the daily / monthly chart was not included in order to simplify the process for the participants, thus minimising the number of dropouts. Also the study did not intend to evaluate in detail the premenstrual symptoms but only menstrual and premenstrual pain and premenstrual so it was considered that the inclusion of the chart would not provide relevant data and instead could be uncomfortable for the participants to fill it out.
- Questions 4 and 5 were added to determine the date of the last visit to the gynaecologist and if the participant had been diagnosed with any pathology
- Question 6 was added to find out whether participants had been pregnant at any time

- Questions 11, 16, 17, 18 and 19 were added to the questionnaire. These relate to the colour of menstrual blood, the quantity of blood, the possible presents of clots and whether pain is alleviated with the application of heat or not, as this data is relevant and decisive for diagnosis in TCM (Flaws 1997) (Maciocia 1998).

3.3.2 Procedure (application of the questionnaire)

A personalised interview was carried out with each of the participants where the study process was explained. In this first interview the participants filled out a retrospective menstrual pain questionnaire (see Appendix XII– initial menstrual pain questionnaire), a tongue photograph was taken and radial pulse were taken. They were given four questionnaires (see Appendix XIII– daily menstrual pain questionnaire) to fill out over the following four menstruations and they were given instructions on how to fill out the forms.

The first questionnaire was filled out **without receiving the pharmacopoeial treatment**. The pharmacopoeial treatment was begun on the first day after the first menstruation and during three menstrual cycles. During these 3 cycles the participants filled out the daily questionnaire during menstruation.

At the end of the fourth cycle a final interview was carried out, where the participants filled out a retrospective questionnaire (see Appendix XIV– final menstrual pain questionnaire) and a second tongue photograph was taken and the characteristics of the radial pulse were annotated.

The data was treated statistically with the Statistical Package for the Social Sciences (SPSS).

3.3.3 Revision of the questionnaire used and proposal of a revised questionnaire for assessment of menstrual pain in PD in TCM

After the application of the questionnaire to the 10 participants the following limitations in the initial menstrual pain questionnaire were detected:

- The questions were not numbered and subsequent numbering was done in order to facilitate results analysis
- Various participants found it difficult to remember their last gynecological visit (question 4) so the addition of different answer possibilities could simplify response
- Question 6 ('Have you ever been pregnant?') could be more useful if it were substituted by 'How many times have you been pregnant?'

Likewise, in the daily questionnaire, the question 'Have you taken medication for pain?' is not specific enough. The question should permit specifying the number of pain killers and dosage.

Lastly, in all of the questionnaires (initial, final and daily), the section for assessment of premenstrual symptoms should not limit responses to a maximum of two days prior to menstruation. It would be more convenient to leave space for the participant to indicate how many days before menstruation their symptoms begin, as in many cases symptoms may begin a week, or even up to two weeks, before the menstrual period.

In spite of this, by carrying out a prior interview and completing the questionnaire along with the participants on an individual basis, the deficiencies that could be derived from the questionnaire were minimised.

In Appendix XIX (XIXa, XIXb and XIXc) a proposal for revised questionnaires is presented for assessment of menstrual pain in PD in TCM for future studies.

3.4 Scope and limitations

The design of the study should be considered as a limitation due to the lack of a control group and because of the small sample size.

Other factors detected throughout the study could also be considered limitations, these being the lack of control over the administration of treatments, the lack of control over the number and weight of analgesic tablets taken as well as a more thorough determination of the number of days participants suffered from premenstrual syndrome.

The questionnaire used would seem to be adequate for the study objectives but needs to be correctly validated. In the light of the lack of validation it was decided to consult with Cristina Larroy for her opinion on the modifications made to the original questionnaire elaborated by her and her team, and at the same time request more detailed evidence on the validity of the original questionnaire. Dr. Larroy kindly collaborated indicating that the modifications made for the adaptation of the questionnaire to TCM seemed to her to be "very appropriate" and added that "many of these questions where included in a personalised self-report that the women in our study filled out along with the menstrual pain questionnaire (MPQ)".

Regarding the validation of the original questionnaire she commented that "the MPQ arose from a previous questionnaire drawn up ad hoc for a pilot study carried out in 1987, based on items in the MSQ and other questionnaires with which there were significant correlations; the instrument became more refined and its validity and reliability were proven in a couple of studies, but I can't give you the data because the process was not published and I don't remember them".

In spite of the fact that the contributions of Dr. Larroy do not validate the questionnaire used for this study, they do however reinforce the idea that this could be an adequate questionnaire and it would be interesting to validate it in future investigations.

4. RESULTS

4.1 Introduction

This study assesses the efficacy of treatment of menstrual pain with modified Xiao Yao Wan with a sample of 10 women. For assessing the evolution of menstrual pain, of premenstrual pain, the number of days with pain, the number of days of use of analgesia and the number of days of abandonment of activities due to pain the SPSS programme was used to apply the Student's t-test for related samples. As well, since the study sample number is small, in order to confirm the results the Wilcoxon test was also used, which makes no assumption as to the normal distribution of the frequency of the variables.

4.2 Data Analysis

4.2.1 Demographic profiles

The demographic characteristics of the participants (n=10) are summarised in the table 4.2.1:

Variable	n=10
Age	
Average (SD)	30.9 (6.6)
Range	22 - 42
Family situation	
Single	4
Married or de facto	6
Separated/divorced	0
Ever pregnant	
Yes	2
No	8
Nationality	
Spanish	8
French	1
Croatian	1
Level of education	
Tertiary	7
Secondary	3
Primary	0
Without studies	0
Work activity	
Professional	5
Semi-professional	1
Non professional	3
Unemployed	1

Table 4.2.1 Demographic characteristics of the participants

The average age of the participants was 30.9 (6.6), eight of them were of Spans nationality, one was French and one was Croatian. Six were married, or living with a partner and four were single. Eight of the participants had never been pregnant; two of them had been and had had one child each.

Seven of the participants had university level education and three had secondary school education. At the time of the study five of them were professionally employed, one in a semi-professional job, three non-professionals and one was unemployed.

4.2.2 General Heath behaviour and characteristics

Eight of the participants were of normal weight (CMI[3] between 18.5 and 24.9) and two were obese (CMI between 30 and 39.9). Seven were smokers, six consumed alcohol regularly and one also took drugs. Half of them normally did regular exercise.

One of the participants had been taking oral contraceptives for 7 years and continued taking them during the study.

The table 4.2.2 summarises the general health behaviours and characteristics:

Variable	n=10
CMI classification	
Slim	0
Normal	8
Overweight	0
Obese	2
Smoker	
Yes	7
No	3
Does physical exercise	
Yes	5
No	5
Alcohol consumption	
Yes	6
No	4
Drug consumption	
Yes	1
No	9
Takes oral contraceptives	
Yes	1
No	9

Table 4.2.2 General health behaviours and characteristics of the participants

4.2.3 Menstrual history

The average age of menarche was 13.5 (2.2), between a minimum age of 10 years and maximum of 17 years. The average number of years suffering pain was 15.7 (7.3), with the average number of years with menstruation 17.4 (6.7). Nine of the participants had normal cycle duration according to TCM parameters (Maciocia, 1998), between 26 and 32 days, however one of the participants had a longer cycle of between 32 and 35 days. Eight of the participants had menstrual periods of normal duration, between 4 and 6

[3] CMI = weight (kg) / height^2 (m) (Beers, Berkow & Merck, 1999)

days, according to the parameters of TCM (Maciocia, 1998), one had short periods of 3 days and one had long periods of 7 days.

Nine of the participants felt relief from pain with the application of heat, one did not know whether the heat alleviated her pain or not.

The maximum pain suffered by the participants was 8.3 (0.82) on average, with a range of between 7 and 10 points. Nine of the participants had suffered pain in the last 6 months, the tenth participant in 4 or 5 of the last 6 cycles. The participants on average suffered pain in 11.5 (1.1) months per year, and took analgesic medication on an average of 9 (3.5) cycles per year.

Nine of the participants suffered from Premenstrual syndrome (PMS) and had to abandon normal activities on average 1.4 (1.1) days each menstruation, with a range of between 0 and 3.

The table 4.2.3 shows a summary of the data presented on the menstrual characteristics of the participants:

Variable	n=10
Menarche	
Average (SD)	13.5 (2.2)
Range	10 - 17
Years of pain	
Average (SD)	15.7 (7.3)
Range	3 - 29
Years of menstruation	
Average (SD)	17.4 (6.7)
Range	8 - 29
Normal duration of menstruation	
3 days	1
4 - 6 days	8
7 days	1
Normal duration of the menstrual cycle	
21 - 26 days	0
Painful menstruations per year	
Average (SD)	11.5 (1.1)
Range	9 - 12
Painful months in the last 6 months	
6	9
4 or 5	1
Menstruations per year that require the use of analgesics	
Average (SD)	9 (3.5)

Range	2 - 12
Premenstrual syndrome (PMS)	
Yes	9
No	1
Days of abandonment of activities due to menstrual pain	
Average (SD)	1.4 (1.1)
Range	0 – 3

Table 4.2.3 Menstrual characteristics of the participants

4.2.4 Disharmony patterns of the participants

All of the participants manifested signs and symptoms of Qi stagnation, nine also manifested Qi/Xue vacuity and six manifested Xue stasis, these were the predominant disharmony patterns. Secondarily there was Fire in three cases, Cold-dampness in three cases, Liv/Kid Yin vacuity in three cases and Yang vacuity in two cases. No cases of Heat-dampness or of Heat due to vacuity were detected. In the table 4.2.4 the disharmony patterns manifested by the participants are summarised:

DISHARMONY PATTERNS	10JN01	18A02	11M01	18A03	13A01	25M01	16M01	20M01	10M01	20A01	Total
Qi stagnation	√	√	√	√	√	√	√	√	√	√	10
+ Fire	√					√			√		3
Xue stasis		√	√			√	√	√	√		6
Cold-dampness			√		√		√				3
Yang vacuity				√						√	2
Heat-dampness											0
Qi/Xue vacuity	√	√	√	√		√	√	√	√	√	9
Liv/Kid Yin vacuity				√					√	√	3
+ Heat											0

Table 4.2.4 Disharmony patterns manifested by the participants

4.2.5 Evolution of menstrual pain

The menstrual pain maximum at the beginning of the study was 7.8 (1.4) and at the end was 4.2 (2.5), the difference is statistically significant ($t=4.07$; $p<0.05$)

In the tables 4.2.5 and 4.2.6 the results of the Student's t-test and the Wilcoxon test can be seen.

Related samples test

		Related differences					t	gl	Sig. (bilateral)
		Mean	Typical deviation.	Typical mean error	95% Confidence interval for the difference Lower	Upper			
Par 1	InMaxP_1 - InMaxP_4	3.60000	2.79682	.88443	1.59927	5.60073	4.070	9	.003

Table 4.2.5 Results of the Student's t-test for the evolution of the peak menstrual pain

Contrast statistics[b]

	InMaxP_4 - Intensity of MAXIMUM pain of cycle 1
Z	-2.558[a]
Asymptotic sig. (bilateral)	.011

a. Based on the positive ranges.
b. Test of ranges with Wilcoxon sign

Table 4.2.6 Results of the Wilcoxon test for the evolution of the peak menstrual pain

In the chart 4.2.7 the representation of the data in bloxpot of the initial and final comparisons can be seen and in the chart 4.2.8 the representation of the initial and final comparisons per participant can be seen:

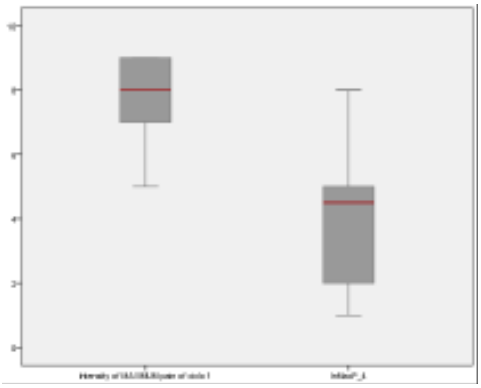


Table 4.2.7 Representation of the data in bloxpot of the initial and final comparisons for the evolution of the peak menstrual pain

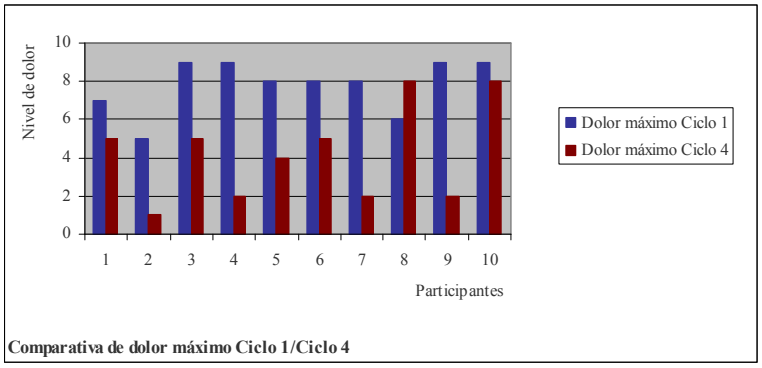


Table 4.2.8 Representation of the initial and final peak menstrual pain comparisons per participant

The menstrual pain average at the beginning of the study was 5.6 (1.3) and at the end was 3.7 (2.1), the difference is not statistically significant (t=1.994; p⩽0.05)

In tables 4.2.9 and 4.2.10 the results of the Student's t-test and the Wilcoxon test can be seen.

Related samples test

		Related differences					t	gl	Sig. (bilateral)
		Mean	Typical deviation.	Typical mean error	95% Confidence interval for the difference Lower	Upper			
Par 1	Level of premenstrual Pain Cycle 1 - LevelPMPain_4	2.35000	3.72715	1.17863	-.31624	5.01624	1.994	9	.077

Table 4.2.9 Results of the Student's t-test for the evolution of the average menstrual pain

Contrast statistics[b]

	LevelPain_4 - Range of Level of pain Cycle 1
Z	-1.886[a]
Asymptotic sig. (bilateral)	.059

a. Based on the positive ranges.
b. Test of ranges with Wilcoxon sign

Table 4.2.10 Results of the Wilcoxon test for the evolution of the average menstrual pain

In the chart 4.2.11 the representation of the data in bloxpot of the initial and final comparisons can be seen:

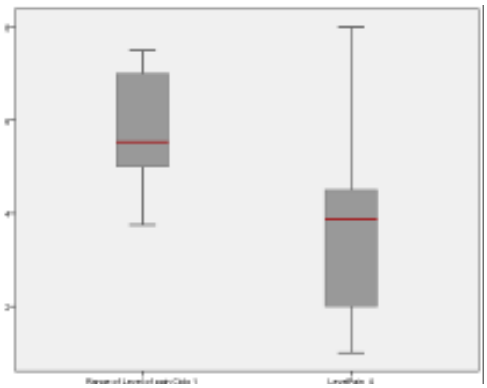


Table 4.2.11 Representation of the data in bloxpot of the initial and final comparisons for the evolution of the average menstrual pain

4.2.6 Evolution of premenstrual pain

The level of premenstrual pain at the beginning of the study was 3.2 (3.0) and at the end was 0.8 (1.4), the difference is not statistically significant (t=2.0; p⩽0.05)

In tables 4.2.12 and 4.2.13 the results of the Student's t-test and the Wilcoxon test can be seen.

Related samples test

		Related differences					t	gl	Sig. (bilateral)
		Mean	Typical deviation.	Typical mean error	95% Confidence interval for the difference				
					Lower	Upper			
Par 1	Level of premenstrual Pain Cycle 1 - LevelPMPain_4	2.35000	3.72715	1.17863	-.31624	5.01624	1.994	9	.077

Table 4.2.12 Results of the Student's t-test for the evolution of the level of premenstrual pain

Contrast statistics[b]

	LevelPMPain_4 - Level of premenstrual Pain Cycle 1
Z	-1.778[a]
Asymptotic sig. (bilateral)	.075

a. Based on the positive ranges.
b. Test of ranges with Wilcoxon sign

Table 4.2.13 Results of the Wilcoxon test for the evolution of the level of premenstrual pain

In the chart 4.2.14 the representation of the data in bloxpot of the initial and final comparisons can be seen:

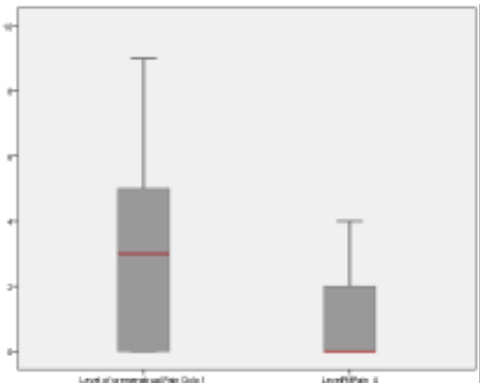


Table 4.2.14 Representation of the data in bloxpot of the initial and final level of premenstrual pain

The number of premenstrual symptoms at the beginning of the study was 4.2 (1.9) and at the end was 2.2 (1.9), the difference is statistically significant ($t=2.4$; $p<0.05$)

In the tables 4.2.15 and 4.2.16 the results of the Student's t-test and the Wilcoxon test can be seen.

Related samples test

		Related differences					t	gl	Sig. (bilateral)
		Mean	Typical deviation.	Typical mean error	95% Confidence interval for the difference Lower	Upper			
Par 1	Number of premenstrual symptoms Cycle 1 - PMSymptoms_4	2.000	2.582	.816	.153	3.847	2.449	9	.037

Table 4.2.15 Results of the Student's t-test for the evolution of the number of premenstrual symptoms

Contrast statistics[b]

	PMSymptoms_4 - Number of premenstrual symptoms Cycle 1
Z	-2.032[a]
Asymptotic sig. (bilateral)	.042

a. Based on the positive ranges.
b. Test of ranges with Wilcoxon sign

Table 4.2.16 Results of the Wilcoxon test for the evolution of the number of premenstrual symptoms

In the chart 4.2.17 the representation of the data in bloxpot of the initial and final comparisons can be seen:

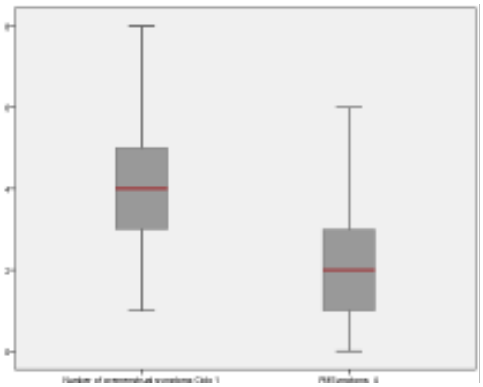


Table 4.2.17 Representation of the data in bloxpot of the initial and final number of premenstrual symptoms

4.2.7 Evolution of the number of days with pain

The number of days of menstrual pain at the beginning of the study was 3.1 (1.3) and at the end was 2.0 (1.1), the difference is statistically significant ($t=2.7$; $p<0.05$)

In the tables 4.2.18 and 4.2.19 the results of the Student's t-test and the Wilcoxon test can be seen.

Related samples test

		Related differences					t	gl	Sig. (bilateral)
		Mean	Typical deviation.	Typical mean error	95% Confidence interval for the difference Lower	Upper			
Par 1	Days of pain Cycle 1 - Pain days_4	1.100	1.287	.407	.180	2.020	2.703	9	.024

Table 4.2.18 Results of the Student's t-test for the evolution of the number of painful days

Contrast statistics[b]

	Pain days_4 - Days of pain Cycle 1
Z	-2.041[a]
Asymptotic sig. (bilateral)	.041

a. Based on the positive ranges.
b. Test of ranges with Wilcoxon sign

Table 4.2.19 Results of the Wilcoxon test for the evolution of the number of painful days

In the chart 4.2.20 the representation of the data in bloxpot of the initial and final comparisons can be seen:

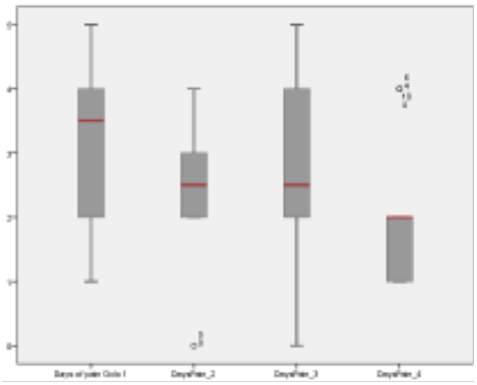


Table 4.2.20 Representation of the data in bloxpot of the initial and final number of painful days

4.2.8 Evolution of the number of days of analgesia use.

The number of days of use of analgesia at the beginning of the study was 3.1 (1.3) and at the end was 2.0 (1.1), the difference is statistically significant ($t=2.7$; $p<0.05$)

In tables 4.2.21 and 4.2.22 the results of the Student's t-test and the Wilcoxon test can be seen.

Related samples test

		Related differences					t	gl	Sig. (bilateral)
		Mean	Typical deviation.	Typical mean error	95% Confidence interval for the difference Lower	Upper			
Par 1	Days of analgesia Cycle 1 - AnalgDays_4	1.100	1.197	.379	.244	1.956	2.905	9	.017

Table 4.2.21 Results of the Student's t-test for the evolution of the number of painful days of analgesia use

Contrast statistics[b]

	AnalgDays_4 - Days of analgesia Cycle 1
Z	-2.209[a]
Asymptotic sig. (bilateral)	.027

a. Based on the positive ranges.

b. Test of ranges with Wilcoxon sign

Table 4.2.22 Results of the Wilcoxon test for the evolution of the number of painful days of analgesia use

In the chart 4.2.23 the representation of the data in bloxpot of the initial and final comparisons can be seen:

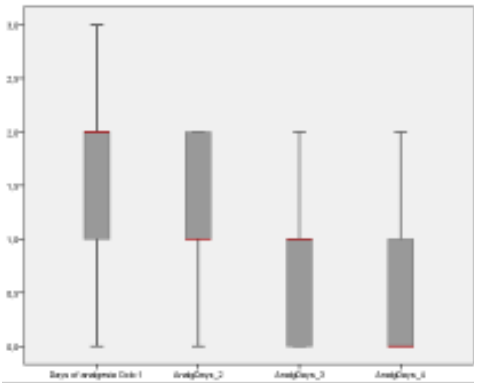


Table 4.2.23 Representation of the data in bloxpot of the initial and final number of days of analgesia use

4.2.9 Evolution of the number of days of abandonment of activities

The number of days of abandonment of normal activities due to pain at the beginning of the study was 1.4 (1.1) and at the end was 0.6 (1.1), the difference is not statistically significant ($t=2.2$; $p<0.05$)

In tables 4.2.24 and 4.2.25 the results of the Student's t-test and the Wilcoxon test can be seen.

Related samples test

		Related differences					t	gl	Sig. (bilateral)
		Mean	Typical deviation.	Typical mean error	95% Confidence interval for the difference Lower	Upper			
Par 1	Days need to abandon activities Cycle 1 - AbanAct_4	.800	1.135	.359	-.012	1.612	2.228	9	.053

Table 4.2.24 Results of the Student's t-test for the evolution of the number of painful days of abandonment of activities

Contrast statistics[b]

	AbanAct_4 - Days need to abandon activities Cycle 1
Z	-1.930[a]
Asymptotic sig. (bilateral)	.054

a. Based on the positive ranges.
b. Test of ranges with Wilcoxon sign

Table 4.2.25 Results of the Wilcoxon test for the evolution of the number of painful days of abandonment of activities

In the chart 4.2.26 the representation of the data in bloxpot of the initial and final comparisons can be seen:

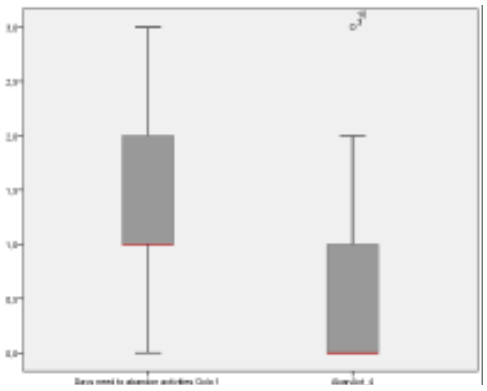


Table 4.2.26 Representation of the data in bloxpot of the initial and final number of days of abandonment of activities

4.2.10 Variations in menstruation and blood characteristics

For the analysis of the study results the characteristics of menstrual bleeding were also considered. In the table 4.2.27 a summary of the evolution of these characteristics from the beginning (Cycle 1) to the end (Cycle 2) can be seen.

TCM considers normal characteristics of menstruation (Maciocia, 1998) to be:

- Colour: bright red
- Quantity: one sanitary napkin or tampon every 3 hours
- Consistency: fluid
- No clots

To simplify the interpretation of the assessment of this data the number of improved and worsened characteristics for each participant was calculated. We can use the case of one participant as an example:

- The participant with code 10JN01 began the study with normal coloured menstrual blood (bright red) with no change at the end of the study. The quantity of menstrual blood was scant both at the beginning and end of the study, and therefore there was neither improvement nor worsening. At the beginning of the study the consistency of the blood was thick and at the end it was fluid, showing improvement in this aspect. At the beginning of the study there were red, medium sized clots and at the end there were no clots, this also being an improvement. If she had had small red clots this would also have been considered an improvement, however if at the end the clots were medium but dark this would have been considered a worsening.

The results were three participants with improvement in three characteristics, four participants with improvement in two characteristics, three participants with improvement in one characteristic and there were no participants that did not experience some kind of improvement.

Only two participants suffered worsening of any of the characteristics

It should be noted that nine of the participants had improvement in the quality or presence of clots.

		10JN01	18A02	11M01	18A03	13A01	25M01	16M01	20M01	10M01	20A01
COLOUR MENSTR	CYCLE 1	Bright red	Bright red	Pale-dark	Bright red	Bright red	Bright red	Bright red	Bright red	Pale, red	Pale
	CYCLE 4	Bright red	Pale-red-dark	Red-dark	Bright red	Bright red	Bright red	Bright red	Pale	Bright red	Bright red
QUANTITY	CYCLE 1	Scant	Abundant	Scant	Abundant	Normal	Normal	Abundant	Normal	Scant	Abundant
	CYCLE 4	Scant	Normal	Scant	Normal	Normal	Normal	Scant	Scant	Normal	Abundant
CONSISTENCY	CYCLE 1	Thick	Fluid	Fluid	With clots	Fluid	Fluid	Thick	With clots	Fluid	Thick
	CYCLE 4	Fluid	Fluid	Fluid	Fluid	Fluid	Fluid	Thick	Fluid	Fluid	Fluid
CLOTS	CYCLE 1	Red, med	Dark, med	Dark, small	Red, large	Red, small	Dark, med	Dark, large	Dark, large	Red, dark, small	Red, med
	CYCLE 4	No	Red, small	Dark, small	Red, med	No	Dark, small	Dark, med	Pale, small	Red, small	Red, small
Changes in clots		√	√	=	√	√	√	√	√	√	√
nº improved		√√	√√	√	√√√	√	√	√√	√√	√√√	√√√
nº worse			↓						↓↓		

Table 4.2.27 Evolution of the characteristics of menstrual bleeding

4.3 Findings

The analysis of the data shows that the predominant disharmony patterns in the participants were Qi stagnation (10), Qi/Xue vacuity (9) and Xue stasis (6).

The statistical analysis of the data shows that the improvement in the menstrual pain maximum, in the number of premenstrual symptoms, in the number of days with menstrual pain and in the number of days with use of analgesia are statistically significant. There was an improvement in the menstrual pain average, premenstrual pain and the number of days of abandonment of activities but these were not statistically significant.

As far as the analysis of the menstrual blood characteristics went, all participants experienced improvement, especially in the presence and characteristics of clots (9 out of 10).

Therefore the results obtained from the data analysis partially confirm the working hypothesis: Xiao Yao Wan is significantly effective ($p \leq 0.05$) for treatment of menstrual pain in primary dysmenorrhea (Xiao Yao Wan is significantly effective

($p \leq 0.05$) for treatment of maximum menstrual pain and reduces the number of **days** with pain in primary dysmenorrhea).

The results also partially confirm the **null hypothesis**: Xiao Yao Wan is not significantly effective ($p > 0.05$) for treatment of menstrual pain in primary dysmenorrhea (Xiao Yao Wan reduces average menstrual pain in primary dysmenorrhea, but is not significantly effective ($p > 0.05$)).

4.4 Summary

The analysis of the data of the study shows improvement in all menstrual characteristics, with some of these being statistically significant and others not.

The analysis of the results partially confirms the working hypothesis, showing that Xiao Yao Wan is significantly effective ($p \leq 0.05$) for treatment of maximum menstrual pain and reduces the number of days with pain in primary dysmenorrhea.

5. DISCUSSION AND CONCLUSIONS

5.1 Discussion

The results of the study seem to indicate that the modified Xiao Yao Wan formula is effective for treatment of menstrual and premenstrual pain and discomfort, although the sample is small and therefore further research is necessary.

All of the participants had improvement in one or more of the aspects investigated, but it is interesting to look closely at the two cases where less improvement of menstrual pain was noted.

The first case that stands out is that of a participant who suffered a two point increase in maximum pain. In cycle 1 (without treatment) she had 4 days of continuous pain with a pain maximum of 6 and a pain average of 3.75. In cycle 4 she had a day with a pain intensity of 10. In the interview it was detected that this pain in the last cycle was felt during approximately 1 hour at night having not felt pain at any other moment during that entire menstrual period. It would seem then that the pain improvement was important however this is not reflected accurately in the data analysis. In spite of this it should also be noted that this participant experienced the greatest worsening of

menstrual bleeding characteristics, beginning with blood bright red and ending with pale blood, beginning with normal quantity and ending with scant bleeding.

The analysis of the second case provided different data and conclusions. This participant had an improvement in pain levels, but less than that of the rest of the participants. In cycle 1 she had 3 days of pain, with an average intensity of 8.3 and a maximum intensity of 10. In cycle 4 she had 4 days of pain (1 more) with an average intensity of 5.5 (lower) and a maximum intensity of 8 (also lower). Therefore this case presented slight improvement. Although this participant presented signs and symptoms of Qi stagnation and Qi/Xue vacuity (for which Xiao Yao Wan is indicated) she also presented important signs and symptoms of both Yin and Yang Kidney vacuity, and it would seem that the noteworthy presence of Kidney vacuity may be one of the reasons that the reduction of pain and discomfort was less than in the rest of the cases.

5.2 Conclusions and implications

- The modified Xiao Yao Wan formula seems to be effective for menstrual pain, reducing significantly ($p<0.05$) the number of days with pain, the menstrual pain maximum, the taking of analgesics and premenstrual discomfort.

- Modified Xiao Yao Wan seems to modify the characteristics of menstrual bleeding, bringing them closer to the ideal according to TCM

- Menstrual pain and discomfort seem to be related to the characteristics of menstrual bleeding as TCM affirms

- The most frequent disharmony patterns that cause dysmenorrhea seem to be Qi stagnation, Qi/Xue vacuity and Xue stasis

- Modified Xiao Yao Wan seems to be most effective for treating menstrual pain and discomfort when the predominant disharmony patterns are Qi stagnation, Qi/Xue vacuity and Xue stasis

- Modified Xiao Yao Wan seems to be most effective for treating menstrual pain and discomfort when there is premenstrual discomfort

- Modified Xiao Yao Wan may well be a safe and effective alternative to treatment of menstrual pain de with CM

5.3 Recommendations for future research

Further work is required to assess the contributions of CHM for treatment of dysmenorrhea using scientific methods. The RCT's are the most recognised studies in terms of the range of scientific evidence and therefore it is recommendable to carry out studies using this design. Currently there is a tendency to question the ethics of the use of placebo as a control technique (Zaslawski, 2010) and therefore it is necessary to go deeper into this aspect in order to guarantee maximum respect for human rights.

For future research it would be recommendable to begin the process validating the proposed questionnaire from this study or another questionnaire that responds to the needs and characteristics of TCM.

It would also be recommendable to add a post-treatment follow up phase to the study in order to assess the perdurability of the effects of the treatment.

It would be recommendable to carry out studies with treatments during the entire menstrual cycle and not limited to some specific days of the cycle.

Finally, would be recommendable to establish a method of control over the administration of the treatment and the taking of analgesics.

5.4 Summary

The results of the study seem to show the effectiveness of treatment of menstrual and premenstrual discomfort in PD with the modified Xiao Yao Wan formula, especially when the predominant disharmony patterns are Qi stagnation, Qi/Xue vacuity and/or el Xue stasis. The study seems to show these as the main TCM disharmony patterns causing dysmenorrhea. There also seems to be a relationship between the characteristics of the menstrual bleeding and the intensity and duration of both menstrual and premenstrual pain.

Further work is required to evaluate the contributions of CHM for dysmenorrhea using scientific methods.

REFERENCES

A. Haywood, P.Slade y H.King (2002) 'Assessing the assessment measures for menstrual cycle symptoms□: A guide for researchers and clinicians', *Jornal of Psychosomatic Research*, 52, [en línea] Available from: https://secure.uoc.edu/science/article/pii/,DanaInfo=www.sciencedirect.com+S0022399902002970 (Accedido 22 Agosto 2011).

Beers, Mark H., Berkow, Robert y Merck (1999) *El Manual Merck de diagnóstico y tratamiento*, Elsevier - Health Sciences Division.

Buela-Casal, Gualberto, Caballo, Vicente E. y Sierra, J. Carlos (1996) *Manual de evaluación en psicología clínica y de la salud*, Siglo XXI de España Editores.

Cox, Daniel J. (1977) 'Menstrual symptom questionnaire: further psychometric evaluation', *Behaviour Research and Therapy*, 15(6), págs. 506-508, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/0005796777900092 (Accedido 27 Agosto 2011).

Chang, Il-Moo (2004) 'Initiative for Developing Evidence-based Standardization of Traditional Chinese Medical Therapy in the Western Pacific Region of the World Health Organization: May 27-29, 2004, Seoul Korea', *eCAM*, 1(3), págs. 337-341, [en línea] Available from: http://ecam.oxfordjournals.org (Accedido 31 Octubre 2010).

Cheng, Jui-Fen, Lu, Zxy-yann Jane, Su, Yi-Chang, Chiang, Li-Chi y Wang, Ruey-Yun (2008) 'A traditional Chinese herbal medicine used to treat dysmenorrhoea among Taiwanese women', *Journal of Clinical Nursing*, 17(19), págs. 2588-2595, [en línea] Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2702.2008.02382.x/full (Accedido 31 Octubre 2010).

Chesney, M. A y Tasto, D. L (1975) 'The development of the menstrual symptom questionnaire', *Behaviour Research and Therapy*, 13(4), págs. 237–244.

Choi, P Y y Salmon, P (1995) 'Symptom changes across the menstrual cycle in competitive sportswomen, exercisers and sedentary women', *The British Journal of Clinical Psychology / the British Psychological Society*, 34 (Pt 3), págs. 447-460, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/8845783 (Accedido 23 Agosto 2011).

DeVellis, Robert F. (2003) *Scale development: theory and applications*, SAGE.

Dmitrovic, Romana, Peter, Branimir, Cvitkovic-Kuzmic, Andrea, Strelec, Mihajlo y Kereshi, Tibor (2003) 'Severity of symptoms in primary dysmenorrhea--a doppler study', *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 107(2), págs. 191-194, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/S030121150200372X.

El Centro Nacional de la Medicina Complementaria y Alternativa (s.f.) 'Los estudios clinicos y la medicina complementaria y alternativa [NCCAM]', [en línea]

Available from: http://nccam.nih.gov/health/espanol/estudiosclinicos/ (Accedido 26 Marzo 2011).

Endicott, J, Nee, J, Cohen, J y Halbreich, U (1986) 'Premenstrual changes: patterns and correlates of daily ratings', *Journal of Affective Disorders*, 10(2), págs. 127-135, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/2941469 (Accedido 23 Agosto 2011).

Ferreira-Valente, Maria Alexandra, Pais-Ribeiro, José Luís y Jensen, Mark P. (2011) 'Validity of four pain intensity rating scales', *PAIN*, [en línea] Available from: https://secure.uoc.edu/science/article/pii/,DanaInfo=www.sciencedirect.com+S0304395911004453 (Accedido 22 Agosto 2011).

Flaws, Bob (1997) *Handbook of menstrual disease in Chinese medicine*, Blue Poppy Press.

Geng, Shan Shan, Li, Hai Zhong, Wu, Xiao Ke, Dang, Jie Ming, et al. (2010) 'Effect of Wujijing Oral Liquid on menstrual disturbance of women', *Journal of Ethnopharmacology*, 128(3), págs. 649-653, [en línea] Available from: http://www.sciencedirect.com/science/article/B6T8D-4Y34V41-6/2/3f282428b22d5608536e540ede488c6c.

Halbreich, Uriel y Endicott, Jean (1985) 'Methodological issues in studies of premenstrual changes', *Psychoneuroendocrinology*, 10(1), págs. 15-32, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/0306453085900368 (Accedido 4 Septiembre 2011).

Hawes, Ellen y Oei, Tian P.S. (1992) 'The menstrual distress questionnaire: Are the critics right?', *Current Psychology*, 11(3), pág. 264, [en línea] Available from: http://search.ebscohost.com/login.aspx?direct=true&AuthType=ip,cookie,url,uid&db=aph&AN=9603201718&site=ehost-live.

Howard, Fred M. (2000) *Pelvic pain: diagnosis and management*, Lippincott Williams & Wilkins.

Jang, Jun-Bock, Yoon, Young-Jin, Park, Jung-Hyun, Jeong, Haeng-Gyu, et al. (2009) 'Therapeutic effects of Chiljehyangbuhwan on primary dysmenorrhea: A randomized, double blind, placebo-controlled study', *Complementary Therapies in Medicine*, 17(3), págs. 123-130, [en línea] Available from: http://www.sciencedirect.com/science/article/B6WCS-4TKXD61-1/2/e05378c907e4ea8ce99211d7087575f3.

Kennedy, S, Jin, X, Yu, H, Zhong, S, et al. (2006) 'Randomized controlled trial assessing a traditional Chinese medicine remedy in the treatment of primary dysmenorrhea', *Fertility and Sterility*, 86(3), págs. 762-764, [en línea] Available from: http://www.fertstert.org/article/S0015-0282(06)00957-5/abstract (Accedido 31 Octubre 2010).

Larroy, C (2002) 'Comparing Visual-Analog and Numeric Scales for Assessing Menstrual Pain', *Behavioral Medicine*, Vol. 27 Issue 4, p179, 3p, [en línea]

Available from: https://secure.uoc.edu/ehost/,DanaInfo=web.ebscohost.com+detail?sid=ddfe1c21-f6c8-48d8-9026-cdd8e81c1b7d%40sessionmgr13&vid=1&hid=12&bdata=JkF1dGhUeXBlPWlwLGNvb2tpZSx1cmwsdWlkJnNpdGU9ZWhvc3QtbGl2ZQ%3d%3d#db=aph&AN=7239629 (Accedido 22 Agosto 2011).

Larroy, C, C., Tabernero, J. A y Alegría Gil, Ana (2001) 'Factorización de los síntomas no dolor osos de la dismenorrea primaria y su cambio a lo la rgo de la edad: estudio en la Comunidad de Madrid Factor structure and evolution of painless', *Clínica y Salud*, vol. 12, núm. 2, 2001, pp. 253-269.

Larroy, C, Meseguer, C y Crespo (2001) 'Dismenorrea funcional en la Comunidad Autónoma de Madrid: estudio de la prevalencia en función de la edad (Revista de la Sociedad Española del Dolor (SED))', *Rev Soc Esp Dolor 8 (2001);1□:11 - 22*, [en línea] Available from: http://www.revista.sedolor.es/articulo.php?ID=207 (Accedido 14 Noviembre 2010).

M. S. Serrano - Atero, J. Caballero** (2002) 'Valoración del dolor (I)', *R e v. Soc. Esp. Dolor*.

Maciocia, Giovanni (1998) *Obstetrics and gynecology in Chinese medicine*, Elsevier Health Sciences.

Martín Arribas, M.C. (2004) 'Diseño y validaciónde cuestionarios', *Matronas Profesión*, vol. 5(17): 23-29.

Martínez, Lorenzo Abad y López, Lorenzo Abad Martínez, Rafael Comino Delgado, Guillermo (López García) (2004) *Obstetricia y ginecología*, Editorial Ariel.

Michelle L Proctor and Cynthia M Farquhar (2006) 'Dysmenorrhoea', *clinical evidence*.

Moos, udolph H. (1968) 'The Development of a Menstrual Distress Questionnaire', *Psychosomatic Medicine*, 30(6), págs. 853-867, [en línea] Available from: http://www.psychosomaticmedicine.org/cgi/content/abstract/30/6/853.

Morales, Alvaro Ruiz y Zárate, Luis Enrique Morillo (2004) *Epidemiología clínica: investigación clínica aplicada*, Ed. Médica Panamericana.

Norvell, Kristine Turner, Gaston-Johansson, Fannie y Fridh, Gerd (1987) 'Remembrance of labor pain: how valid are retrospective pain measurements?', *Pain*, 31(1), págs. 77-86, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/030439598790008X.

Palacios (2000) *Salud y Medicina de la mujer*, Elsevier España.

Peilin, Sun (2002) *The treatment of pain with Chinese herbs and acupuncture*, Elsevier Health Sciences.

Price, D D, McGrath, P A, Rafii, A y Buckingham, B (1983) 'The validation of visual analogue scales as ratio scale measures for chronic and experimental pain', *Pain*, 17(1), págs. 45-56, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/6226917 (Accedido 27 Marzo 2011).

Prieto, José Lombardía (2007) *Ginecología y obstetricia: manual de consulta rápida*, Ed. Médica Panamericana.

Proctor, Michelle y Farquhar, Cynthia (2006) 'Diagnosis and management of dysmenorrhoea', *BMJ*, 332(7550), págs. 1134 -1138, [en línea] Available from: http://www.bmj.com/content/332/7550/1134.short (Accedido 1 Noviembre 2010).

Riley, Dagmar (2003) *Treating pain with traditional Chinese medicine*, Paradigm.

Rosier, Elisa M., Iadarola, Michael J. y Coghill, Robert C. (2002) 'Reproducibility of pain measurement and pain perception', *Pain*, 98(1-2), págs. 205-216, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/S0304395902000489.

Ross, C., Coleman, G. y Stojanovska, C. (2003) 'Factor structure of the modified Moos Menstrual Distress Questionnaire: Assessment of prospectively reported follicular, menstrual and premenstrual symptomatology - Journal of Psychosomatic Obstetrics and Gynecology | HighBeam Research', *J Psychosom Obstet Gyneco*, 24:163-174, [en línea] Available from: http://www.highbeam.com/doc/1P3-471812521.html (Accedido 22 Agosto 2011).

Smith, Caroline A., Crowther, Caroline A., Petrucco, Oswald, Beilby, Justin y Dent, Hannah (2010) 'Acupuncture to Treat Primary Dysmenorrhea in Women: A Randomized Controlled Trial', *eCAM*, pág. nep239, [en línea] Available from: http://ecam.oxfordjournals.org/cgi/content/abstract/nep239v1 (Accedido 31 Octubre 2010).

Smith, Roger P. (2004) *Netter obstetricia, ginecología y salud de la mujer*, Elsevier España.

Stephenson, Laura A., Denney, Douglas R. y Aberger, Edward W. (1983) 'Factor structure of the menstrual symptom questionnaire: Relationship to oral contraceptives, neuroticism and life stress', *Behaviour Research and Therapy*, 21(2), págs. 129-135, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/0005796783901572 (Accedido 5 Septiembre 2011).

Sundell, G, Milsom, I y Andersch, B (1990) 'Factors influencing the prevalence and severity of dysmenorrhoea in young women', *British Journal of Obstetrics and Gynaecology*, 97(7), págs. 588-594, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/2390501 (Accedido 6 Febrero 2011).

Taylor, J. W (1979) 'The timing of menstruation ‐ related symptoms assessed by a daily symptom rating scale', *Acta Psychiatrica Scandinavica*, 60(1), págs. 87-105, [en línea] Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1600-0447.1979.tb00268.x/abstract (Accedido 23 Agosto 2011).

Terry, Rohini H., Niven, Catherine A., Brodie, Eric E., Jones, Ray B. y Prowse, Morag A. (2008) 'Memory for Pain? A Comparison of Nonexperiential Estimates and Patients' Reports of the Quality and Intensity of Postoperative Pain', *The Journal of Pain*, 9(4), págs. 342-349, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/S1526590007010206.

Tseng, Ying-Fen, Chen, Chung-Hey y Yang, Yi-Hsin (2005) 'Rose Tea for Relief of Primary Dysmenorrhea in Adolescents: A Randomized Controlled Trial in Taiwan', *Journal of Midwifery & Women's Health*, 50(5), pág. e51-e57, [en línea] Available from: http://www.sciencedirect.com/science/article/B6W6R-4H2F7JB-1C/2/8f9a7b0cb082c32cb4588e51f80b2914.

Villoria, Clemente Muriel (2007) *Dolor Cronico - Diagnóstico, clínica y tratamiento*, Arán Ediciones.

Webster, Sandra K., Martin, Harry J., Uchalik, Deborah y Gannon, Linda (1979) 'The menstrual symptom questionnaire and spasmodic/congestive dysmenorrhea: Measurement of an invalid construct', *Journal of Behavioral Medicine*, 2(1), págs. 1-19, [en línea] Available from: http://www.springerlink.com/content/n535034p7676702g/ (Accedido 1 Noviembre 2010).

Weissman, Alicia M., Hartz, Arthur J., Hansen, Michael D. y Johnson, Susan R. (2004) 'The natural history of primary dysmenorrhoea: a longitudinal study', *BJOG: An International Journal of Obstetrics and Gynaecology*, 111(4), págs. 345-352, [en línea] Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1471-0528.2004.00090.x/pdf (Accedido 6 Febrero 2011).

Wildman, Beth G. y White, Pamela A. (1986) 'Assessment of dysmenorrhea using the menstrual symptom questionnaire: Factor structure and validity', *Behaviour Research and Therapy*, 24(5), págs. 547-551, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/0005796786900355 (Accedido 27 Agosto 2011).

Wong, Chooi L, Farquhar, Cindy, Roberts, Helen y Proctor, Michelle (2009) 'Oral contraceptive pill for primary dysmenorrhoea', En The Cochrane Collaboration y Wong, C. L. (eds.), *Cochrane Database of Systematic Reviews*, Chichester, UK, John Wiley & Sons, Ltd, [en línea] Available from: http://www2.cochrane.org/reviews/en/ab002120.html (Accedido 6 Febrero 2011).

Xiaoshu Zhu, Michelle Proctor, Alan Bensoussan, Emily Wu y Caroline A Smith (2010) 'Chinese herbal medicine for primary dysmenorrhoea', [en línea] Available from: http://onlinelibrary.wiley.com/o/cochrane/clsysrev/articles/CD005288/frame.html (Accedido 19 Diciembre 2010).

Yarnitsky, David, Sprecher, Elliot, Zaslansky, Ruth y Hemli, Jeshayachu A. (1996) 'Multiple session experimental pain measurement', *Pain*, 67(2-3), págs. 327-333, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/0304395996031107 (Accedido 3 Septiembre 2011).

Yeh, Lan Lan Liang, Liu, Jah-Yao, Lin, Kao-Si, Liu, Yu-Shen, et al. (2007) 'A Randomised Placebo-Controlled Trial of a Traditional Chinese Herbal Formula in the Treatment of Primary Dysmenorrhoea', *PLoS ONE*, 2(8), pág. e719, [en línea] Available from: http://dx.doi.org/10.1371/journal.pone.0000719 (Accedido 31 Octubre 2010).

Zaslawski, Christopher (2010) 'Ethical Considerations for Acupuncture and Chinese Herbal Medicine Clinical Trials: A Cross-cultural Perspective', *eCAM*, 7(3), págs. 295-301, [en línea] Available from: http://ecam.oxfordjournals.org/cgi/content/abstract/7/3/295 (Accedido 31 Octubre 2010).

Zhang, Zhongjing (1987) *Synopsis of prescriptions of the golden chamber (jinkui yaolue fanglun)*, New World Press.

Zuo Yanfu, Tan Yong y He Guizxiang (2006) *Gynecology of traditional chinese medicine*, A Newly Compiled Practical English-Chinese Library of Traditional Chinese Medicine, Publishing House of Shanghai University of Traditional Chinese Medicine.

Zuo, Yanfu (2003) *A newly compiled practical English-Chinese library of traditional Chinese medicine*, Shanghai University of Traditional Chinese Medicine.

BIBLIOGRAPHY

A. Haywood, P.Slade y H.King (2002) 'Assessing the assessment measures for menstrual cycle symptoms□: A guide for researchers and clinicians', *Jornal of Psychosomatic Research*, 52, [en línea] Available from: https://secure.uoc.edu/science/article/pii/,DanaInfo=www.sciencedirect.com+S0022399902002970 (Accedido 22 Agosto 2011).

Agarwal, Anupriya y Venkat, Annapoorna (2009) 'Questionnaire Study on Menstrual Disorders in Adolescent Girls in Singapore', *Journal of Pediatric and Adolescent Gynecology*, 22(6), págs. 365-371, [en línea] Available from: http://www.sciencedirect.com/science/article/B6W68-4WWPFYV-1/2/02aea33263581cdf5210d2d418cea07d.

Aisong, Guo y Qingyi, Meng (2008) 'Acupuncture Combined with Spinal Tui Na for Treatment of Primary Dysmenorrhea in 30 Cases', *Journal of Traditional Chinese Medicine*, 28(1), págs. 7-9, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/S0254627208600035.

Alaettin Unsal, Unal Ayranci, Mustafa Tozun, Gul Arslan y Elif Calik (2010) 'Prevalence of dysmenorrhea and its effect on quality of life among a group of female university students', [en línea] Available from: http://informahealthcare.com/doi/abs/10.3109/03009730903457218 (Accedido 31 Octubre 2010).

Alonso, Carmen y Coe, Christopher L. (2001) 'Disruptions of social relationships accentuate the association between emotional distress and menstrual pain in young women.', *Health Psychology*, 20(6), págs. 411-416, [en línea] Available from: https://secure.uoc.edu/ehost/,DanaInfo=web.ebscohost.com+detail?sid=e928a1f4-d211-48d3-8ec9-4bbac3c8d22f%40sessionmgr10&vid=1&hid=7&bdata=JkF1dGhUeXBlPWlwLGNvb2tpZSx1cmwsdWlkJnNpdGU9ZWhvc3QtbGl2ZQ%3d%3d#db=pdh&AN=hea-20-6-411 (Accedido 4 Septiembre 2011).

Allais, G, Voghera, D, De Lorenzo, C, Mana, O y Benedetto, C (2000) 'Access to databases in complementary medicine', *Journal of Alternative and Complementary Medicine (New York, N.Y.)*, 6(3), págs. 265-274, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/10890337 (Accedido 18 Diciembre 2010).

Anon (2006) 'Calidad de un ensayo clínico', *e-Digitalis*.

Anon (s.f.) 'Cochrane Handbook for Systematic Reviews of Interventions', [en línea] Available from: http://www.mrc-bsu.cam.ac.uk/cochrane/handbook/index.htm#chapter_5/5_1_1_rationale_for_well-formulated_questions.htm (Accedido 22 Abril 2011a).

Anon (s.f.) 'Construcción, validación y resultados de un cuestionario sobre factores relacionados con el uso de los protocolos de fisioterapia - Editorial Elsevier', [en línea] Available from: http://www.elsevier.es/en/node/2024910 (Accedido 23 Agosto 2011b).

Anon (s.f.) 'Las revisiones sistemáticas', [en línea] Available from: http://www.fisterra.com/guias2/fmc/rrss.asp (Accedido 18 Diciembre 2010c).

Anon (s.f.) 'pub79_ThemcGillpainquestionairre.pdf', [en línea] Available from: http://heblab.research.yale.edu//pub_pdf/pub79_ThemcGillpainquestionairre.pdf (Accedido 23 Agosto 2011d).

Baker, Fiona C., Driver, Helen S., Rogers, Geoffrey G., Paiker, Janice y Mitchell, Duncan (1999) 'High nocturnal body temperatures and disturbed sleep in women with primary dysmenorrhea', *Am J Physiol Endocrinol Metab*, 277(6), págs. E1013-1021, [en línea]

Available from: http://ajpendo.physiology.org/cgi/content/abstract/277/6/E1013 (Accedido 1 Noviembre 2010).

Banikarim, Chantay, Chacko, Mariam R. y Kelder, Steve H. (2000) 'Prevalence and Impact of Dysmenorrhea on Hispanic Female Adolescents', *Archives of Pediatrics Adolescent Medicine*, 154(12), págs. 1226-1229, [en línea] Available from: http://archpedi.ama-assn.org/cgi/content/abstract/154/12/1226.

Beers, Mark H., Berkow, Robert y Merck (1999) *El Manual Merck de diagnóstico y tratamiento*, Elsevier - Health Sciences Division.

Bensky, Dan, Clavey, Steven y Stöger, Erich (2004) *Chinese herbal medicine: materia medica*, Eastland Press.

Bone, Kerry (2005) 'Phytotherapy for Pain Management in Dysmenorrhea.', *Townsend Letter for Doctors & Patients*, (258), págs. 57-59.

Brotto, Lori A., Krychman, Michael y Jacobson, Pamela (2008) 'Eastern Approaches for Enhancing Women's Sexuality: Mindfulness, Acupuncture, and Yoga (CME)', *Journal of Sexual Medicine*, 5(12), págs. 2741-2748, [en línea] Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1743-6109.2008.01071.x/abstract (Accedido 1 Noviembre 2010).

Brown, D. (1997) 'Management of Primary Dysmenorrhea with a Kampo Medicine.', *Quarterly Review of Natural Medicine*, pág. 283.

Buela-Casal, Gualberto, Caballo, Vicente E. y Sierra, J. Carlos (1996) *Manual de evaluación en psicología clínica y de la salud*, Siglo XXI de España Editores.

Cohen, Michael H. (2000) 'The Role of Informed Consent in the Delivery of Complementary and Alternative Medical Therapies', *Complementary Health Practice Review*, 6(1), págs. 21 -28, [en línea] Available from: http://chp.sagepub.com/content/6/1/21.short (Accedido 1 Noviembre 2010).

Collins, Nancy H., Lessey, Elizabeth C., DuSell, Carolyn D., McDonnell, Donald P., et al. (2009) 'Characterization of Antiestrogenic Activity of the Chinese Herb, Prunella vulgaris, Using In Vitro and In Vivo (Mouse Xenograft) Models', *Biology of Reproduction*, 80(2), págs. 375 -383, [en línea] Available from: http://www.biolreprod.org/content/80/2/375.abstract (Accedido 31 Octubre 2010).

Cox, Daniel J. (1977) 'Menstrual symptom questionnaire: further psychometric evaluation', *Behaviour Research and Therapy*, 15(6), págs. 506-508, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/0005796777900092 (Accedido 27 Agosto 2011).

Chang, Anne M., Chau, Janita P.C. y Holroyd, Eleanor (1999) 'Translation of questionnaires and issues of equivalence', *Journal of Advanced Nursing*, 29(2), págs. 316-322, [en línea] Available from: https://secure.uoc.edu/ehost/,DanaInfo=web.ebscohost.com+detail?sid=dd55d6f2-e865-46f0-a433-706868613f6a%40sessionmgr15&vid=1&hid=10&bdata=JkF1dGhUeXBlPWlwLGNvb2tpZSx1cmwsdWlkJnNpdGU9ZWhvc3QtbGl2ZQ%3d%3d#db=aph&AN=5866778 (Accedido 22 Agosto 2011).

Chang, Il-Moo (2004) 'Initiative for Developing Evidence-based Standardization of Traditional Chinese Medical Therapy in the Western Pacific Region of the World Health Organization: May 27-29, 2004, Seoul Korea', *eCAM*, 1(3), págs. 337-341, [en línea] Available from: http://ecam.oxfordjournals.org (Accedido 31 Octubre 2010).

Chantler, Ingrid, Mitchell, Duncan y Fuller, Andrea (2009) 'Diclofenac Potassium Attenuates Dysmenorrhea and Restores Exercise Performance in Women With Primary

Dysmenorrhea', *The Journal of Pain*, 10(2), págs. 191-200, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/S1526590008007335.

Cheng, Jui-Fen, Lu, Zxy-yann Jane, Su, Yi-Chang, Chiang, Li-Chi y Wang, Ruey-Yun (2008) 'A traditional Chinese herbal medicine used to treat dysmenorrhoea among Taiwanese women', *Journal of Clinical Nursing*, 17(19), págs. 2588-2595, [en línea] Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2702.2008.02382.x/full (Accedido 31 Octubre 2010).

Chesney, M. A y Tasto, D. L (1975) 'The development of the menstrual symptom questionnaire', *Behaviour Research and Therapy*, 13(4), págs. 237–244.

Cho, Seung-Hun y Hwang, Eui-Whan (2010) 'Acupressure for primary dysmenorrhoea: A systematic review', *Complementary Therapies in Medicine*, 18(1), págs. 49-56, [en línea] Available from: http://www.sciencedirect.com/science/article/B6WCS-4XT2CKS-1/2/0b2f0501148ac398e52da1e34729796b.

Cho, S-H y Hwang, E-W (2010) 'Acupuncture for primary dysmenorrhoea: a systematic review', *BJOG: An International Journal of Obstetrics & Gynaecology*, 117(5), págs. 509-521, [en línea] Available from: https://secure.uoc.edu/doi/10.1111/j.1471-0528.2010.02489.x/,DanaInfo=onlinelibrary.wiley.com+abstract (Accedido 3 Noviembre 2010).

Choi, Jungmi, Baek, Ji Hyun, Noh, Jihae, Kim, Ji Sun, et al. (2011) 'Association of seasonality and premenstrual symptoms in Bipolar I and Bipolar II disorders', *Journal of Affective Disorders*, 129(1-3), págs. 313-316, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/S0165032710005124.

Choi, P Y y Salmon, P (1995) 'Symptom changes across the menstrual cycle in competitive sportswomen, exercisers and sedentary women', *The British Journal of Clinical Psychology / the British Psychological Society*, 34 (Pt 3), págs. 447-460, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/8845783 (Accedido 23 Agosto 2011).

Chou, Patsy B, Morse, Carol A y Xu, Hong (2008) 'A controlled trial of Chinese herbal medicine for premenstrual syndrome', *Journal of Psychosomatic Obstetrics and Gynaecology*, 29(3), págs. 185-192, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/18608825 (Accedido 7 Septiembre 2011).

Dandenell, Lars‐Otto, Lalos, Othon, Lisciak, Jan, Sandström, Bo, et al. (1979) 'CLINICAL EXPERIENCE OF NAPROXEN IN THE TREATMENT OF PRIMARY DYSMENORRHEA', *Acta Obstetricia et Gynecologica Scandinavica*, 58(S87), págs. 95-100, [en línea] Available from: http://onlinelibrary.wiley.com/doi/10.3109/00016347909157800/abstract (Accedido 3 Septiembre 2011).

Daniels, J. P. y Khan, K. S. (2010) 'Chronic pelvic pain in women', *BMJ*, 341(oct05 2), pág. c4834-c4834, [en línea] Available from: http://www.bmj.com/content/341/bmj.c4834.full?sid=587c28bd-ba9f-48d6-b0d2-1de79c43dd88 (Accedido 1 Noviembre 2010).

Dawood, M. Yusoff y Huang, Jaou-Chen (1998) 'Uterine vascular function and menstruction', *Current Obstetrics & Gynaecology*, 8(2), págs. 66-72, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/S0957584798800176.

Dawood, M. Yusoff y Khan-Dawood, Firyal S. (2007) 'Differential suppression of menstrual fluid prostaglandin F2a, prostaglandin E2, 6-keto prostaglandin F1a and thromboxane B2 by suprofen in women with primary dysmenorrhea', *Prostaglandins & Other Lipid Mediators*, 83(1-2), págs. 146-153, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/S109888230600164X.

Dawood, M.Yusoff (1993) 'Dysmenorrhea', *Current Obstetrics & Gynaecology*, 3(4), págs. 219-224, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/095758479390042N.

Deng, Hai-xia, Zhu, Nan-sun y Wang, Cai-wen (2003) 'Effect of jiawei mojie tablet on plasma oxytocin level in patients with primary dysmenorrhea in menstrual period', *Zhongguo Zhong Xi Yi Jie He Za Zhi Zhongguo Zhongxiyi Jiehe Zazhi = Chinese Journal of Integrated Traditional and Western Medicine / Zhongguo Zhong Xi Yi Jie He Xue Hui, Zhongguo Zhong Yi Yan Jiu Yuan Zhu Ban*, 23(5), págs. 354-356, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/12800418 (Accedido 31 Octubre 2010).

DeVellis, Robert F. (2003) *Scale development: theory and applications*, SAGE.

Dmitrovic, Romana, Peter, Branimir, Cvitkovic-Kuzmic, Andrea, Strelec, Mihajlo y Kereshi, Tibor (2003) 'Severity of symptoms in primary dysmenorrhea--a doppler study', *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 107(2), págs. 191-194, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/S030121150200372X.

Durain, Dawn (Noviembre) 'Primary dysmenorrhea: Assessment and management update', *Journal of Midwifery & Women's Health*, 49(6), págs. 520-528, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/S1526952304003903.

Ebenezar, Kesavarao K y Smith, Francine G (2007) 'Prostaglandins in the patent literature', *Expert Opinion on Therapeutic Patents*, 17(9), págs. 1131-1145, [en línea] Available from: http://informahealthcare.com/doi/abs/10.1517/13543776.17.9.1131.

Eccles, Nyjon K. (2005) 'A Randomized, Double-Blinded, Placebo-Controlled Pilot Study to Investigate the Effectiveness of a Static Magnet to Relieve Dysmenorrhea', *Journal of Alternative and Complementary Medicine*, 11(4), págs. 681-687, [en línea] Available from: http://web.ebscohost.com.ezproxy.wales.ac.uk:2048/ehost/delivery?vid=3&hid=110&sid=1cdba16c-89db-41e4-8e8d-7450884cf101%40sessionmgr114 (Accedido 1 Noviembre 2010).

El Centro Nacional de la Medicina Complementaria y Alternativa (s.f.) 'Los estudios clinicos y la medicina complementaria y alternativa [NCCAM]', [en línea] Available from: http://nccam.nih.gov/health/espanol/estudiosclinicos/ (Accedido 26 Marzo 2011).

Endicott, J, Nee, J, Cohen, J y Halbreich, U (1986) 'Premenstrual changes: patterns and correlates of daily ratings', *Journal of Affective Disorders*, 10(2), págs. 127-135, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/2941469 (Accedido 23 Agosto 2011).

Fernandez, N, Mear, I, Moos, R y Johannes, EJ (Noviembre) 'PIH22 LINGUISTIC VALIDATION OF THE MENSTRUAL DISTRESS QUESTIONNAIRE (MDQ) IN AN INTERNATIONAL STUDY FOR A NEW COMBINED ORAL CONTRACEPTIVE PILL', *Value in Health*, 9(6), pág. A259, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/S1098301510633803.

Ferreira-Valente, Maria Alexandra, Pais-Ribeiro, José Luís y Jensen, Mark P. (2011) 'Validity of four pain intensity rating scales', *PAIN*, [en línea] Available from: https://secure.uoc.edu/science/article/pii/,DanaInfo=www.sciencedirect.com+S0304395911004453 (Accedido 22 Agosto 2011).

Finney-Brown, Tessa (2009) 'Reviews of articles on medicinal herbs.', *Australian Journal of Medical Herbalism*, 21(3), págs. 79-81.

Flaws, Bob (1997) *Handbook of menstrual disease in Chinese medicine*, Blue Poppy Press.

Flaws, Bob (1996) 'The TCM Acupuncture Treatment of Dysmenorrhea.', *Oriental Medicine Journal*, 5(1), pág. 58.

Gath, D, Osborn, M, Bungay, G, Iles, S, et al. (1987) 'Psychiatric disorder and gynaecological symptoms in middle aged women: a community survey.', *British Medical Journal (Clinical research ed.)*, 294(6566), págs. 213 -218, [en línea] Available from: http://www.bmj.com/content/294/6566/213.abstract (Accedido 1 Noviembre 2010).

Geirsson, Reynir Tómas (2008) 'A new uterus, a new beginning.', *Acta Obstetricia & Gynecologica Scandinavica*, 87(11), págs. 1095-1096, [en línea] Available from: http://search.ebscohost.com/login.aspx?direct=true&AuthType=ip,cookie,url,uid&db=aph&AN=35295100&site=ehost-live.

Geng, Shan Shan, Li, Hai Zhong, Wu, Xiao Ke, Dang, Jie Ming, et al. (2010) 'Effect of Wujijing Oral Liquid on menstrual disturbance of women', *Journal of Ethnopharmacology*, 128(3), págs. 649-653, [en línea] Available from: http://www.sciencedirect.com/science/article/B6T8D-4Y34V41-6/2/3f282428b22d5608536e540ede488c6c.

Gonda, X., Telek, T., Juhsz, G., Lazary, J., et al. (2008) 'Patterns of mood changes throughout the reproductive cycle in healthy women without premenstrual dysphoric disorders', *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 32(8), págs. 1782-1788, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/S0278584608002327.

Halbreich, Uriel y Endicott, Jean (1985) 'Methodological issues in studies of premenstrual changes', *Psychoneuroendocrinology*, 10(1), págs. 15-32, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/0306453085900368 (Accedido 4 Septiembre 2011).

Hawes, Ellen y Oei, Tian P.S. (1992) 'The menstrual distress questionnaire: Are the critics right?', *Current Psychology*, 11(3), pág. 264, [en línea] Available from: http://search.ebscohost.com/login.aspx?direct=true&AuthType=ip,cookie,url,uid&db=aph&AN=9603201718&site=ehost-live.

He, Dong-Yi y Dai, Sheng-Ming (s.f.) 'Anti-Inflammatory and Immunomodulatory Effects of Paeonia Lactiflora Pall., a Traditional Chinese Herbal Medicine', 2.

Health, National Center for Complementary and Alternative Medicine National Institutes of (2008) 'Paying for Complementary and Alternative Medicine Treatment: Information for Patients', *Journal of Pain and Palliative Care Pharmacotherapy*, 22(2), págs. 153-157, [en línea] Available from: http://informahealthcare.com/doi/abs/10.1080/15360280801992165.

Howard, Fred M. (2000) *Pelvic pain: diagnosis and management*, Lippincott Williams & Wilkins.

Hsieh, Shu-Ching, Lai, Jung-Nien, Lee, Chuan-Fang, Hu, Fu-Chang, et al. (2008) 'The prescribing of Chinese herbal products in Taiwan: a cross-sectional analysis of the national health insurance reimbursement database', *Pharmacoepidemiology and Drug Safety*, 17(6), págs. 609-619, [en línea] Available from: http://dx.doi.org/10.1002/pds.1611.

Hsu, C.-S., Yang, J.-K. y Yang, L.-L. (2006) 'Effect of «Dang-Qui-Shao-Yao-San» a Chinese medicinal prescription for dysmenorrhea on uterus contractility in vitro', *Phytomedicine*, 13(1-2), págs. 94-100, [en línea] Available from: http://www.sciencedirect.com/science/article/B7GVW-4G9Y4HN-1/2/c5edc715d19c3195ca730cc00444496b.

Hsu, Chun-Sen, Yang, J-Kay y Yang, Ling-Ling (2003) 'Effect of a dysmenorrhea Chinese medicinal prescription on uterus contractilityin vitro', *Phytotherapy Research*, 17(7), págs. 778-783, [en línea] Available from: http://onlinelibrary.wiley.com/doi/10.1002/ptr.1235/abstract (Accedido 31 Octubre 2010).

Hua, Y.Q., Su, S.L., Duan, J.A., Wang, Q.J., et al. (2008) 'Danggui-Shaoyao-San, a traditional Chinese prescription, suppresses PGF2[alpha] production in endometrial epithelial cells by inhibiting COX-2 expression and activity', *Phytomedicine*, 15(12), págs. 1046-1052, [en línea] Available from: http://www.sciencedirect.com/science/article/B7GVW-4T719SK-1/2/892584717ce5b1cd09007bf326df3c8b.

Huan Yang, Cun-Zhi Liu, Xu Chen, Liang-Xiao Ma, et al. (2008) 'Systematic review of clinical trials of acupuncture-related therapies for primary dysmenorrhea.', *Acta Obstetricia & Gynecologica Scandinavica*, 87(11), págs. 1114-1122, [en línea] Available from: http://search.ebscohost.com/login.aspx?direct=true&AuthType=ip,cookie,url,uid&db=aph&AN=35295097&site=ehost-live.

Huang, Jaou-Chen, Ruan, Cheng-Huai, Tang, Kathy y Ruan, Ke-He (2006) 'Prunella stica inhibits the proliferation but not the prostaglandin production of Ishikawa cells', *Life Sciences*, 79(5), págs. 436-441, [en línea] Available from: http://www.sciencedirect.com/science/article/B6T99-4J8D8SJ-3/2/b6d1da91691a7cb17eba3ff1dc9a402f.

Imai, A, Horibe, S, Fuseya, S, Iida, K, et al. (1995) 'Possible evidence that the herbal medicine shakuyaku-kanzo-to decreases prostaglandin levels through suppressing arachidonate turnover in endometrium', *Journal of Medicine*, 26(3-4), págs. 163-174, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/8558097 (Accedido 31 Octubre 2010).

Indusekhar, Radha, Usman, Sa'adatu Bose y O'Brien, Shaughn (2007) 'Psychological aspects of premenstrual syndrome', *Best Practice & Research Clinical Obstetrics & Gynaecology*, 21(2), págs. 207-220, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/S1521693406001349.

Iorno, V., Burani, R., Bianchini, B., Minelli, E., et al. (2008) 'Acupuncture Treatment of Dysmenorrhea Resistant to Conventional Medical Treatment', *eCAM*, 5(2), págs. 227-230, [en línea] Available from: http://ecam.oxfordjournals.org/cgi/content/abstract/5/2/227 (Accedido 31 Octubre 2010).

Jadad, Alejandro R., Moore, R. Andrew, Carroll, Dawn, Jenkinson, Crispin, et al. (1996) 'Assessing the quality of reports of randomized clinical trials: Is blinding necessary?', *Controlled Clinical Trials*, 17(1), págs. 1-12, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/0197245695001344 (Accedido 10 Septiembre 2011).

Jang, Jun-Bock, Yoon, Young-Jin, Park, Jung-Hyun, Jeong, Haeng-Gyu, et al. (2009) 'Therapeutic effects of Chiljehyangbuhwan on primary dysmenorrhea: A randomized, double blind, placebo-controlled study', *Complementary Therapies in Medicine*, 17(3), págs. 123-130, [en línea] Available from: http://www.sciencedirect.com/science/article/B6WCS-4TKXD61-1/2/e05378c907e4ea8ce99211d7087575f3.

Jia, Wei, Wang, Xiaorong, Xu, Desheng, Zhao, Aihua y Zhang, Yongyu (2006) 'Common traditional Chinese medicinal herbs for dysmenorrhea', *Phytotherapy Research*, 20(10), págs. 819-824, [en línea] Available from:

http://onlinelibrary.wiley.com/doi/10.1002/ptr.1905/abstract (Accedido 31 Octubre 2010).

Jian-li NI (2008) 'Laws of compound traditional Chinese medicine in treatment of dysmenorrhea', *Zhong Xi Yi Jie He Xue Bao.*

Juang, Chi-Mou, Yen, Ming-Shien, Twu, Nae-Fong, Horng, Huann-Cheng, et al. (2006) 'Impact of pregnancy on primary dysmenorrhea', *International Journal of Gynecology & Obstetrics*, 92(3), págs. 221-227, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/S002072920500634X.

Jun, Eun-Mi, Chang, Soonbok, Kang, Duck-Hee y Kim, Sue (2007) 'Effects of acupressure on dysmenorrhea and skin temperature changes in college students: A non-randomized controlled trial', *International Journal of Nursing Studies*, 44(6), págs. 973-981, [en línea] Available from: http://www.sciencedirect.com/science/article/B6T7T-4K6CPX0-1/2/5dab14630ae0f39adea3fd91a9c72c5a.

Kane, Mark (2004) *Research made easy in complementary and alternative medicine*, Elsevier Health Sciences.

Kashefi, Farzaneh, Ziyadlou, Samaneh, Khajehei, Marjan, Ashraf, Ali Reza, et al. (2010) 'Effect of acupressure at the Sanyinjiao point on primary dysmenorrhea: A randomized controlled trial', *Complementary Therapies in Clinical Practice*, 16(4), págs. 198-202, [en línea] Available from: http://www.sciencedirect.com/science/article/B7MFN-5046W5N-1/2/ae92ed827d5b704fc2dc2b649c480fef.

Kennedy, S, Jin, X, Yu, H, Zhong, S, et al. (2006) 'Randomized controlled trial assessing a traditional Chinese medicine remedy in the treatment of primary dysmenorrhea', *Fertility and Sterility*, 86(3), págs. 762-764, [en línea] Available from: http://www.fertstert.org/article/S0015-0282(06)00957-5/abstract (Accedido 31 Octubre 2010).

Kido, Aki, Togashi, Kaori, Kataoka, Masako, Maetani, Yoji, et al. (2007) 'The effect of oral contraceptives on uterine contractility and menstrual pain: an assessment with cine MR imaging', *Human Reproduction*, 22(7), págs. 2066 -2071, [en línea] Available from: http://humrep.oxfordjournals.org/content/22/7/2066.abstract (Accedido 1 Noviembre 2010).

Kokjohn, K., Schmidt, D.M., Triano, J.J. y Brennan, P.C. (1992) 'The effect of spinal manipulation on pain and prostaglandin levels in women with primary dysmenorrhea.', *Journal of the Canadian Chiropractic Association*, 36(3), pág. 178.

Kotani, N, Oyama, T, Sakai, I, Hashimoto, H, et al. (1997) 'Analgesic effect of a herbal medicine for treatment of primary dysmenorrhea--a double-blind study', *The American Journal of Chinese Medicine*, 25(2), págs. 205-212, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/9288368 (Accedido 31 Octubre 2010).

Larroy, C (2002) 'Comparing Visual-Analog and Numeric Scales for Assessing Menstrual Pain', *Behavioral Medicine*, Vol. 27 Issue 4, p179, 3p, [en línea] Available from: https://secure.uoc.edu/ehost/,DanaInfo=web.ebscohost.com+detail?sid=ddfe1c21-f6c8-48d8-9026-cdd8e81c1b7d%40sessionmgr13&vid=1&hid=12&bdata=JkF1dGhUeXBlPWlwLGNvb2tpZSx1cmwsdWlkJnNpdGU9ZWhvc3QtbGl2ZQ%3d%3d#db=aph&AN=7239629 (Accedido 22 Agosto 2011).

Larroy, C (2001) 'Prevalencia de los síntomas no dolorosos de la dismenorrea funcional en la Comunidad de Madrid. Su evolución en función de la edad - Clínica y Salud', *Clínica y Salud*, vol. 12, núm. 3, 2001, pp. 327-340, [en línea] Available from: http://redalyc.uaemex.mx/src/inicio/ArtPdfRed.jsp?iCve=180618319003# (Accedido 4 Septiembre 2011).

Larroy, C, C., Tabernero, J. A y Alegría Gil, Ana (2001) 'Factorización de los síntomas no dolor osos de la dismenorrea primaria y su cambio a lo la rgo de la edad: estudio en la Comunidad de Madrid Factor structure and evolution of painless', *Clínica y Salud*, vol. 12, núm. 2, 2001, pp. 253-269.

Larroy, C, Meseguer, C y Crespo (2001) 'Dismenorrea funcional en la Comunidad Autónoma de Madrid: estudio de la prevalencia en función de la edad (Revista de la Sociedad Española del Dolor (SED))', *Rev Soc Esp Dolor 8 (2001);1 :11 - 22*, [en línea] Available from: http://www.revista.sedolor.es/articulo.php?ID=207 (Accedido 14 Noviembre 2010).

Latthe, Pallavi, Mignini, Luciano, Gray, Richard, Hills, Robert y Khan, Khalid (2006) 'Factors predisposing women to chronic pelvic pain: systematic review', *BMJ*, 332(7544), págs. 749 -755, [en línea] Available from: http://www.bmj.com/content/332/7544/749.abstract (Accedido 1 Noviembre 2010).

Lete, Iñaki, Dueñas, José Luis, Serrano, Isabel, Doval, José Luis, et al. (2011) 'Attitudes of Spanish women toward premenstrual symptoms, premenstrual syndrome and premenstrual dysphoric disorder: results of a nationwide survey', *European Journal of Obstetrics & Gynecology and Reproductive Biology*, [en línea] Available from: http://linkinghub.elsevier.com/retrieve/pii/S030121151100399X (Accedido 22 Agosto 2011).

Li LF, Zhang JX (2007) 'Effects of Fufang Xiaojingtong capsules on uterine activity of animals', *Zhongguo Zhong Yao Za Zhi*.

Liang, Shangdong, Xu, Changshui, Li, Guilin y Gao, Yun (2010) 'P2X receptors and modulation of pain transmission: Focus on effects of drugs and compounds used in traditional Chinese medicine', *Neurochemistry International*, 57(7), págs. 705-712, [en línea] Available from: http://www.sciencedirect.com/science/article/B6T0B-512K1JP-1/2/3584a28f51d8439a8bfae82d380fe897.

Liao, Zheng-Gen, Liang, Xin-Li, Zhu, Jing-Yun, Zhao, Guo-Wei, et al. (2010) 'Correlation between synergistic action of Radix Angelica dahurica extracts on analgesic effects of Corydalis alkaloid and plasma concentration of dl-THP', *Journal of Ethnopharmacology*, 129(1), págs. 115-120, [en línea] Available from: http://www.sciencedirect.com/science/article/B6T8D-4YN5PG2-1/2/0b03ed3859680ec9375e5ff680fc60c3.

Liu, J X (1994) 'Clinical study of the treatment of endometriosis with traditional Chinese medicine', *Zhongguo Zhong Xi Yi Jie He Za Zhi Zhongguo Zhongxiyi Jiehe Zazhi = Chinese Journal of Integrated Traditional and Western Medicine / Zhongguo Zhong Xi Yi Jie He Xue Hui, Zhongguo Zhong Yi Yan Jiu Yuan Zhu Ban*, 14(6), págs. 337-339, 323-324, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/8000220 (Accedido 31 Octubre 2010).

Liu, J, Li, X y Hu, X (1998) 'Clinical observations on treatment of endometriosis by tonifying kidney and removing blood stasis', *Zhongguo Zhong Xi Yi Jie He Za Zhi Zhongguo Zhongxiyi Jiehe Zazhi = Chinese Journal of Integrated Traditional and Western Medicine / Zhongguo Zhong Xi Yi Jie He Xue Hui, Zhongguo Zhong Yi Yan Jiu Yuan Zhu Ban*, 18(3), págs. 145-147, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/11367661 (Accedido 31 Octubre 2010).

Liu, J.-Y., Liu, Y.-S., Liang Yeh, L.L., Lin, K.-S., et al. (2007) 'Uterine blood flow change in a randomized double-blind clinical trial of a traditional Chinese herbal formula treating primary dysmenorrhea', *Fertility and Sterility*, 88(Supplement 1), pág. S192-S193, [en línea] Available from: http://www.sciencedirect.com/science/article/B6T6K-4PM8WKS-NH/2/828acc7e2d0a272a46d4e2962ff4b65b.

Liu, Pei, Duan, Jin-ao, Hua, Yong-qing, Tang, Yu-ping, et al. (2010) 'Effects of Xiang-Fu-Si-Wu Decoction and Its Main Components for Dysmenorrhea on Uterus Contraction', *Journal of Ethnopharmacology*, In Press, Accepted Manuscript, [en línea] Available from: http://www.sciencedirect.com/science/article/B6T8D-51BBKWB-1/2/2df7b92f33412148a7537f991f457212.

Liu, Yan, Gold, Ellen B., Lasley, Bill L. y Johnson, Wesley O. (2004) 'Factors Affecting Menstrual Cycle Characteristics', *American Journal of Epidemiology*, 160(2), págs. 131 -140, [en línea] Available from: http://aje.oxfordjournals.org/content/160/2/131.abstract (Accedido 4 Septiembre 2011).

Lloyd, Kimberly Braxton y Hornsby, Lori B. (2009) 'Complementary and Alternative Medications for Women's Health Issues', *Nutrition in Clinical Practice*, 24(5), págs. 589 -608, [en línea] Available from: http://ncp.sagepub.com/content/24/5/589.abstract (Accedido 1 Noviembre 2010).

M. A. L. van Tilburg, M. C. Becht y A. J. J. M. Vingerhoets (2009) 'Self-reported crying during the menstrual cycle: Sign of discomfort and emotional turmoilor erroneous beliefs?', [en línea] Available from: https://secure.uoc.edu/doi/abs/10.3109/,DanaInfo=informahealthcare.com+01674820309074689 (Accedido 3 Noviembre 2010).

M. S. Serrano - Atero, J. Caballero** (2002) 'Valoración del dolor (I)', *R e v. Soc. Esp. Dolor*.

Ma, Hongyue, Su, Shulan, Duan, Jinao, Tang, Yuping, et al. (2010) 'Evaluation of the analgesic activities of the crude aqueous extract and fractions of Shao Fu Zhu Yu decoction', *Pharmaceutical Biology*, págs. 1-9, [en línea] Available from: http://informahealthcare.com/doi/abs/10.3109/13880209.2010.504965 (Accedido 31 Octubre 2010).

Maciocia y G (2009) *La práctica de la medicina china*, Elsevier España.

Maciocia, Giovanni (1998) *Obstetrics and gynecology in Chinese medicine*, Elsevier Health Sciences.

Martín Arribas, M.C. (2004) 'Diseño y validación de cuestionarios', *Matronas Profesión*, vol. 5(17): 23-29.

Martínez, Lorenzo Abad y López, Lorenzo Abad Martínez, Rafael Comino Delgado, Guillermo (López García) (2004) *Obstetricia y ginecología*, Editorial Ariel.

Michelle L Proctor and Cynthia M Farquhar (2006) 'Dysmenorrhoea', *clinical evidence*.

Milsom, Ian, Minic, Milos, Dawood, M. Yusoff, Akin, Mark D., et al. (2002) 'Comparison of the efficacy and safety of nonprescription doses of naproxen and naproxen sodium with ibuprofen, acetaminophen, and placebo in the treatment of primary dysmenorrhea: a pooled analysis of five studies', *Clinical Therapeutics*, 24(9), págs. 1384-1400, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/S0149291802800431.

Moos, udolph H. (1968) 'The Development of a Menstrual Distress Questionnaire', *Psychosomatic Medicine*, 30(6), págs. 853-867, [en línea] Available from: http://www.psychosomaticmedicine.org/cgi/content/abstract/30/6/853.

Morales, Alvaro Ruiz y Zárate, Luis Enrique Morillo (2004) *Epidemiología clínica: investigación clínica aplicada*, Ed. Médica Panamericana.

Mowrey, Daniel B. y Mowrey, Daniel (1998) *The scientific validation of herbal medicine*, McGraw-Hill Professional.

Nahid, Khodakrami, Fariborz, Moatar, Ataolah, Ghahiri y Solokian, Shahdan (2009) 'The Effect of an Iranian Herbal Drug on Primary Dysmenorrhea: A Clinical Controlled Trial', *Journal of Midwifery & Women's Health*, 54(5), págs. 401-404, [en línea]

Available from: http://www.sciencedirect.com/science/article/B6W6R-4X3X83B-J/2/3fc2c78c2be9a8268e81a3e30105b1b5.

Negriff, S., Dorn, L. D., Hillman, J. B. y Huang, B. (2009) 'The measurement of menstrual symptoms: Factor structure of the menstrual symptom questionnaire in adolescent girls', *Journal of Health Psychology*, 14(7), págs. 899-908, [en línea] Available from: https://secure.uoc.edu/content/14/7/,DanaInfo=hpq.sagepub.com+899 (Accedido 22 Agosto 2011).

Nelson, Anita L. (2006) 'Extended-Regimen Contraception Effects on Menstrual Symptoms and Quality of Life.', *Journal of Family Practice*, 55(2), pág. S1-S8, [en línea] Available from: http://search.ebscohost.com/login.aspx?direct=true&db=a9h&AN=19791724&site=ehost-live.

Norvell, Kristine Turner, Gaston-Johansson, Fannie y Fridh, Gerd (1987) 'Remembrance of labor pain: how valid are retrospective pain measurements?', *Pain*, 31(1), págs. 77-86, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/030439598790008X.

Ochir, Sarangowa, Ishii, Kouta, Park, ByoungJae, Matsuta, Tomohiko, et al. (2010) 'Botanical origin of mei-gui hua (petal of a Rosa species)', *Journal of Natural Medicines*, 64(4), págs. 409-416, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/20467822 (Accedido 2 Junio 2011).

Oya, Atsuko, Oikawa, Tetsuro, Nakai, Akihito, Takeshita, Toshiyuki y Hanawa, Toshihiko (2008) 'Clinical efficacy of Kampo medicine (Japanese traditional herbal medicine) in the treatment of primary dysmenorrhea', *Journal of Obstetrics and Gynaecology Research*, 34(5), págs. 898-908, [en línea] Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1447-0756.2008.00847.x/abstract (Accedido 31 Octubre 2010).

Palacios (2000) *Salud y Medicina de la mujer*, Elsevier España.

Pan, Si-Yuan, Chen, Si-Bao, Dong, Hong-Guang, Yu, Zhi-Ling, et al. (2010) 'New Perspectives on Chinese Herbal Medicine (Zhong-Yao) Research and Development', *eCAM*, pág. neq056, [en línea] Available from: http://ecam.oxfordjournals.org/cgi/content/abstract/neq056v1 (Accedido 1 Noviembre 2010).

Peilin, Sun (2002) *The treatment of pain with Chinese herbs and acupuncture*, Elsevier Health Sciences.

Peterson, Drew (2007) 'Research Update: Oriental Medicine Research Abstracts', *California Journal of Oriental Medicine (CJOM)*, 18(2), págs. 30-31.

Pirotta, Marie (2008) 'Commentary on the Cochrane Review of Chinese Herbal Medicine for Dysmenorrhea', *EXPLORE: The Journal of Science and Healing*, 4(6), págs. 389-391, [en línea] Available from: http://www.sciencedirect.com/science/article/B7MF9-4TT9DXV-F/2/b9e2b862a55f0b22ff407c5616e1788b.

Price, D D, McGrath, P A, Rafii, A y Buckingham, B (1983) 'The validation of visual analogue scales as ratio scale measures for chronic and experimental pain', *Pain*, 17(1), págs. 45-56, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/6226917 (Accedido 27 Marzo 2011).

Prieto, José Lombardía (2007) *Ginecología y obstetricia: manual de consulta rápida*, Ed. Médica Panamericana.

Proctor, Michelle y Farquhar, Cynthia (2006) 'Diagnosis and management of dysmenorrhoea', *BMJ*, 332(7550), págs. 1134 -1138, [en línea] Available from: http://www.bmj.com/content/332/7550/1134.short (Accedido 1 Noviembre 2010).

Proctor, Michelle y Murphy, Patricia A (2001) 'Herbal and dietary therapies for primary and secondary dysmenorrhoea', En The Cochrane Collaboration y Proctor, M. (eds.), *Cochrane Database of Systematic Reviews*, Chichester, UK, John Wiley & Sons, Ltd, [en línea] Available from: http://onlinelibrary.wiley.com/o/cochrane/clsysrev/articles/CD002124/abstract.html (Accedido 1 Noviembre 2010).

Qing-Zhu, Fu, Shou-Zhong, Yang y Da-Wei, Liu (1992) *Fu Qing-Zhu's Gynecology*, Blue Poppy Enterprises, Inc.

Rapkin, Andrea J., Berman, Steven M., Mandelkern, Mark A., Silverman, Daniel H.S., et al. (2011) 'Neuroimaging Evidence of Cerebellar Involvement in Premenstrual Dysphoric Disorder', *Biological Psychiatry*, 69(4), págs. 374-380, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/S0006322310009984.

Riley, Dagmar (2003) *Treating pain with traditional Chinese medicine*, Paradigm.

Rivera-Tovar, Ana D., Pilkonis, Paul y Frank, Ellen (1992) 'Symptom patterns in late luteal-phase dysphoric disorder', *Journal of Psychopathology and Behavioral Assessment*, 14(2), págs. 189-199, [en línea] Available from: http://www.springerlink.com/content/k1w8qk836354gp0t/ (Accedido 4 Septiembre 2011).

Rosier, Elisa M., Iadarola, Michael J. y Coghill, Robert C. (2002) 'Reproducibility of pain measurement and pain perception', *Pain*, 98(1-2), págs. 205-216, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/S0304395902000489.

Ross, C., Coleman, G. y Stojanovska, C. (2003) 'Factor structure of the modified Moos Menstrual Distress Questionnaire: Assessment of prospectively reported follicular, menstrual and premenstrual symptomatology - Journal of Psychosomatic Obstetrics and Gynecology | HighBeam Research', *J Psychosom Obstet Gyneco*, 24:163-174, [en línea] Available from: http://www.highbeam.com/doc/1P3-471812521.html (Accedido 22 Agosto 2011).

Rowlands, Dewi Kenneth, Cui, Yu Gui, Wong, Hau Yan, Gou, Yu Lin y Chan, Hsiao Chang (2009) 'Traditional Chinese medicine Bak Foong Pills alters uterine quiescence - Possible role in alleviation of dysmenorrhoeal symptoms', *Cell Biology International*, 33(12), págs. 1207-1211, [en línea] Available from: http://www.sciencedirect.com/science/article/B6WCB-4VYP9C1-1/2/2284980c9e931e438abe0b8732ddd43a.

Sampalis, Fotini, Bunea, Roxandra, Pelland, Marie France, Kowalski, Odile, et al. (2003) 'Evaluation of the Effects of Neptune Krill Oil™ on the Management of Premenstrual Syndrome and Dysmenorrhea.', *Alternative Medicine Review*, 8(2), págs. 171-179.

Satoshi Usuki, Tomoko Nakauchi, Sawako Higa y Katsumi Someya (2001) 'The Improvement of Luteal Insufficiency in Fecund Women by Tokishakuyakusan Treatment', *The American Journal of Chinese Medicine (AJCM)*, Volume: 30, Issues: 2-3(2002) pp. 327-338, [en línea] Available from: http://www.worldscinet.com/ajcm/30/3002n03/S0192415X02000247.html (Accedido 1 Noviembre 2010).

Shang, Aijing, Huwiler, Karin, Nartey, Linda, Jüni, Peter y Egger, Matthias (2007) 'Placebo-controlled trials of Chinese herbal medicine and conventional medicine—comparative study', *International Journal of Epidemiology*, 36(5), págs. 1086 -1092, [en línea] Available from: http://ije.oxfordjournals.org/content/36/5/1086.abstract (Accedido 31 Octubre 2010).

Sharp, B. A. C. (2002) 'Cyclic Perimenstrual Pain and Discomfort: The Scientific Basis for Practice', *Journal of Obstetric, Gynecologic, and Neonatal Nursing*, 31(6), págs. 637-

649, [en línea] Available from: http://onlinelibrary.wiley.com/doi/10.1177/0884217502239207/abstract (Accedido 1 Noviembre 2010).

Shibata, T, Morimoto, T, Suzuki, A, Saito, H y Yanaihara, T (1996) 'The effect of Shakuyaku-kanzo-to on prostaglandin production in human uterine myometrium', *Nippon Sanka Fujinka Gakkai Zasshi*, 48(5), págs. 321-327, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/8847457 (Accedido 31 Octubre 2010).

Smith, Caroline A., Crowther, Caroline A., Petrucco, Oswald, Beilby, Justin y Dent, Hannah (2010) 'Acupuncture to Treat Primary Dysmenorrhea in Women: A Randomized Controlled Trial', *eCAM*, pág. nep239, [en línea] Available from: http://ecam.oxfordjournals.org/cgi/content/abstract/nep239v1 (Accedido 31 Octubre 2010).

Smith, Roger P. (2004) *Netter obstetricia, ginecología y salud de la mujer*, Elsevier España.

Stephenson, Laura A., Denney, Douglas R. y Aberger, Edward W. (1983) 'Factor structure of the menstrual symptom questionnaire: Relationship to oral contraceptives, neuroticism and life stress', *Behaviour Research and Therapy*, 21(2), págs. 129-135, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/0005796783901572 (Accedido 5 Septiembre 2011).

Sundell, Gunilla, Milsom, Ian y Andersch, Bjorn (1990) 'Factors influencing the prevalence and severity of dysmenorrhoea in young women', *BJOG: An International Journal of Obstetrics and Gynaecology*, 97(7), págs. 588-594, [en línea] Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1471-0528.1990.tb02545.x/abstract (Accedido 1 Noviembre 2010).

Tanaka, T (2003) 'A novel anti-dysmenorrhea therapy with cyclic administration of two Japanese herbal medicines', *Clinical and Experimental Obstetrics & Gynecology*, 30(2-3), págs. 95-98, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/12854851 (Accedido 31 Octubre 2010).

Tang, Jin-Ling (2006) 'Research priorities in traditional Chinese medicine', *BMJ*, 333(7564), págs. 391 -394, [en línea] Available from: http://www.bmj.com/content/333/7564/391.short (Accedido 1 Noviembre 2010).

Taylor, Diana, Miaskowski, Christine y Kohn, Joel (2002) 'A Randomized Clinical Trial of the Effectiveness of An Acupressure Device (Relief Brief) for Managing Symptoms of Dysmenorrhea', *Journal of Alternative and Complementary Medicine*, 8(3), págs. 357-370, [en línea] Available from: http://www.liebertonline.com/doi/abs/10.1089%2F10755530260128050 (Accedido 31 Octubre 2010).

Taylor, Helen M. (1942) 'A Clinical Study of Menstruation with Special Reference to Primary Dysmenorrhoea', *BJOG: An International Journal of Obstetrics and Gynaecology*, 49(4), págs. 341-367, [en línea] Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1471-0528.1942.tb05736.x/abstract (Accedido 1 Noviembre 2010).

Taylor, J. W (1979) 'The timing of menstruation ‐ related symptoms assessed by a daily symptom rating scale', *Acta Psychiatrica Scandinavica*, 60(1), págs. 87-105, [en línea] Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1600-0447.1979.tb00268.x/abstract (Accedido 23 Agosto 2011).

Terry, Rohini H., Niven, Catherine A., Brodie, Eric E., Jones, Ray B. y Prowse, Morag A. (2008) 'Memory for Pain? A Comparison of Nonexperiential Estimates and Patients' Reports of the Quality and Intensity of Postoperative Pain', *The Journal of Pain*, 9(4),

págs. 342-349, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/S1526590007010206.

Tillburt, Jon C y Kaptchuck, Ted J (s.f.) 'Herbal medicine research and global health: an ethical anylisis',.

Trudi M. Walsh, Leeanne LeBlanc y Patrick J. McGrath (2003) 'Menstrual Pain Intensity, Coping, and Disability: The Role of Pain Catastrophizing', *Pain Medicine*, Volume 4, Number 4 (December 01, 2003), [en línea] Available from: http://ejournals.ebsco.com/Article.asp?ContributionID=5476370 (Accedido 1 Noviembre 2010).

Tseng, Ying-Fen, Chen, Chung-Hey y Yang, Yi-Hsin (2005) 'Rose Tea for Relief of Primary Dysmenorrhea in Adolescents: A Randomized Controlled Trial in Taiwan', *Journal of Midwifery & Women's Health*, 50(5), pág. e51-e57, [en línea] Available from: http://www.sciencedirect.com/science/article/B6W6R-4H2F7JB-1C/2/8f9a7b0cb082c32cb4588e51f80b2914.

Tugwell, P., Petticrew, M., Kristjansson, E., Welch, V., et al. (2010) 'Assessing equity in systematic reviews: realising the recommendations of the Commission on Social Determinants of Health', *BMJ*, 341(sep13 1), pág. c4739-c4739, [en línea] Available from: http://www.bmj.com/cgi/doi/10.1136/bmj.c4739 (Accedido 1 Noviembre 2010).

Villoria, Clemente Muriel (2007) *Dolor Cronico - Diagnóstico, clínica y tratamiento*, Arán Ediciones.

Vincent, Katy, Warnaby, Catherine, Stagg, Charlotte J., Moore, Jane, et al. (2011) 'Dysmenorrhoea is associated with central changes in otherwise healthy women', *PAIN*, 152(9), págs. 1966-1975, [en línea] Available from: https://secure.uoc.edu/science/article/pii/,DanaInfo=www.sciencedirect.com+S0304395911002211 (Accedido 22 Agosto 2011).

Wang H, Tang Y (2010) 'Antidysmenorrheic effects of Radix angelica and Rhizoma Chuanxiong with different proportions and preparation methods on dysmenorrhea model mice', *Zhongguo Zhong Yao Za Zhi*.

Wang, L, Wang, X, Wang, W, Chen, C, et al. (2004) 'Stress and dysmenorrhoea: a population based prospective study', *Occupational and Environmental Medicine*, 61(12), págs. 1021 -1026, [en línea] Available from: http://oem.bmj.com/content/61/12/1021.abstract (Accedido 31 Octubre 2010).

Wang, Mei-Chuan, Hsu, Mei-Chi, Chien, Li-Wei, Kao, Chien-Huei y Liu, Chi-Feng (2009) 'Effects of Auricular Acupressure on Menstrual Symptoms and Nitric Oxide for Women with Primary Dysmenorrhea', *The Journal of Alternative and Complementary Medicine*, 15(3), págs. 235-242, [en línea] Available from: http://www.liebertonline.com/doi/abs/10.1089/acm.2008.0164 (Accedido 31 Octubre 2010).

Webster, Sandra K., Martin, Harry J., Uchalik, Deborah y Gannon, Linda (1979) 'The menstrual symptom questionnaire and spasmodic/congestive dysmenorrhea: Measurement of an invalid construct', *Journal of Behavioral Medicine*, 2(1), págs. 1-19, [en línea] Available from: http://www.springerlink.com/content/n535034p7676702g/ (Accedido 1 Noviembre 2010).

Weissman, Alicia M., Hartz, Arthur J., Hansen, Michael D. y Johnson, Susan R. (2004) 'The natural history of primary dysmenorrhoea: a longitudinal study', *BJOG: An International Journal of Obstetrics and Gynaecology*, 111(4), págs. 345-352, [en línea] Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1471-0528.2004.00090.x/full (Accedido 31 Octubre 2010).

Werbach, Melvyn R. (1993) 'Nutritional Influences on Illness: Dysmenorrhea (Painful Menstruation).', *Townsend Letter for Doctors & Patients*, (120), pág. 674.

Wiffen, Philip J (2010) 'Evidence-Based Pain Management and Palliative Care in Issue Four for 2009 of The Cochrane Library', *Journal of Pain and Palliative Care Pharmacotherapy*, 24(1), págs. 48-52, [en línea] Available from: http://informahealthcare.com/doi/abs/10.3109/15360280903583131.

Wildman, Beth G. y White, Pamela A. (1986) 'Assessment of dysmenorrhea using the menstrual symptom questionnaire: Factor structure and validity', *Behaviour Research and Therapy*, 24(5), págs. 547-551, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/0005796786900355 (Accedido 27 Agosto 2011).

Witt, Claudia M, Reinhold, Thomas, Brinkhaus, Benno, Roll, Stephanie, et al. (2008) 'Acupuncture in patients with dysmenorrhea: a randomized study on clinical effectiveness and cost-effectiveness in usual care', *American Journal of Obstetrics and Gynecology*, 198(2), págs. 166.e1-8, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/18226614 (Accedido 31 Octubre 2010).

Wong, C.L., Lai, K.Y. y Tse, H.M. (2010) 'Effects of SP6 acupressure on pain and menstrual distress in young women with dysmenorrhea', *Complementary Therapies in Clinical Practice*, 16(2), págs. 64-69, [en línea] Available from: http://www.sciencedirect.com/science/article/B7MFN-4XP8TF6-1/2/da5c568ac46fc7a91cafaaba6cbf31cf.

Wong, Chooi L, Farquhar, Cindy, Roberts, Helen y Proctor, Michelle (2009) 'Oral contraceptive pill for primary dysmenorrhoea', En The Cochrane Collaboration y Wong, Chooi L (eds.), *Cochrane Database of Systematic Reviews*, Chichester, UK, John Wiley & Sons, Ltd, [en línea] Available from: http://www2.cochrane.org/reviews/en/ab002120.html (Accedido 6 Febrero 2011).

Wu, Q, Chen, Y y Niu, J (1998) 'Clinical observation of forty cases in adolescent dysmenorrhea treated by traditional Chinese medicine', *Zhongguo Zhong Xi Yi Jie He Za Zhi Zhongguo Zhongxiyi Jiehe Zazhi = Chinese Journal of Integrated Traditional and Western Medicine / Zhongguo Zhong Xi Yi Jie He Xue Hui, Zhongguo Zhong Yi Yan Jiu Yuan Zhu Ban*, 18(10), págs. 610-611, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/11477846 (Accedido 31 Octubre 2010).

Wu, R y Han, T Y (1989) 'Cold dysmenorrhea with blood stagnation treated with zhuyu wengong decoction', *Zhong Xi Yi Jie He Za Zhi = Chinese Journal of Modern Developments in Traditional Medicine / Zhongguo Zhong Xi Yi Jie He Yan Jiu Hui (chou), Zhong Yi Yan Jiu Yuan, Zhu Ban*, 9(8), págs. 455-457, 451, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/2598345 (Accedido 31 Octubre 2010).

Xiaoshu Zhu, Michelle Proctor, Alan Bensoussan, Emily Wu y Caroline A Smith (2010) 'Chinese herbal medicine for primary dysmenorrhoea', [en línea] Available from: http://onlinelibrary.wiley.com/o/cochrane/clsysrev/articles/CD005288/frame.html (Accedido 19 Diciembre 2010).

Xie, C (1990) 'Effects of danggui shaoyao powder on blood rheological indexes and prostaglandin F2 alpha in dysmenorrhea patients', *Zhong Xi Yi Jie He Za Zhi = Chinese Journal of Modern Developments in Traditional Medicine / Zhongguo Zhong Xi Yi Jie He Yan Jiu Hui (chou), Zhong Yi Yan Jiu Yuan, Zhu Ban*, 10(7), págs. 410-412, 389, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/2208420 (Accedido 31 Octubre 2010).

Xie, Yan, Xuan, Zhen-yu, Yu, Li y Guo, Jing (2008) 'Effects of Shujing Ketong soft capsules on uterine activity of animals', *Zhongguo Zhong Yao Za Zhi = Zhongguo*

Zhongyao Zazhi = China Journal of Chinese Materia Medica, 33(12), págs. 1466-1469, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/18837358 (Accedido 31 Octubre 2010).

Yao, Min y Li, Pei (2007) 'Clinical study on treatment of primary dysmenorrhea with Qihuang herbal warm bag', *Journal of Acupuncture and Tuina Science*, 5(5), págs. 304-306, [en línea] Available from: http://www.springerlink.com/content/777331665q126w32/ (Accedido 1 Noviembre 2010).

Yarnitsky, David, Sprecher, Elliot, Zaslansky, Ruth y A. Hemli, Jeshayachu (1996) 'Multiple session experimental pain measurement', *Pain*, Volume 67, Issues 2-3, [en línea] Available from: https://secure.uoc.edu/science/article/pii/,DanaInfo=www.sciencedirect.com+03043959 96031107 (Accedido 4 Septiembre 2011).

Yeh, Lan Lan Liang, Liu, Jah-Yao, Lin, Kao-Si, Liu, Yu-Shen, et al. (2007) 'A Randomised Placebo-Controlled Trial of a Traditional Chinese Herbal Formula in the Treatment of Primary Dysmenorrhoea', *PLoS ONE*, 2(8), pág. e719, [en línea] Available from: http://dx.doi.org/10.1371/journal.pone.0000719 (Accedido 31 Octubre 2010).

Yeh, Lan Lan Liang, Liu, Jah-Yao, Liu, Yu-Shen, Lin, Kao-Si, et al. (2009) 'Anemia-Related Hemogram, Uterine Artery Pulsatility Index, and Blood Pressure for the Effects of Four-Agents-Decoction (Si Wu Tang) in the Treatment of Primary Dysmenorrhea', *The Journal of Alternative and Complementary Medicine*, 15(5), págs. 531-538, [en línea] Available from: http://www.liebertonline.com/doi/abs/10.1089/acm.2008.0208 (Accedido 31 Octubre 2010).

Yi, Tao, Zhao, Zhong-Zhen, Yu, Zhi-Ling y Chen, Hu-Biao (2010) 'Comparison of the anti-inflammatory and anti-nociceptive effects of three medicinal plants known as «Snow Lotus» herb in traditional Uighur and Tibetan medicines', *Journal of Ethnopharmacology*, 128(2), págs. 405-411, [en línea] Available from: http://www.sciencedirect.com/science/article/B6T8D-4Y6452N-5/2/7bba3fe17f3460f494ae977c887d50a7.

Zahradnik, Hans-Peter, Hanjalic-Beck, Aida y Groth, Klaus (2010) 'Nonsteroidal anti-inflammatory drugs and hormonal contraceptives for pain relief from dysmenorrhea: a review', *Contraception*, 81(3), págs. 185-196, [en línea] Available from: http://www.sciencedirect.com/science/article/pii/S0010782409004454.

Zaslawski, Christopher (2010) 'Ethical Considerations for Acupuncture and Chinese Herbal Medicine Clinical Trials: A Cross-cultural Perspective', *eCAM*, 7(3), págs. 295-301, [en línea] Available from: http://ecam.oxfordjournals.org/cgi/content/abstract/7/3/295 (Accedido 31 Octubre 2010).

ZHANG, Li-ling, ZHANG, Gang y ZHANG, Li-ping (2009) 'Prof. ZHANG Zhi-jun's Experience in the Combined Treatment with Acupuncture and Chinese Herbs -- A Report of 3 Illustrative Cases', *Journal of Traditional Chinese Medicine*, 29(4), págs. 279-282, [en línea] Available from: http://www.sciencedirect.com/science/article/B8JH6-4Y121WN-B/2/0ec1d82f48e144986ca81ccea041ba78.

Zhang, Y, Hou, G y Yue, Y (2000) 'The analgesic action of semen coicis on severe functional dysmenorrhea--a sequential trial observation', *Journal of Traditional Chinese Medicine = Chung I Tsa Chih Ying Wen Pan / Sponsored by All-China Association of Traditional Chinese Medicine, Academy of Traditional Chinese Medicine*, 20(4), págs. 293-296, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/11263287 (Accedido 31 Octubre 2010).

Zhang, Zhongjing (1987) *Synopsis of prescriptions of the golden chamber (jinkui yaolue fanglun)*, New World Press.

Zhao Wang, Pei-Lin Zhang y Yong Ju (2004) 'Effect of leonurine on the activity of creatine kinase.', *Journal of Asian Natural Products Research*, 6(4), págs. 281-287.

ZHAO, Li y LI, Pei (2009) 'A Survey of Acupuncture Treatment for Primary Dysmenorrhea', *Journal of Traditional Chinese Medicine*, 29(1), págs. 71-76, [en línea] Available from: http://www.sciencedirect.com/science/article/B8JH6-4VYNNJC-J/2/fd6cef21cbd3b160bfd453ff7590094a (Accedido 7 Abril 2011).

Zhou, Jue y Qu, Fan (2009) 'Treating gynaecological disorders with traditional Chinese medicine: a review', *African Journal of Traditional, Complementary, and Alternative Medicines: AJTCAM / African Networks on Ethnomedicines*, 6(4), págs. 494-517, [en línea] Available from: http://www.ncbi.nlm.nih.gov/pubmed/20606770 (Accedido 31 Octubre 2010).

Zhou, Wei, Su, Shu-Lan, Duan, Jin-Ao, Guo, Jian-Ming, et al. (2010) 'Characterization of the Active Constituents in Shixiao San Using Bioactivity Evaluation Followed by UPLC-QTOF and Markerlynx Analysis', *Molecules*, 15(9), págs. 6217-6230, [en línea] Available from: http://www.mdpi.com/search/?q=Characterization+of+the+Active+Constituents+in+Shixiao+San+Using+Bioactivity+Evaluation+Followed+by&s_journal=molecules&s_volume=&s_authors=&s_section=0&s_issue=&s_article_type=0&s_special_issue=0&s_page=&s_search=Search (Accedido 3 Noviembre 2010).

Zhu, Xiaoshu, Bensoussan, Alan, Zhu, Lin, Qian, Jing, et al. (2009) 'Primary dysmenorrhoea: A comparative study on Australian and Chinese women', *Complementary Therapies in Medicine*, 17(3), págs. 155-160, [en línea] Available from: http://www.complementarytherapiesinmedicine.com/article/S0965-2299(08)00125-8/abstract (Accedido 31 Octubre 2010).

Zhu, Xiaoshu, Wong, Felix, Bensoussan, Alan, Lo, Sing Kai, et al. (2010) 'Are there any cross-ethnic differences in menstrual profiles? A pilot comparative study on Australian and Chinese women with primary dysmenorrhea', *Journal of Obstetrics and Gynaecology Research*, 36(5), págs. 1093-1101, [en línea] Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1447-0756.2010.01250.x/full (Accedido 6 Febrero 2011).

Zuo Yanfu, Tan Yong y He Guizxiang (2006) *Gynecology of traditional chinese medicine*, A Newly Compiled Practical English-Chinese Library of Traditional Chinese Medicine, Publishing House of Shanghai University of Traditional Chinese Medicine.

Zuo, Yanfu (2003) *A newly compiled practical English-Chinese library of traditional Chinese medicine*, Shanghai University of Traditional Chinese Medicine.

APPENDICES

APPENDIX I – Poster advertisement

¿DO YOU HAVE PAINFUL PERIODS?

Participa en un estudio sobre la efectividad del tratamiento del dolor menstrual

Cindy Méndez Pendavis, terapeuta licenciada en Medicina Tradicional China, está realizando un estudio sobre el dolor menstrual con el apoyo de ISMET y Centre Equilibrium.

El estudio titulado "Estudio naturalístico sobre la efectividad de la Farmacopea China para el tratamiento de la dismenorrea primaria" tiene como objetivo **evaluar la eficacia de diferentes fórmulas chinas de plantas para el tratamiento del dolor menstrual**.

Si tienes entre 18 y 50 años y estás padeciendo dolor durante el período, o conoces a alguien que pueda estar interesada en obtener más información o en participar en el estudio, por favor ponte en contacto con Cindy Méndez en el **93 000 53 23** o escríbele a dismenorrea@centreequilibrium.com.

Más información en el artículo ¿Tienes dolor menstrual? en la web de Centre Equlibrium.

APPENDIX II – Social network announcement

¿Do you have painful periods? or ¿Do you know someone with painful periods?

Receive FREE treatment of Chinese herbs taking part of a trial I'm conducting with The University of East London. For more information please contact me or read the following article:

http://centreequilibrium.com/2011/03/%C2%BFtienes-dolor-menstrual/

APPENDIX III – Article in Web pages

¿Tienes dolor menstrual?

Participa en un estudio sobre la efectividad del tratamiento del dolor menstrual con farmacopea china

La **dismenorrea primaria es la presencia de dolor severo relacionado con la menstruación** en ausencia de patología pélvica que lo justifique (Howard 2000) (Smith et al. 2010).
Entre el 52 y el 90% de las mujeres padecen dismenorrea (Weissman et al. 2004) y es una causa de absentismo laboral y escolar frecuente. En Estados Unidos se estima que se pierden 600 millones de horas de trabajo al año por esta causa, suponiendo aproximadamente 2 millones de dólares por año. (Howard 2000)

En la Comunidad Autónoma de Madrid se llevó a cabo un estudio para recoger datos fiables y válidos sobre la incidencia de la dismenorrea funcional (Larroy, C et al. 2001). Los resultados sugieren que el 61,9% de las mujeres sufren dolor menstrual y que la intensidad del dolor depende de la edad, así como del número de niños. La correlación entre la intensidad del dolor y la frecuencia de dolor fue alta y significativa. El dolor se reportó principalmente en la región abdominal, seguido del dolor lumbar, el dolor mamario y por último, dolor en los muslos. (Larroy, C et al. 2001)

Enfoques de tratamiento

Hay tres enfoques convencionales para la gestión de la dismenorrea primaria: farmacológico, no farmacológico y quirúrgico. El tratamiento convencional incluye medicamentos antiinflamatorios no esteroideos (AINEs), los anticonceptivos orales, danazol, agonistas de la hormona liberadora de gonadotropina, el acetato de medroxiprogesterona, neurectomía presacra, neurectomía uterosacra y la estimulación nerviosa eléctrica transcutánea (Howard 2000). Es interesante destacar la inclusión de la acupuntura en algunos libros de medicina convencional como tratamiento para el dolor pélvico (Howard 2000).
Existen estudios que evidencian la eficacia del uso de agentes farmacológicos como los AINEs (Wong et al. 2009), o como los anticonceptivos orales (Sundell et al. 1990) para aliviar el dolor menstrual, sin embargo, **el tratamiento convencional para la dismenorrea primaria tiene una tasa de fracaso del 20% al 25% y puede estar contraindicado o no tolerado por algunas mujeres** (Xiaoshu Zhu et al. 2010). La Medicina Herbal China puede ser una alternativa adecuada para todas aquellas mujeres que no puedan o no quieran tratarse con tratamientos convencionales.
La Biblioteca Cochrane (una colección de bases de datos sobre ensayos clínicos controlados en medicina y otra áreas de la salud) publicó una revisión reciente. En ella se detectaron **evidencias que avalan el uso del tratamiento con Farmacopea Tradicional China** en comparación con el placebo, con tratamientos de Medicina Convencional como los AINEs y la píldora anticonceptiva oral, con la ausencia de tratamiento, o en comparación con otros tratamientos como la acupuntura, o la aplicación de calor. Así mismo no se observaron efectos adversos significativos. (Zhu X 2007). Sin embargo, los autores de la revisión también concluyeron que los resultados están limitados por la escasez de estudios y por la baja calidad metodológica de los mismos, lo que no permite ninguna conclusión definitiva. (Xiaoshu Zhu et al. 2010)

Un nuevo estudio en marcha

Cindy Méndez Pendavis, terapeuta Licenciada en Medicina Tradicional China, está realizando un **estudio sobre el dolor menstrual,** en Barcelona, con el apoyo de **ISMET** y **Centre Equilibrium**. El estudio titulado "Estudio naturalístico sobre la efectividad de la Fitoterapia China para el tratamiento de la dismenorrea primaria" tiene como objetivo evaluar la eficacia de diferentes fórmulas chinas de plantas para el tratamiento del dolor menstrual, así como validar la importancia de la diferenciación de síndromes en el tratamiento con farmacopea.

Para este estudio se están **reclutando participantes** mujeres en edad reproductiva, con ciclos menstruales entre 21 y 35 días, de entre 3 y 7 días de duración, que hayan experimentado dolor en 4 períodos consecutivos en los últimos 6 meses no relacionado con dismenorrea secundaria, que no están embarazas, que están de acuerdo en tomar medidas anticonceptivas no hormonales durante el estudio, y que en caso de tomar anticonceptivos orales, hayan estado tomándolos durante como mínimo los últimos 6 meses y que están de acuerdo en seguir tomándolos durante la duración del estudio. Las mujeres incluidas en el estudio no deben estar utilizando dispositivo intrauterino (DIU), no deben haber sido diagnosticadas de una enfermedad grave y no deben estar recibiendo tratamiento de Medicina Tradicional China.

Las participantes recibirán como tratamiento una formulación tradicional de hierbas chinas durante tres períodos menstruales que será elegida de manera personalizada con base en la causa del dolor según la Medicina Tradicional China. Las formulaciones a base de hierbas que se utilizarán en este estudio son fórmulas comercializadas por Fitoki (www.fitoki.com) que se recetarán sin coste económico para las participantes.

Referencias

Howard, F.M., 2000. *Pelvic pain: diagnosis and management*, Lippincott Williams & Wilkins.

Larroy , C, Meseguer , C & Crespo, 2001. Dismenorrea funcional en la Comunidad Autónoma de Madrid: estudio de la prevalencia en función de la edad (Revista de la Sociedad Española del Dolor (SED)). *Rev Soc Esp Dolor 8 (2001);1 :11 – 22*. Available at: http://www.revista.sedolor.es/articulo.php?ID=207

Proctor, M. & Farquhar, C., 2006. Diagnosis and management of dysmenorrhoea. *BMJ*, 332(7550), 1134 -1138.

Smith, C.A. et al., 2010. Acupuncture to Treat Primary Dysmenorrhea in Women: A Randomized Controlled Trial. *eCAM*, nep239.

Sundell, G., Milsom, I. & Andersch, B., 1990. Factors influencing the prevalence and severity of dysmenorrhoea in young women. *British Journal of Obstetrics and Gynaecology*, 97(7), 588-594.

Weissman, A.M. et al., 2004. The natural history of primary dysmenorrhoea: a longitudinal study. *BJOG: An International Journal of Obstetrics and Gynaecology*, 111(4), 345-352.

Wong, C.L. et al., 2009. Oral contraceptive pill for primary dysmenorrhoea. En The Cochrane Collaboration & C. L. Wong, eds. *Cochrane Database of Systematic Reviews*. Chichester, UK:

John Wiley & Sons, Ltd. Available at: http://www2.cochrane.org/reviews/en/ab002120.html

Xiaoshu Zhu et al., 2010. Chinese herbal medicine for primary dysmenorrhoea. Available at: http://onlinelibrary.wiley.com/o/cochrane/clsysrev/articles/CD005288/frame.html

Zhu X, P.M., 2007. Chinese herbal medicine for primary dysmenorrhoea. *Cochrane Database Syst Rev*.

APPENDIX IV – Telephone script for preliminary assessment of candidates

Buenas tardes, quería hablar con ----

Mi nombre es Cindy y me pongo en contacto contigo por una solicitud que nos has hecho para participar en un estudio sobre dolor menstrual.

El estudio que estamos realizando investiga la efectividad de la farmacopea china en el tratamiento del dolor menstrual.

A continuación voy a hacerte unas preguntas para evaluar si cumples con los requisitos para participar en el estudio. Toda la información que me proporciones será tratada de modo absolutamente confidencial, y en caso de no cumplir con los requisitos la destruiremos. ¿Estás de acuerdo con que te haga las preguntas?

Respuestas:

- Este es un requisito indispensable para participar en el estudio, por lo que no podemos incluirte. De todas maneras te agradecemos tu interés, y en cualquier caso tienes mi contacto por si algún día necesitas realizarme cualquier consulta. Muchas gracias y hasta pronto

- Felicidades, cumples con lo requisitos para participar en el estudio. A continuación voy a explicarte los siguientes pasos. El estudio tendrá una duración de 4 meses. Durante el estudio realizaremos dos entrevistas presenciales, una al inicio y otra al final. Tendremos una tercera entrevista 2 o 3 semanas después de iniciar la toma de las plantas que podrá ser presencial o telefónica.

  ¿Cuándo tuviste la última menstruación y para cuando esperas la siguiente? Ahora concertaremos la primera entrevista, en ella te explicaré el proceso con más detalle, e iniciaremos a rellenar los impresos para el estudio. En la entrevista evaluaremos el dolor que has tenido en las últimas menstruaciones, y te daré unos impresos para que rellenes cuando tengas la siguiente menstruación, y a partir del último día podrás empezar a tomar las plantas.

  Bien ---, nos vemos entonces el --- de abril, ¿puedes apuntar la dirección? Calle XXX, XX

  Metro
  L1 (Espanya, Rocafort)
  L3 (Espanya, Poble Sec)

  Ferrocarriles Catalanes
  Espanya

  Autobuses
  13-38-50-52-53-55-57-65-91-141

Muchas gracias por participar en el estudio, nos vemos el –---

APPENDIX V – Preliminary assessment of candidates questionnaire

I will ask you some questions to assess whether you are eligible to participate in this study. All information you provide will be treated confidentiality, and if they do not meet the requirements will be destroyed.

Do you agree to answer my questions?

Name _____

Email address _____

Teléfono_____

Have you age of majority? Yes □ No □ ok □
Requirement: Yes
Age: ___
How long is your menstrual cycle normally? ___ ok □
Requirement: between 21 and 35 days long
How long is your menstrual period normally? ___ ok □
Requirement: between 3 and 7 days long
In the past 6 months, how many periods have been painful? __ ok □
Requirement: who have experienced pain in 4 consecutive periods in the last 6 months
Did you visit a gynaecologist for this reason? Yes □ No □
Have you been diagnosed with any gynecological condition? Yes □ No □
Requirement: Not associated with secondary dysmenorrhea
Which? _____ ok □
Are you pregnant? Yes □ No □ ok □
Requirement: No
Do you use intrauterine device (IUD)? Yes □ No □ ok □
Requirement: No
Do you use hormonal contraceptives? Yes □ No □
Requirement: If taking oral contraceptives, have been taking them for at least the last 6 months and agree to continue taking them for the duration of the study.
How long? ___
Requirement: more than 6 months
You agree to keep using this method of contraception as long as duration of the study? Yes □ No □ ok □
Requirement: Yes
Do you agree to use non-hormonal contraceptive measures during the time duration of the study? Yes □ No □ ok □
Requirement: Yes
Have you been diagnosed with any illness? Yes □ No □
Which? _____
Do you take any medication or do any treatment? ¿Which?
_____
Requirement: Must not have been diagnosed with a serious illness ok □
Are you following any TCM treatment? Yes □ No □ ok □
Requirement: No

The candidate meets the Requirements? Yes □ No □

APPENDIX VI – Composition of the formula used in the study

NOMBRE EN PIN YIN	NOMBRE FARMACEÚTICO	Dosis diaria CP (Polvo concentrado)*
F019 - XIAO YAO WAN		
CHAI HU	Radix Bupleurum	395,46
DANG GUI	Radix Angelica sinensis	602,64
BAI SHAO YAO	Radix Paeoniae alba	451,98
BAI ZHU	Radix Atractylodis macrocephalae	602,64
FU LING	Sclerotium Poria cocos	602,64
GAN CAO	Radix et Rizoma Glycyrrhizae uralensis	113,04
CHEN PI	Pericarpium Citri reticulatae	395,46
CHUAN XIONG	Rizoma Ligustici wallichi	602,64
TOTAL XIAO YAO WAN		3766,5
V010 REGULAR LA MENSTRUACIÓN (REGULATE THE PERIOD)		
YU JIN	Radix Curcumae	627,78
CHUANG XIONG	Rizoma Ligustici wallichi	627,78
ZE LAN	Herba Lycopi	627,78
JI XUE TENG	Caulis Spatholobus	627,78
TOTAL REGULAR MENSTRUACIÓN		2511,12
TOTAL DIARIO		**6277,62**

Table VI.1 Composition of the formula used in the study | Photo © Carles Garay, Jordi Sales

*Extraction ratio CP: Fresh Herb 5:1

CHAI HU **Radix Bupleuri** 柴胡	**DANG GUI** **Radix Angelica sinensis** 当归	**BAI SHAO YAO** **Radix Paeoniae alba** 白芍藥	**BAI ZHU** **Rizoma Atractylodis macrocephalae** 白术	**FU LING** **Sclerotium Poria cocos** 茯苓	**GAN CAO** **Radix et Rizoma Glycyrhizae uralensis** 甘草
					
Liberate Biao Removes heat Unlock the Liver Qi Elevate Yang Qi Harmonize Shao Yang	Nourish the Blood Activate theBlood Calm pain Moisten the intestines	Nourishes the Blood Nourishes Liver Yin Regulates the Liver Relieves pain Subdue Liver Yang	Activates Qi Strengthens the Spleen Removes Damp Activates the metabolism of liquids Contains sweating Calms the fetus	Removes Damp Strengthens the Spleen Calms the Shen	Tonify Spleen Qi Tonify and Hydrates Lung Eliminates Phlegm Stop coughing Relieves spasms Relieves pain Eliminates Heat and Toxins Moderate and harmonize and formulas

CHEN PI **Pericarpium Citri reticulatae** **陈皮**	**CHUAN XIONG** **Rizoma Ligustici wallichi** **川芎**	**YU JIN** **Radix Curcumae** **郁金**	**ZE LAN** **Herba Lycopi** **泽兰**	**JI XUE TENG** **Caulis Spatholobus** **鸡血藤**
				
Regulates the Spleen and Lung Qi Eliminate Dampness and Phlegm	Activate Blood and Qi Eliminate wind Analgesic	Activate Blood Eliminates Blood stasis Mobilize the Qi Relieve pain Cool the Blood Eliminate Heat Remove Heart Damp Stimulate bile secretion and treate jaundice	Activate Blood Eliminate Blood stasis Stimulate diuresis Reduce edema	Nourish the Blood Activate Blood Relax the tendons Unlock the meridians

Table VI.2 Functions of materias in the formula used in the study | Photo © Carles Garay, Jordi Sales

APPENDIX VII- Traditional composition of Xiao Yan San

XIAO YAO SAN
Rambling Powder
(xiāo yáo sǎn)
逍遙散

Source: Tai Ping Hui Min He Ji Ju Fang (太平惠民和劑局方**,** Formulary of the Tai Ping Era). Imperial Department of Medicine (1085).

The formula book, "He Ji Ju Fang" was edited by the office of "He Ji Ju" of the Song Dynasty (960-1279). He Ji Ju was an official agency that oversaw the management and business of herbs and herbal formulae during that time. Later, during the year of Shaoxing (A.D. 1136－1141) of later Southern Song, the name of the agency was changed to "Tai Ping Hui Min Ju,太 平惠民局" meaning "office of peaceful benefiting the people". Thereafter the book has been known as "Tai Ping Hui Min He Ji Ju Fang". Fang means formulae. Now, there are ten volumes in existence, and there are three volumes of appendices on general instruction. There are 788 formulae listed in the book.[4]

Formula

Pin Yin Name	Pharmaceutic Name	g. *	%**
CHAI HU	Radix Bupleuri	9,00	14,50
DANG GUI	Radix Angelicae Sinensis	9,00	14,50
BAI SHAO YAO	Radix Paeoniae Lactiflorae	9,00	14,50
BAI ZHU	Rhizoma Atractylodis Macrocephalae	9,00	14,50
FU LING	Sclerotium Poriae Cocos	9,00	14,50
ZHI GAN CAO	Radix Glycyrrhizae Uralensis (honey fried)	6,00	9,00
WEI SHENG JIANG	Rhizoma Zingiberis Officinalis Recens (roasted)	6,00	14,50
BO HE	Herba Menthae Haplocalycis	3,00	4,00
		60	100

* Grams (Bensky, Barolet 1990:147)
** Percentages (Marié 1991:456)

Analysis of Formula

CHIEF HERB
CHAI HU (Radix Bupleuri): Bitter | Slightly cold | Channels: Liver, Gall Bladder, Pericardium, Triple Heather

DEPUTIES
DANG GUI (Radix Angelicae Sinensis): Sweet, pungent | Warm | Channels: Liver, Heart, Spleen

BAI SHAO YAO (Radix Paeoniae Lactiflorae): Bitter, sour | Slightly cold | Channels: liver, Spleen

ASSISTANTS
BAI ZHU (Rhizoma Atractylodis Macrocephalae): Bitter, sweet | Warm | Channels: Spleen, stomach

FU LING (Sclerotium Poriae Cocos): Sweet, bland | Mild | Channels: Heart, spleen, kidney

[4] Joe Hing Kwok Chu. Tai Ping Hui Min He Ji Ju Fang [Internet]. Accessed 2011-09-23. Available at http://alternativehealing.org/tai_ping_hui_min_he_ji_ju_fang.htm

ZHI GAN CAO (Radix Glycyrrhizae Uralensis honey fried): Sweet | Mild | Heart, lung, spleen, stomach

ENVOYS
SHENG JIANG (Rhizoma Zingiberis Officinalis Recens roasted): Pungent | Warm | Lung, spleen, stomach

BO HE (Herba Menthae Haplocalycis): Pungent | Cool | Lung, liver

Preparation and dosis
The original formula is powdered, but this formula could be prepared in two ways: in decoction and powder. For the decoction, boil the ingredients in 1 liter of water and let reduce to 40 cl. Bo He should be added at the end of the decoction. The 40cl should be taken in one day in 3 times.

For preparing powder herbs are picked, they are ground until they are just dust, and 6-9g are taken with warm water 3 times a day.

Acciones
- Smooth the liver
- Tonify Spleen
- Nourish Blood
- Armoniza Hígado y Bazo

Indications
- Oppression of Liver Qi and deficiency of Blood
- Disharmony between Liver and Spleen due to excessive control of Liver over Spleen

Symptoms[5]
- Amenorrea
- Anemia
- Bitter taste
- Bloating
- Chronic hepatitis
- Digestive disorders
- Dizziness
- Dysmenorrhea
- Fatigue
- Fibrocystic breast
- Functional sterility
- Gastritis
- Headache
- Hiccup
- Irregular menstruation
- Leukorrhea
- Menorrhagia

[5] Xiao Yao San [Internet] Accessed 2011-09-26. Available at http://www.tcmassistant.com/search/index.asp?stype=f1

- Pain of the hypochondrium
- Peptic ulcer
- Poor appetite
- Premenstrual síndrome
- Dry mouth
- Dry throat
- Hypoglycemia
- Nervous breakdown
- Pleurisy
- Poor vision
- Retinitis
- Slight, chronic fever
- Pale-red tongue
- Weak-Wiry pulse (Ruo Xian); Wiry-Empty pulse (Xian Xu)

CHIEF HERB

Chai Hu harmonizes and relieves liver constraint

DEPUTIES

Chai Hu and Bai Shao Yao nourish the blood and soften edginess that results from liver constraint

ASSISTANTS

Bai Zhu and Fu Ling strengthen the spleen and tus its transforming and transporting functions. Zhi Gan Cao tonifies the spleen and combined with Bai Shao Yao moderates the spasmodic abdominal pain.

ENVOYS

Bo He and Sheng Jiang harmonize and control Qi and prevent rebellious Qi. Therefore Bo He helps Chai Hu to relieve liver constraint.

Figure VII.1 Xiao Yao San Hierarchy composition | Photo © Carles Garay, Jordi Sales

APPENDIX VIII – Laboratory quality certificates

Agència de
Protecció de la Salut

REGISTRE SANITARI D'INDÚSTRIES I PRODUCTES ALIMENTARIS DE CATALUNYA
REGISTRO SANITARIO DE INDUSTRIAS Y PRODUCTOS ALIMENTARIOS DE CATALUÑA
(RSIPAC)

D'acord amb la sol·licitud presentada i havent tramitat l'expedient corresponent, ha quedat **REVALIDADA** l'autorització sanitària de funcionament i la inscripció de l'empresa de referència en el Registre sanitari d'indústries i productes alimentaris de Catalunya (RSIPAC), amb les dades següents:

*De conformidad con la solicitud presentada y tramitado el expediente correspondiente, ha quedado **CONVALIDADA** la autorización sanitaria de funcionamiento y la inscripción de la empresa de referencia en el Registro sanitario de industrias y productos alimentarios de Cataluña (RSIPAC), con los datos siguientes:*

IDENTIFICACIÓ DE L'EMPRESA/*IDENTIFICACIÓN DE LA EMPRESA*

Raó social /*razón social*
PLANTAS MEDICINALES DE CATALUNYA SA

NIF
A60386539

Adreça social /*domicilio social*
Rambla Marina, 371 Nave A
08907 L'HOSPITALET DE LLOBREGAT

Adreça industrial /*domicilio industrial*
Rambla Marina, 371 Nave A
08907 L'HOSPITALET DE LLOBREGAT

Núm. RSIPAC: 24.04079/CAT **Núm. RGS: 24.00755/B**

Període de vigència /*Período de vigencia*

Data Inscripció /Fecha inscripción: 04/11/1994
Data revalidació / Fecha convalidación: 14/04/2009
Vàlida fins/Válida hasta: 14/04/2014

ACTIVITATS AUTORITZADES / *ACTIVIDADES AUTORIZADAS*

Clau: 24

Codi	Descripció
02/03	Envasament de condiments i espècies
03/03	Distribució de condiments i espècies
04/03	Emmagatzematge de condiments i espècies
05/03	Importació de condiments i espècies

Generalitat de Catalunya
Departament de Salut

Pàgina 1 de 2

MINISTERIO DE SANIDAD, POLITICA SOCIAL E IGUALDAD

agencia española de seguridad alimentaria y nutrición

MINISTERIO DE SANIDAD Y POLITICA SOCIAL
SUBDIRECCIÓN GENERAL DE GESTIÓN DE RIESGOS ALIMENTARIOS
- 9 FEB 2011
SALIDA Nº 618

SUBDIRECCIÓN GENERAL DE GESTION DE RIESGOS ALIMENTARIOS
REGISTRO GENERAL SANITARIO DE ALIMENTOS

1/1

1.	Nombre o Razon Social **FITOTERAPIA CHINA S.L.**		
2.	Domicilio Social C/ FLORIDABLANCA 18 BARCELONA		BARCELONA
3.	Actividad de la Industria **DISTRIBUCION** **DE COMPLEMENTOS ALIMENTICIOS**		
4.	Domicilio Industrial C/ FLORIDABLANCA 18 BARCELONA		BARCELONA
5.	Clave 26	Categ. / Act./s 0325	Núm. Registro Sanitario **26.12411/B**

De conformidad con lo dispuesto en el articulo segundo del Real Decreto 1712/1991, de 29 de noviembre (B.O.E. de 4 de diciembre), y a tenor de la autorización concedida, ha quedado inscrita la industria de referencia en el Registro General Sanitario de Alimentos con el número arriba indicado.

Madrid, 08 de Febrero de 2011

EL TÉCNICO SUPERIOR

MINISTERIO DE SANIDAD Y POLITICA SOCIAL
REGISTRO GENERAL SANITARIO DE ALIMENTOS

Miguel Ángel Casas Paulet

AREA DE AUTORIZACIONES Y REGISTROS (DIVISION DE GESTION DE RIESGOS)
AGENCIA DE PROTECCION DE LA SALUD
BARCELONA

C/ Alcalá, 56.- 28071 - Madrid
Telf. 91-338.03.96
Fax. 91-338.09.32

APPENDIX IX – Precepts of the law "Law 29/2006, of the 26th of July" of guarantees and rational use of medicaments and health care products

Artículo 51. Medicamentos de plantas medicinales.

1. Las plantas y sus mezclas, así como los preparados obtenidos de plantas en forma de extractos, liofilizados, destilados, tinturas, cocimientos o cualquier otra preparación galénica que se presente con utilidad terapéutica, diagnóstica o preventiva **seguirán el régimen de las fórmulas magistrales, preparados oficinales o medicamentos industriales, según proceda y con las especificidades que reglamentariamente se establezcan**.

2. El Ministerio de Sanidad y Consumo establecerá una lista de plantas cuya venta al público estará restringida o prohibida por razón de su toxicidad.

3. Podrán venderse libremente al público las plantas tradicionalmente consideradas como medicinales y que se ofrezcan sin referencia a propiedades terapéuticas, diagnósticas o preventivas, quedando prohibida su venta ambulante.

En primer lugar tenemos que la legislación estatal regula los medicamentos homeopático como medicamentos legales y autorizados para su fabricación y consumo humano. Asimismo también están permitidas las plantas medicinales incluso su venta libre al público. En este sentido los productos propios de la homeopatía y plantas tradicionalmente consideradas como medicinales tienen su permisión legal. Cosa diferente es su dispensación.

El Artículo 19. **de la citada ley respecto de las Condiciones de prescripción y dispensación de medicamentos, que al respecto previene que :**

1. En la autorización del medicamento, la Agencia Española de Medicamentos y Productos Sanitarios determinará sus condiciones de prescripción clasificándolo, según corresponda, en las siguientes categorías:

Medicamento sujeto a prescripción médica.

Medicamento no sujeto a prescripción médica.

2. Estarán en todo caso sujetos a prescripción médica los medicamentos que se encuentren en alguno de los siguientes supuestos:

Puedan presentar un peligro, directa o indirectamente, incluso en condiciones normales de uso, si se utilizan sin control médico.

Se utilicen frecuentemente, y de forma muy considerable, en condiciones anormales de utilización, y ello pueda suponer, directa o indirectamente, un peligro para la salud.

Contengan sustancias o preparados a base de dichas sustancias, cuya actividad y/o reacciones adversas sea necesario estudiar más detalladamente.

Se administren por vía parenteral, salvo casos excepcionales, por prescripción médica.

3. La Agencia Española de Medicamentos y Productos Sanitarios podrá establecer, en los medicamentos que sólo pueden dispensarse bajo prescripción médica, las siguientes subcategorías:

a. Medicamentos de dispensación bajo prescripción médica renovable o no renovable.

b. Medicamentos sujetos a prescripción médica especial.

c. Medicamentos de dispensación bajo prescripción médica restringida, de utilización reservada a determinados medios especializados.

Reglamentariamente se establecerán los criterios para su aplicación.

La Agencia Española de Medicamentos y Productos Sanitarios podrá calificar como medicamentos no sujetos a prescripción médica aquéllos que vayan destinados a procesos o condiciones que no necesiten un diagnóstico preciso y cuyos datos de evaluación toxicológica, clínica o de su utilización y vía de administración no exijan prescripción médica, de modo que dichos medicamentos puedan ser utilizados para autocuidado de la salud, mediante su dispensación en la oficina de farmacia por un farmacéutico, que informará, aconsejará e instruirá sobre su correcta utilización.

5. Los prospectos y el etiquetado de los medicamentos que no requieran prescripción médica contendrán aquellas advertencias que convengan a su naturaleza y, en especial, las orientadas a prevenir su uso indebido.

6. El Ministerio de Sanidad y Consumo establecerá los requisitos mínimos, características y plazo de validez de las recetas médicas y prescripciones hospitalarias, así como los requisitos especiales para la prescripción y dispensación de los medicamentos de sustancias psicoactivas y otros que por su naturaleza lo requieran o para tratamientos peculiares.

7. La dispensación de medicamentos se ajustará a las condiciones de prescripción establecidas.

En este sentido lo medicamentos homeopáticos son medicamentos cuya dispensa no precisa, de acuerdo con las autoridades sanitarias de receta médica, lo que supone de acuerdo con el precepto estudiado que, por parte del estado pueden ser adquiridas por cualquier ciudadano en una farmacia, y repetimos por cualquier ciudadano. Lo que el homeópata realiza es una recomendación sobre un medicamento homeopático concreto, medicamento que el paciente debe adquirir en una farmacia, dicho medicamento nunca será dispensado por el homeópata. Sin embargo el farmacéutico podrá entregar dicho medicamento sin receta médica y ello porque de acuerdo con la norma estudiada dicho medicamento no se encuentra se encuentren en ninguno de los siguientes supuestos:

Puedan presentar un peligro, directa o indirectamente, incluso en condiciones normales de uso, si se utilizan sin control médico.

Se utilicen frecuentemente, y de forma muy considerable, en condiciones anormales de utilización, y ello pueda suponer, directa o indirectamente, un peligro para la salud.

Contengan sustancias o preparados a base de dichas sustancias, cuya actividad y/o reacciones adversas sea necesario estudiar más detalladamente.

Y porque dicho medicamento homeopático va destinados a procesos o condiciones que no necesitan un diagnóstico preciso y cuyos datos de evaluación toxicológica, clínica o de su utilización y vía de administración no exigen prescripción médica,

de modo que dichos medicamentos pueden ser utilizados para autocuidado de la salud, mediante su dispensación en la oficina de farmacia por un farmacéutico, que informará, aconsejará e instruirá sobre su correcta utilización.

En definitiva, sin someternos a grandes interpretaciones retóricas, sino con una sencilla lectura de las normas estudiadas las conclusiones a las que llegamos son las siguientes:

1. Lo medicamentos homeopáticos están regulados por el Estado así como las plantas medicinales, por tanto son medicamentos que deben reunir una serie de requisitos y autorizaciones para su venta en farmacias.

2. La dispensa de dichos medicamentos es sin receta médica de acuerdo con la ley estatal existente al respecto, por lo que cualquier ciudadano puede comprarlo sin la receta ni recomendación de un profesional sanitario.

La consideración estatal de tales medicamentos, por tanto, es que **van destinados a procesos o condiciones que no necesitan un diagnóstico preciso y cuyos datos de evaluación toxicológica, clínica o de su utilización y vía de administración no exigen prescripción médica, de modo que dichos medicamentos pueden ser utilizados para autocuidado de la salud, mediante su dispensación en la oficina de farmacia por un farmacéutico, que informarán, aconsejará e instruirá sobre su correcta utilización.** Por tanto, un práctico en terapias naturales dedicado a la homeopatía puede, por la legislación existente a fecha de hoy recomendar un medicamento homeopático a un ciudadano, pues este medicamento puede ser adquirido por el ciudadano sin esta previa recomendación, ya que el farmacéutico se lo deberá dispensar tanto en un caso como en otro, porque la legislación estatal permite dicha dispensa sin receta médica, esto es, sin la intervención de un profesional sanitario

Sin más rodeos, llegar a otras conclusiones y hacer juegos semánticos supone alejarse de la **legislación estatal vigente al respecto** y estudiada, pues es clara y ninguna duda ofrece al respecto de los medicamentos homeopáticos.

APPENDIX X – Informed consent

Title of study: Effectiveness of Chinese herbal medicine for the treatment of primary dysmenorrhea: a naturalistic study

Principal investigator: Cindy Méndez Pendavis

My name is Cindy Méndez Pendavis and you are invited to participate in a research clinical trial as part of an MSc course awarded by the University of East London, UK.
The purpose of this study is to investigate the efficacy of Chinese herbal medicine in the treatment of primary dysmenorrhea, that is, pain during menstrual period. I would like to invite you to join this research study.

Procedures

This study will recruit women in reproductive age, with menstrual cycles between 21 to 35 days, menstrual periods of 3 to 7 days, which have experienced pain in 4 consecutive periods in the last 6 months not related to secondary dysmenorrhea and who are not pregnant and agree to take non-hormonal contraceptive measures during the study. Women included in the study, should not be using intrauterine contraceptive device. In order to participate, you should not have been diagnosed with a severe disease that may interfere with the symptoms or with the treatment and you should not be currently receiving treatment with Traditional Chinese Medicine. Participants will take an herbal formulation during three periods. This formulation may be changed after one or two periods if the clinician deems it clinically appropriate. The herbal formulations that will be used in this study are commercialised by Fitoki (www.fitoki.com). In some of the visits the study a photo of the tongue will be taken and the radial pulse will be assessed.

Possible risks or benefits

The herbal formulations used in this study have been used in numerous previous studies and are commercialised in Spain for their consumption in an over the counter basis. No significant side effects have been reported for any of the formulations that will be used in this study. However, some women may experience mild gastrointestinal problems such as discomfort, pain, nausea or vomiting. If you experience any of these or any other symptom, whether or not it is suspected to be associated with the herbal prescription, please contact the researcher Cindy Méndez Pendavis on 647430072 or by email on cindymendez@centreequilibrium.com or contact your doctor for advice. Any symptoms should disappear soon after discontinuing the herbs.

As a participant in this study, there is no direct financial compensation associated with participating in this study. However, all the clinical visits will be free of cost for you and the Chinese herbal formulations will be provided for free during the duration of the study.

Right of refusal to participate and withdrawal

You are free to choose to participate in the study. You may refuse to participate without any loss of benefit that you are otherwise entitled to. You may also withdraw any time from the study without any adverse effect on management.

Confidentiality

The information provided by you will remain confidential. Nobody except Cindy Méndez and her assistant will have access to it. Your name and identity will not be disclosed at any time. However the data may be published in a journal or elsewhere without giving your name or disclosing your identity.

AUTHORIZATION

I have read and understand this consent form, and I volunteer to participate in this research study. I understand that I will receive a copy of this form. I voluntarily choose to participate, but I understand that my consent does not take away any legal rights in the case of negligence or other legal fault of anyone who is involved in this study. I further understand that nothing in this consent form is intended to replace any applicable laws.

I understand that I will receive a copy of this form. I voluntarily choose to participate, but I understand that my consent is not a pound of any legal rights in case of fault or negligence of any other legal entity that is involved in this study. I further understand that nothing in this consent form is intended to replace applicable laws.

Participant's Name (Printed or Typed):
Date:

Principal Investigator's Signature: Cindy Méndez Pendavis
Date:

APPENDIX XI – Organic Law on Data Protection

Pursuant to the provisions of Law 15/1999 of December 13, Protection of Personal Data (PPD) and its implementing regulations, we inform you that your personal data will be included in a file named "Participants dysmenorrhea study " owned by Centre Equilibrium - Sun Si Miao SLL Barcelona in order to maintain the professional relationship with you, and only send information related to the study entitled 'A naturalistic study on the effectiveness of traditional Chinese Pharmacopoeia for the treatment of Primary dysmenorrhea '. You can exercise at any time the right of access, rectification, cancellation and opposition of your personal information, please contact: Centre Equilibrium - Sun Si Miao Barcelona, SLL, c / Castillejos 343, entlo 3 ª, 08025 Barcelona or in the following email address: centreequilibrium@centreequilibrium.com

According: (Name and national identity number)

Date and signature:

APPENDIX XII – Initial menstrual pain questionnaire

Thank you for completing this questionnaire. The information provided by you will remain confidential. Nobody except Cindy Méndez and her assistant will have access to it. Your name and identity will not be disclosed at any time. However, the data may be published in a scientific journal and elsewhere without giving your name or disclosing your identity.
Your collaboration will be very helpful for this study about pain during menstruation.

1. Age:
2. Job:
3. Level of studies:

   No studies □ Primary school □ Secondary school □ University □
4. When was your last visit to the gynaecologist?
5. Were you diagnosed with any disease?
6. Have you ever been pregnant? □ No □ Yes
7. How many children do you have? _____
8. For how many years have you have had your period (approx.)? _____
9. Score in the following scale the intensity of the pain in the last period (circle one)

0	1	2	3	4	5	6	7	8	9	1 0
No pain										**Intense pain**

10. Score in the following scale the mean intensity of the pain in your periods (circle one)

0	1	2	3	4	5	6	7	8	9	1 0
No pain										**Intense pain**

11. Can the pain be relieved with local application of heat? □ No □ Yes
12. How many of your periods have been painful during the last 12 months?

0	1	2	3	4	5	6	7	8	9	1 0	11	12

13. For how many years have you been having painful periods? _____
14. Have you ever visited a gynaecologist for menstrual pain? □ N o □ Yes
15. During menstruation, the pain is located in (mark an X in the correct alternatives):

    Belly □ Lower back □ Thighs (internal side) □

    Tension in breasts □ Other places (specify) _____
16. What is the colour of your menstrual blood today?

Pale	**Vivid red**	**Dark**
(Pink, red, lilac)		(Brown, blackish, purple)

17. How much do you normally bleed?

Scant	**Normal**	**Abundant**
(1 sanitary towel/tampon every 6h or more)	(1 st/t every 3h)	(1 st/t every 1h or less or having to change it during the night)

18. How is your menstrual blood?

Fluid	**Thick**	**With clots**

19. If you had clots, how were they?

Pale	**Red**	**Dark**

Small	**Medium size**	**Large**
(like lentils or rice grains)	(like chickpeas)	(like a date)

20. Before or during menstruation, do you have any of these symptoms? (Mark with X)

Bad temper □ Sadness □

Swollen belly □ Swollen, painful breasts □

Intestinal problems □ (e.g. diarrhoea, dizziness, vomiting . . .)

Other (specify) _____

21. Pain or menstrual cramps usually begin:

Two days before menstruation □ One day before menstruation □

On the same day of menstruation □

Sometimes the day before and sometimes the same day □

22. Do you take medication for pain relief?

□ N o □ Yes what? :

23. How many periods (in the last year)?

0	1	2	3	4	5	6	7	8	9	1 0	11	12

24. Are you relieved by the medication?

No relief □ Slightly relieved □ Fairly relieved □ Very relieved □

25. How many periods (in the last 12 months) did medication succeed in relieving your pain?

0	1	2	3	4	5	6	7	8	9	1 0	11	12

26. Do you need to stop what you are doing because of the pain? □ N o □ Yes

27. How many periods (in one year) do you need to stop what you are doing because of pain? (Circle one)

0	1	2	3	4	5	6	7	8	9	1 0	11	12

28. How long do you abandon what you are doing? (Mark with X)

Less than one hour □ One to 6 hours □ Whole day □

29. When you are not menstruating, do you suffer from any of these? (Mark all that are present)

Cold hands or feet □ Headache □ High blood pressure □

Low back pain □ Neck pain □ Stomach or abdomen pain □

Allergy □ Changes in your cardiac rhythm □

We've finished. Thank you very much for your cooperation. Remember, your data is anonymous and will be treated confidentially.

APPENDIX XIII – Daily menstrual pain questionnaire

Thank you for completing this questionnaire. The information provided by you will remain confidential. Nobody except Cindy Méndez and her assistant will have access to it. Your name and identity will not be disclosed at any time. However, the data may be published in a scientific journal and elsewhere without giving your name or disclosing your identity.
Your collaboration will be very helpful for this study about pain during menstruation.

PREMENSTRUAL PERIOD

Did you feel pain in the days before the menstruation? Yes No

Please score the intensity of pain in the days before the menstruation.

0	1	2	3	4	5	6	7	8	9	1 0

No pain **Intense pain**

Can the pain be relieved with local application of heat? Yes No

Please score the intensity of pain according to location.

Abdomen

0	1	2	3	4	5	6	7	8	9	1 0

Lower back

0	1	2	3	4	5	6	7	8	9	1 0

Inner side of the thighs

0	1	2	3	4	5	6	7	8	9	1 0

Tension in breasts

0	1	2	3	4	5	6	7	8	9	1 0

Other - please explain:

0	1	2	3	4	5	6	7	8	9	1 0

Please circle the symptoms you had in the days previous to menstruation

Bad temper	Low mood	Swollen belly	Tension in breasts
Intestinal problems (diarrhoea, dizziness, vomiting …)			Headache
Swollen legs/arms	Dizziness		Other (specify)

DAY 1 of menstruation
Please circle your answers for every one of the questions below

What was the colour of your menstrual blood today?

Pale	**Vivid red**	**Dark**
(Pink, red, lilac)		(Brown, blackish, purple)

How much did you bleed today?

Scant	**Normal**	**Abundant**
(1 sanitary towel/tampon every 6h or more)	(1 st/t every 3h)	(1 st/t every 1h or less or having to change it during the night)

How was your menstrual blood today?

Fluid	**Thick**	**With clots**

If you had clots, how were they?

Pale	**Red**	**Dark**

Small	**Medium size**	**Large**
(like lentils or rice grains)	(like chickpeas)	(like a date)

Has your period been painful today? Yes No

Please circle the number that best reflects the intensity of the pain:

0	1	2	3	4	5	6	7	8	9	1 0
No pain										**Intense pain**

Please score the intensity of pain according to location.

Abdomen

0	1	2	3	4	5	6	7	8	9	10

Lower back

0	1	2	3	4	5	6	7	8	9	10

Inner side of the thighs

0	1	2	3	4	5	6	7	8	9	10

Tension in breasts

0	1	2	3	4	5	6	7	8	9	10

Other - please explain:

0	1	2	3	4	5	6	7	8	9	10

Can the pain be relieved with local application of heat? Yes No

Please circle the symptoms you have had today

Bad temper	Low mood	Swollen belly	Tension in breasts

Intestinal problems (diarrhoea, nausea, vomit…)	Headache

Swollen legs/arms	Dizziness	Other (please specify)

Did you have the need to stop your activities? Yes No

If so, for how long?

Less than 1 hour	Between 1 - 6 hours	Whole day

Has you take medication for pain relief today? Yes No

Have you relieved by the medication?

No relief □ Slightly relieved □ Fairly relieved □ Very relieved □

DAY 2 of menstruation
Please circle your answers for every one of the questions below

What was the colour of your menstrual blood today?

Pale	**Vivid red**	**Dark**
(Pink, red, lilac)		(Brown, blackish, purple)

How much did you bleed today?

Scant	**Normal**	**Abundant**
(1 sanitary towel/tampon every 6h or more)	(1 st/t every 3h)	(1 st/t every 1h or less or having to change it during the night)

How was your menstrual blood today?

Fluid	**Thick**	**With clots**

If you had clots, how were they?

Pale	**Red**	**Dark**

Small	**Medium size**	**Large**
(like lentils or rice grains)	(like chickpeas)	(like a date)

Has your period been painful today? Yes No

Please circle the number that best reflects the intensity of the pain:

0	1	2	3	4	5	6	7	8	9	1 0

No pain **Intense pain**

Please score the intensity of pain according to location.

Abdomen

0	1	2	3	4	5	6	7	8	9	10

Lower back

0	1	2	3	4	5	6	7	8	9	10

Inner side of the thighs

0	1	2	3	4	5	6	7	8	9	10

Tension in breasts

0	1	2	3	4	5	6	7	8	9	10

Other - please explain:

0	1	2	3	4	5	6	7	8	9	10

Can the pain be relieved with local application of heat? Yes No
Please circle the symptoms you have had today

Bad temper	Low mood	Swollen belly	Tension in breasts

Intestinal problems (diarrhoea, nausea, vomit…)	Headache

Swollen legs/arms	Dizziness	Other (please specify)

Did you have the need to stop your activities? Yes No

If so, for how long?

Less than 1 hour	Between 1 - 6 hours	Whole day

Has you take medication for pain relief today? Yes No
Have you relieved by the medication?

No relief □ Slightly relieved □ Fairly relieved □ Very relieved □

DAY 3 of menstruation
Please circle your answers for every one of the questions below

What was the colour of your menstrual blood today?

Pale	**Vivid red**	**Dark**
(Pink, red, lilac)		(Brown, blackish, purple)

How much did you bleed today?

Scant	**Normal**	**Abundant**
(1 sanitary towel/tampon every 6h or more)	(1 st/t every 3h)	(1 st/t every 1h or less or having to change it during the night)

How was your menstrual blood today?

Fluid	**Thick**	**With clots**

If you had clots, how were they?

Pale	**Red**	**Dark**

Small	**Medium size**	**Large**
(like lentils or rice grains)	(like chickpeas)	(like a date)

Has your period been painful today? Yes No

Please circle the number that best reflects the intensity of the pain:

0	1	2	3	4	5	6	7	8	9	1 0

No pain **Intense pain**

Please score the intensity of pain according to location.

Abdomen

0	1	2	3	4	5	6	7	8	9	10

Lower back

0	1	2	3	4	5	6	7	8	9	10

Inner side of the thighs

0	1	2	3	4	5	6	7	8	9	10

Tension in breasts

0	1	2	3	4	5	6	7	8	9	10

Other - please explain:

0	1	2	3	4	5	6	7	8	9	10

Can the pain be relieved with local application of heat? Yes No

Please circle the symptoms you have had today

Bad temper	Low mood	Swollen belly	Tension in breasts

Intestinal problems (diarrhoea, nausea, vomit…)	Headache

Swollen legs/arms	Dizziness	Other (please specify)

Did you have the need to stop your activities? Yes No

If so, for how long?

Less than 1 hour	Between 1 - 6 hours	Whole day

Has you take medication for pain relief today? Yes No

Have you relieved by the medication?

No relief □ Slightly relieved □ Fairly relieved □ Very relieved □

DAY 4 of menstruation
Please circle your answers for every one of the questions below

What was the colour of your menstrual blood today?

Pale (Pink, red, lilac)	**Vivid red**	**Dark** (Brown, blackish, purple)

How much did you bleed today?

Scant (1 sanitary towel/tampon every 6h or more)	**Normal** (1 st/t every 3h)	**Abundant** (1 st/t every 1h or less or having to change it during the night)

How was your menstrual blood today?

Fluid	**Thick**	**With clots**

If you had clots, how were they?

Pale	**Red**	**Dark**

Small (like lentils or rice grains)	**Medium size** (like chickpeas)	**Large** (like a date)

Has your period been painful today? Yes No

Please circle the number that best reflects the intensity of the pain:

0	1	2	3	4	5	6	7	8	9	1 0

No pain **Intense pain**

Please score the intensity of pain according to location.

Abdomen

0	1	2	3	4	5	6	7	8	9	10

Lower back

0	1	2	3	4	5	6	7	8	9	10

Inner side of the thighs

0	1	2	3	4	5	6	7	8	9	10

Tension in breasts

0	1	2	3	4	5	6	7	8	9	10

Other - please explain:

0	1	2	3	4	5	6	7	8	9	10

Can the pain be relieved with local application of heat? Yes No

Please circle the symptoms you have had today

Bad temper	Low mood	Swollen belly	Tension in breasts

Intestinal problems (diarrhoea, nausea, vomit…)	Headache

Swollen legs/arms	Dizziness	Other (please specify)

Did you have the need to stop your activities? Yes No

If so, for how long?

Less than 1 hour	Between 1 - 6 hours	Whole day

Has you take medication for pain relief today? Yes No

Have you relieved by the medication?

No relief □ Slightly relieved □ Fairly relieved □ Very relieved □

DAY 5 of menstruation
Please circle your answers for every one of the questions below

What was the colour of your menstrual blood today?

Pale	**Vivid red**	**Dark**
(Pink, red, lilac)		(Brown, blackish, purple)

How much did you bleed today?

Scant	**Normal**	**Abundant**
(1 sanitary towel/tampon every 6h or more)	(1 st/t every 3h)	(1 st/t every 1h or less or having to change it during the night)

How was your menstrual blood today?

Fluid	**Thick**	**With clots**

If you had clots, how were they?

Pale	**Red**	**Dark**

Small	**Medium size**	**Large**
(like lentils or rice grains)	(like chickpeas)	(like a date)

Has your period been painful today? Yes No

Please circle the number that best reflects the intensity of the pain:

0	1	2	3	4	5	6	7	8	9	1 0

No pain **Intense pain**

Please score the intensity of pain according to location.

Abdomen

0	1	2	3	4	5	6	7	8	9	10

Lower back

0	1	2	3	4	5	6	7	8	9	10

Inner side of the thighs

0	1	2	3	4	5	6	7	8	9	10

Tension in breasts

0	1	2	3	4	5	6	7	8	9	10

Other - please explain:

0	1	2	3	4	5	6	7	8	9	10

Can the pain be relieved with local application of heat? Yes No

Please circle the symptoms you have had today

Bad temper	Low mood	Swollen belly	Tension in breasts

Intestinal problems (diarrhoea, nausea, vomit…)	Headache

Swollen legs/arms	Dizziness	Other (please specify)

Did you have the need to stop your activities? Yes No

If so, for how long?

Less than 1 hour	Between 1 - 6 hours	Whole day

Has you take medication for pain relief today? Yes No

Have you relieved by the medication?

No relief □ Slightly relieved □ Fairly relieved □ Very relieved □

DAY 6 of menstruation
Please circle your answers for every one of the questions below

What was the colour of your menstrual blood today?

Pale	**Vivid red**	**Dark**
(Pink, red, lilac)		(Brown, blackish, purple)

How much did you bleed today?

Scant	**Normal**	**Abundant**
(1 sanitary towel/tampon every 6h or more)	(1 st/t every 3h)	(1 st/t every 1h or less or having to change it during the night)

How was your menstrual blood today?

Fluid	**Thick**	**With clots**

If you had clots, how were they?

Pale	**Red**	**Dark**

Small	**Medium size**	**Large**
(like lentils or rice grains)	(like chickpeas)	(like a date)

Has your period been painful today? Yes No

Please circle the number that best reflects the intensity of the pain:

0	1	2	3	4	5	6	7	8	9	1 0

No pain **Intense pain**

Please score the intensity of pain according to location.

Abdomen

0	1	2	3	4	5	6	7	8	9	10

Lower back

0	1	2	3	4	5	6	7	8	9	10

Inner side of the thighs

0	1	2	3	4	5	6	7	8	9	10

Tension in breasts

0	1	2	3	4	5	6	7	8	9	10

Other - please explain:

0	1	2	3	4	5	6	7	8	9	10

Can the pain be relieved with local application of heat? Yes No
Please circle the symptoms you have had today

Bad temper	Low mood	Swollen belly	Tension in breasts

Intestinal problems (diarrhoea, nausea, vomit…)	Headache

Swollen legs/arms	Dizziness	Other (please specify)

Did you have the need to stop your activities? Yes No

If so, for how long?

Less than 1 hour	Between 1 - 6 hours	Whole day

Has you take medication for pain relief today? Yes No
Have you relieved by the medication?

No relief □ Slightly relieved □ Fairly relieved □ Very relieved □

DAY 7 of menstruation
Please circle your answers for every one of the questions below

What was the colour of your menstrual blood today?

Pale (Pink, red, lilac)	**Vivid red**	**Dark** (Brown, blackish, purple)

How much did you bleed today?

Scant (1 sanitary towel/tampon every 6h or more)	**Normal** (1 st/t every 3h)	**Abundant** (1 st/t every 1h or less or having to change it during the night)

How was your menstrual blood today?

Fluid	**Thick**	**With clots**

If you had clots, how were they?

Pale	**Red**	**Dark**

Small (like lentils or rice grains)	**Medium size** (like chickpeas)	**Large** (like a date)

Has your period been painful today? Yes No

Please circle the number that best reflects the intensity of the pain:

0	1	2	3	4	5	6	7	8	9	1 0

No pain **Intense pain**

Please score the intensity of pain according to location.

Abdomen

0	1	2	3	4	5	6	7	8	9	10

Lower back

0	1	2	3	4	5	6	7	8	9	10

Inner side of the thighs

0	1	2	3	4	5	6	7	8	9	10

Tension in breasts

0	1	2	3	4	5	6	7	8	9	10

Other - please explain:

0	1	2	3	4	5	6	7	8	9	10

Can the pain be relieved with local application of heat? Yes No

Please circle the symptoms you have had today

Bad temper	Low mood	Swollen belly	Tension in breasts

Intestinal problems (diarrhoea, nausea, vomit…)	Headache

Swollen legs/arms	Dizziness	Other (please specify)

Did you have the need to stop your activities? Yes No

If so, for how long?

Less than 1 hour	Between 1 - 6 hours	Whole day

Has you take medication for pain relief today? Yes No

Have you relieved by the medication?

No relief □ Slightly relieved □ Fairly relieved □ Very relieved □

APPENDIX XIV – Final menstrual pain questionnaire

Thank you for completing this questionnaire. The information provided by you will remain confidential. Nobody except Cindy Méndez and her assistant will have access to it. Your name and identity will not be disclosed at any time. However, the data may be published in a scientific journal and elsewhere without giving your name or disclosing your identity.
Your collaboration will be very helpful for this study about pain during menstruation.

Score the characteristics of your menstruation after the treatment

1. Score in the following scale the intensity of the pain in the last period (circle one)

0	1	2	3	4	5	6	7	8	9	1 0

No pain **Intense pain**

2. Can the pain be relieved with local application of heat? □ No □ Yes

3. During menstruation, the pain is located in (mark an X in the correct alternatives):

Belly □ Lower back □ Thighs (internal side) □

Tension in breasts □ Other places (specify) _____

4. What is the colour of your menstrual blood today?

Pale	**Vivid red**	**Dark**
(Pink, red, lilac)		(Brown, blackish, purple)

5. How much do you normally bleed?

Scant	**Normal**	**Abundant**
(1 sanitary towel/tampon every 6h or more)	(1 st/t every 3h)	(1 st/t every 1h or less or having to change it during the night)

6. How is your menstrual blood?

Fluid	**Thick**	**With clots**

7. If you had clots, how were they?

Pale	**Red**	**Dark**

Small	**Medium size**	**Large**
(like lentils or rice grains)	(like chickpeas)	(like a date)

8. Before or during menstruation, do you have any of these symptoms? (Mark with X)

Bad temper □ Sadness □

Swollen belly □ Swollen, painful breasts □

Intestinal problems □ (e.g. diarrhoea, dizziness, vomiting . . .)

Other (specify) _____

9. Pain or menstrual cramps usually begin:

Two days before menstruation □ One day before menstruation □

On the same day of menstruation □

Sometimes the day before and sometimes the same day □

10. Do you take medication for pain relief?

□ N o □ Yes what? :

11. Are you relieved by the medication?

No relief □ Slightly relieved □ Fairly relieved □ Very relieved □

12. Do you need to stop what you are doing because of the pain? □ N o □ Yes

13. How long do you abandon what you are doing? (Mark with X)

Less than one hour □ One to 6 hours □ Whole day □

14. When you are not menstruating, do you suffer from any of these? (Mark all that are present)

Cold hands or feet □ Headache □ High blood pressure □

Low back pain □ Neck pain □ Stomach or abdomen pain □

Allergy □ Changes in your cardiac rhythm □

We've finished. Thank you very much for your cooperation. Remember, your data is anonymous and will be treated confidentially.

APPENDIX XV – Adverse effects report

No significant side effects have been reported for the formulas used in this study. However, exceptionally, some people may experience gastrointestinal discomfort including nausea, diarrhea or vomiting. If you feel any discomfort suspected to be associated with taking the formulas, please contact Cindy Mendez phone 647430072 or email cindymendez@centreequilibrium.com Any symptoms will reduce or eliminating disappear stopping the oral taking of the formula. Also, thank you for register on the following schedule the day when you experience some discomfort that you suspect may be associated with taking formulas.

MONTH
DAY:
Disconfort:

MONTH
DAY:
Disconfort:

MONTH
DAY:
Disconfort:

MONTH
DAY:
Disconfort:

APPENDIX XVI – Medication report

Thank you for register in the following calendar the day you take any medication during the study, this is important data to analyze the results.

MONTH
DAY:
Type of medication:

MONTH
DAY:
Type of medication:

MONTH
DAY:
Type of medication:

MONTH
DAY:
Type of medication:

MONTH
DAY:
Type of medication:

APPENDIX XVII - Reliability and validity of a questionnaire

The **factors that determine whether a questionnaire is adequate for use** are its reliability and its validity. Martín Arribas defines these parameters in the following way: (Martín Arribas, M.C., 2004).

Reliability: is the degree of precision of the measuring instrument. The reliability of a measuring instrument is assessed through the consistency, temporal stability and interobserver agreement:

- **Consistency**: the degree by which the different questions in the questionnaire relate to each other. There are different statistical methods used to determine this, the most widely used being Cronbach's Alpha Coefficient (which uses a scale between 0 and 1). It is usually considered that there is acceptable internal consistency when the score is greater than 0.7

- **Temporal stability or test-retest reliability**: concordance of the responses and results obtained in a test when the same sample group is assessed by the same assessor in two different situations. This is normally measured with the intra-class correlation coefficient (ICC) and a correlation of 70% indicates that the measuring instrument has acceptable temporal stability.

- **Interobserver reliability**: This can be analysed using the correlation percentage and the Kappa index and represents the degree of consistency obtained when the same sample group is assessed in the same conditions but by two different assessors, or at different times.

- **Validity** is the degree to which a measuring instrument serves the purpose for which is was built, so that it really measures what it is intended to measure. Different types of validity can be described, however, in reality it is a unitary process which allows correct interpretation of point scores obtained from tests and to correlate them with the variable of that which is being measured.

- **Content validity**: Refers to whether the questionnaire and therefore the chosen items in it are indicators of that which is to be measured. This is qualitative assessment done by researchers and experts who must judge the capacity of the questionnaire to assess all the dimensions that need to be measured.

- **Construct validity**: Construct validity is the degree to which the results obtained from the questionnaire may be considered and used as a true measure of the phenomenon being measured. This can be calculated by different methods but the most frequent are factor analysis and the multi-risk - multi-method model.

- **Criterion validity**: Relation between the score of each subject with a *Gold Standard* that guarantees to measure that which it is intended to measure. Reference indicators are not always available, so often, in practice, measuring instruments that have been supported by other studies or research and can offer guarantees for measuring what needs to be measured are used. Depending on the type of variables Pearson's correlation coefficient may be used for quantitative variables and calculation of sensitivity and specificity for qualitative variables.

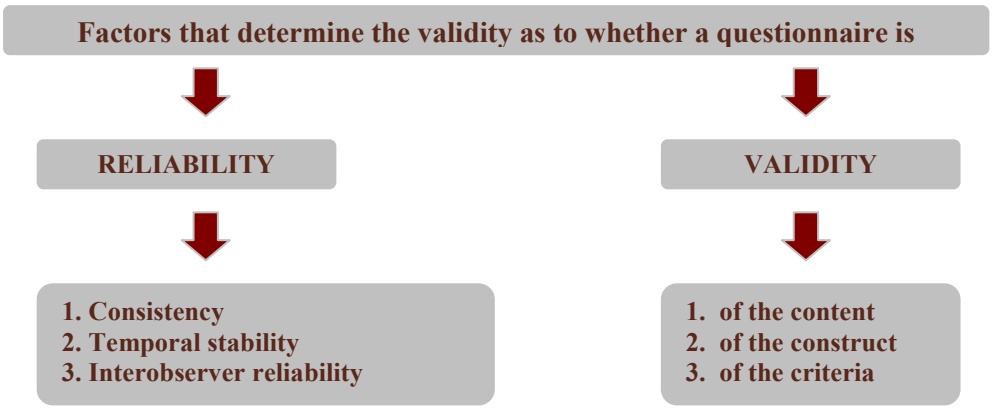


Figure 3.2 Factors that determine the validity of a questionnaire

APPENDIX XVIII– Larroy menstrual pain questionnaire

Thank you for completing this questionnaire. The information provided by you will remain confidential. Your name and identity will not be disclosed at any time. Your collaboration will be very helpful to carry out an epidemiological study on menstrual pain that is conducting the School of Psychology at the Universidad Complutense. Please answer all questions as quickly and accurately as possible. DO NOT HESITATE TO ASK IF IN DOUBT.

DO NOT FILL IN THE QUESTIONNAIRE IF YOU. USE ANY TYPE OF ORAL CONTRACEPTIVES OR IUD OR IF YOU HAVE BEEN DIAGNOSED WITH A GYNECOLOGICAL DISORDER.

1. Age:

2. Job:

3. Number of children:

4. Level of studies:

No studies ❍ Primary school ❍ Secondary school ❍ University ❍

5. For how many years have you have had your period (approx.)?

6. Is your menstruation painful? ❍ N o ❍ Yes

7. Score in the following scale the intensity of the pain in the last period (circle one)

0 1 2 3 4 5 6 7 8 9 1 0

No pain Intense pain

8. Mark with an X on the next line which has been the intensity of pain in the last period

No pain Intense pain

9. How many of your periods have been painful during the last 12 months?

0 1 2 3 4 5 6 7 8 9 1 0

10. For how many years have you been having painful periods? (aprox.)

11. For how many years have you been having painful periods? ❍ N o ❍ Yes

12. During menstruation, the pain is located in (mark an X in the correct alternatives):

Belly ❍ Lower back ❍ Thighs (internal side) ❍

Tension in breasts ❍ Other places (specify) _____

13. Before or during menstruation, do you have any of these symptoms? (Mark with X)

Bad temper ❍ Sadness ❍ Swollen belly ❍

Swollen, painful breasts ❍ Intestinal problems ❍ (e.g. diarrhoea, dizziness, vomiting . . .)

Other (specify) _____

14. Pain or menstrual cramps usually begin:

Two days before menstruation ❍ One day before menstruation ❍

On the same day of menstruation ❍

Sometimes the day before and sometimes the same day ❍

15. Do you take medication for pain relief??

❍ N o ❍ Yes what? :

16. How many periods (in the last year)?

0 1 2 3 4 5 6 7 8 9 1 0 11 12

17. Are you relieved by the medication?

No relief ❍ Slightly relieved ❍ Fairly relieved ❍ Very relieved ❍

18. How many periods (in one year) are you relieved by the medication?

0 1 2 3 4 5 6 7 8 9 1 0 11 12

19. Do you need to stop what you are doing because of the pain? ❍ N o ❍ Yes

20. How many periods (in one year) do you need to stop what you are doing because of pain? (Circle one)

0 1 2 3 4 5 6 7 8 9 1 0 11 12

21. How long do you abandon what you are doing? (Mark with X)

Less than half an hour ❍ Between half an hour and one hour ❍

Between one hour and three ❍ Between three hours and six ❍

Between six hours and one day ❍ More than a day ❍

22. When you are not menstruating, do you suffer from any of these? (Mark all that are present)

Allergy ❍ Headache ❍ High blood pressure ❍

Low back pain ❍ Stomach or abdomen pain ❍ Neck pain ❍

Cold hands or feet ❍

Changes in your cardiac rhythm ❍

23. The table below shows the days of a month. Please indicate with an Me in the table on which day your last period started (if you do not remember exactly, indicate the approximate date) and the days it lasted. Please also appeared on what days you suffer symptoms, each symptom using the symbol below:

Mood changes = M	Belly swelling = B
Chest Swelling = C	Irritability = I
Depression = D	Headache = H
Gastric disorders = G	

For example, if your period started on day 13, marked Me in the box that corresponds to that day, and the following (as well as duration of the period) in the first row, if you had breast swelling and the day before day of menstruation, will mark a signal in the tables for 12 and 13 in the rows corresponding to the symbol P, if in addition, since two days before to two days after the onset of menstruation suffered headaches, will a sign on the tables for the 11, 12, 13, 14 and 15 in the row for the symbol C. Now, please answer the following table appeared on what days of menstruation and the symptoms (if sustained) during the last month (if not remember the exact date, indicate the approximate dates). Write a sign in the row for the appropriate symbol.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
M																															
C																															
D																															
G																															
B																															
I																															
H																															
Me																															

We have finished done. Thank you very much for your cooperation. Remember, your data is anonymous and treated confidentially.

APPENDIX XIXa – Proposal for initial assessment of menstrual pain in PD in TCM questionnaire

Thank you for completing this questionnaire. The information provided by you will remain confidential. Nobody except Cindy Méndez and her assistant will have access to it. Your name and identity will not be disclosed at any time. However, the data may be published in a scientific journal and elsewhere without giving your name or disclosing your identity.

PLEASE DO NOT FILL THE QUESTIONNAIRE IF YOU HAVE BEEN DIAGNOSED WITH A GYCOLOGICAL DISOREDE

Your collaboration will be very helpful for this study about pain during menstruation.

Participant code:

1. Age:

2. Job:

3. Level of studies:

No studies □ Primary school □ Secondary school □ University □

4. When was your last visit to the gynaecologist?

6 months or less □ Between 6 months and 1 year □

Between 1 and 2 years □ More than 2 years □

5. How many times have you been pregnant? _____

6. How many children do you have? _____

7. For how many years have you have had your period (approx.)? _____

8. Score in the following scale the intensity of the pain in the last period (circle one)

0	1	2	3	4	5	6	7	8	9	1 0
No pain										**Intense pain**

9. Score in the following scale the mean intensity of the pain in your periods (circle one)

0	1	2	3	4	5	6	7	8	9	1 0
No pain										**Intense pain**

10. Can the pain be relieved with local application of heat? □ No □ Yes

11. How many of your periods have been painful during the last 12 months?

0	1	2	3	4	5	6	7	8	9	1 0	11	12

12. For how many years have you been having painful periods? _____

13. Have you ever visited a gynaecologist for menstrual pain? □ N o □ Yes

14. During menstruation, the pain is located in (mark an X in the correct alternatives):

Belly □ Lower back □ Thighs (internal side) □

Tension in breasts □ Other places (specify) _____

15. What is the colour of your menstrual blood today?

Pale	**Vivid red**	**Dark**
(Pink, red, lilac)		(Brown, blackish, purple)

16. How much do you normally bleed?

Scant	**Normal**	**Abundant**
(1 sanitary towel/tampon every 6h or more)	(1 st/t every 3h)	(1 st/t every 1h or less or having to change it during the night)

17. How is your menstrual blood?

Fluid	**Thick**	**With clots**

18. If you had clots, how were they?

Pale	**Red**	**Dark**

Small	**Medium size**	**Large**
(like lentils or rice grains)	(like chickpeas)	(like a date)

19. Before or during menstruation, do you have any of these symptoms? (Mark with X)

Bad temper □ Sadness □

Swollen belly □ Swollen, painful breasts □

Intestinal problems □ (e.g. diarrhoea, dizziness, vomiting . . .)

Other (specify) _____

20. Pain or menstrual cramps usually begin:

Two days before menstruation □ One day before menstruation □

On the same day of menstruation □

Sometimes the day before and sometimes the same day □

21. Do you take medication for pain relief?

□ N o □ Yes what? :

22. How many periods (in the last year)?

0	1	2	3	4	5	6	7	8	9	1 0	11	12

23. Are you relieved by the medication?

No relief □ Slightly relieved □ Fairly relieved □ Very relieved □

24. How many periods (in the last 12 months) did medication succeed in relieving your pain?

0	1	2	3	4	5	6	7	8	9	1 0	11	12

25. Do you need to stop what you are doing because of the pain? □ N o □ Yes

26. How many periods (in one year) do you need to stop what you are doing because of pain? (Circle one)

0	1	2	3	4	5	6	7	8	9	1 0	11	12

27. How long do you abandon what you are doing? (Mark with X)

Less than one hour □ One to 6 hours □ Whole day □

28. When you are not menstruating, do you suffer from any of these? (Mark all that are present)

Cold hands or feet □	Headache □	High blood pressure □
Low back pain □	Neck pain □	Stomach or abdomen pain □
Allergy □	Changes in your cardiac rhythm □	

We've finished. Thank you very much for your cooperation. Remember, your data is anonymous and will be treated confidentially.

APPENDIX XIXb – Proposal for daily assessment of menstrual pain in PD in TCM questionnaire

Thank you for completing this questionnaire. The information provided by you will remain confidential. Nobody except Cindy Méndez and her assistant will have access to it. Your name and identity will not be disclosed at any time. However, the data may be published in a scientific journal and elsewhere without giving your name or disclosing your identity.
Your collaboration will be very helpful for this study about pain during menstruation.

PREMENSTRUAL PERIOD

1. Did you feel pain in the days before the menstruation? Yes No

2. If yes, please score the intensity of pain in the days before the menstruation.

0	1	2	3	4	5	6	7	8	9	1 0
No pain										**Intense pain**

3. How many days before the onset of menstruation did you feel pain? _____
4. Please score the intensity of pain according to location.

Abdomen

0	1	2	3	4	5	6	7	8	9	1 0

Lower back

0	1	2	3	4	5	6	7	8	9	1 0

Inner side of the thighs

0	1	2	3	4	5	6	7	8	9	1 0

Tension in breasts

0	1	2	3	4	5	6	7	8	9	1 0

Other - please explain:

0	1	2	3	4	5	6	7	8	9	1 0

5. Please circle the symptoms you had in the days previous to menstruation

Bad temper	Low mood	Swollen belly	Tension in breasts
Intestinal problems (diarrhoea, dizziness, vomiting …)			Headache
Swollen legs/arms	Dizziness		

Other (specify)_____

DAY 1 of menstruation

1. What was the colour of your menstrual blood today?

Pale (Pink, red, lilac)	**Vivid red**	**Dark** (Brown, blackish, purple)

2. How much did you bleed today?

Scant (1 sanitary towel/tampon every 6h or more)	**Normal** (1 st/t every 3h)	**Abundant** (1 st/t every 1h or less or having to change it during the night)

3. How was your menstrual blood today?

Fluid	**Thick**	**With clots**

4. If you had clots, how were they?

Pale	**Red**	**Dark**

Small (like lentils or rice grains)	**Medium size** (like chickpeas)	**Large** (like a date)

5. Has your period been painful today? Yes No

6. If yes, please circle the number that best reflects the intensity of the pain:

0	1	2	3	4	5	6	7	8	9	1 0

No pain **Intense pain**

7. Please score the intensity of pain according to location.

Abdomen

0	1	2	3	4	5	6	7	8	9	10

Lower back

0	1	2	3	4	5	6	7	8	9	10

Inner side of the thighs

0	1	2	3	4	5	6	7	8	9	10

Tension in breasts

0	1	2	3	4	5	6	7	8	9	10

Other - please explain:

0	1	2	3	4	5	6	7	8	9	10

8. Please circle the symptoms you have had today

Bad temper	Low mood	Swollen belly	Tension in breasts

Intestinal problems (diarrhoea, nausea, vomit…)	Headache

Swollen legs/arms	Dizziness

Other (please specify)_____

9. Did you have the need to stop your activities? Yes No

10. If so, for how long?

Less than 1 hour	Between 1 - 6 hours	Whole day

11. Has you take medication for pain relief today? Yes No

What medication? _____ How many tablets? _____ How many grams? _____

12. Have you relieved by the medication?

No relief □ Slightly relieved □ Fairly relieved □ Very relieved □

DAY 2 of menstruation

1. What was the colour of your menstrual blood today?

Pale (Pink, red, lilac)	**Vivid red**	**Dark** (Brown, blackish, purple)

2. How much did you bleed today?

Scant (1 sanitary towel/tampon every 6h or more)	**Normal** (1 st/t every 3h)	**Abundant** (1 st/t every 1h or less or having to change it during the night)

3. How was your menstrual blood today?

Fluid	**Thick**	**With clots**

4. If you had clots, how were they?

Pale	**Red**	**Dark**

Small (like lentils or rice grains)	**Medium size** (like chickpeas)	**Large** (like a date)

5. Has your period been painful today? Yes No

6. If yes, please circle the number that best reflects the intensity of the pain:

0	1	2	3	4	5	6	7	8	9	1 0

No pain **Intense pain**

7. Please score the intensity of pain according to location.

Abdomen

0	1	2	3	4	5	6	7	8	9	10

Lower back

0	1	2	3	4	5	6	7	8	9	10

Inner side of the thighs

0	1	2	3	4	5	6	7	8	9	10

Tension in breasts

0	1	2	3	4	5	6	7	8	9	10

Other - please explain:

0	1	2	3	4	5	6	7	8	9	10

8. Please circle the symptoms you have had today

Bad temper	Low mood	Swollen belly	Tension in breasts

Intestinal problems (diarrhoea, nausea, vomit…)	Headache

Swollen legs/arms	Dizziness

Other (please specify)_____

9. Did you have the need to stop your activities? Yes No

10. If so, for how long?

Less than 1 hour	Between 1 - 6 hours	Whole day

11. Has you take medication for pain relief today? Yes No

What medication? _____ How many tablets? _____ How many grams? _____

12. Have you relieved by the medication?

No relief □ Slightly relieved □ Fairly relieved □ Very relieved □

DAY 3 of menstruation

1. What was the colour of your menstrual blood today?

Pale (Pink, red, lilac)	**Vivid red**	**Dark** (Brown, blackish, purple)

2. How much did you bleed today?

Scant (1 sanitary towel/tampon every 6h or more)	**Normal** (1 st/t every 3h)	**Abundant** (1 st/t every 1h or less or having to change it during the night)

3. How was your menstrual blood today?

Fluid	**Thick**	**With clots**

4. If you had clots, how were they?

Pale	**Red**	**Dark**

Small (like lentils or rice grains)	**Medium size** (like chickpeas)	**Large** (like a date)

5. Has your period been painful today? Yes No

6. If yes, please circle the number that best reflects the intensity of the pain:

0	1	2	3	4	5	6	7	8	9	1 0

No pain **Intense pain**

7. Please score the intensity of pain according to location.

Abdomen

0	1	2	3	4	5	6	7	8	9	10

Lower back

0	1	2	3	4	5	6	7	8	9	10

Inner side of the thighs

0	1	2	3	4	5	6	7	8	9	10

Tension in breasts

0	1	2	3	4	5	6	7	8	9	10

Other - please explain:

0	1	2	3	4	5	6	7	8	9	10

8. Please circle the symptoms you have had today

Bad temper	Low mood	Swollen belly	Tension in breasts

Intestinal problems (diarrhoea, nausea, vomit…)	Headache

Swollen legs/arms	Dizziness

Other (please specify)_____

9. Did you have the need to stop your activities? Yes No

10. If so, for how long?

Less than 1 hour	Between 1 - 6 hours	Whole day

11. Has you take medication for pain relief today? Yes No

What medication? _____ How many tablets? _____ How many grams? _____

12. Have you relieved by the medication?

No relief □ Slightly relieved □ Fairly relieved □ Very relieved □

DAY 4 of menstruation

1. What was the colour of your menstrual blood today?

Pale (Pink, red, lilac)	**Vivid red**	**Dark** (Brown, blackish, purple)

2. How much did you bleed today?

Scant (1 sanitary towel/tampon every 6h or more)	**Normal** (1 st/t every 3h)	**Abundant** (1 st/t every 1h or less or having to change it during the night)

3. How was your menstrual blood today?

Fluid	**Thick**	**With clots**

4. If you had clots, how were they?

Pale	**Red**	**Dark**

Small (like lentils or rice grains)	**Medium size** (like chickpeas)	**Large** (like a date)

5. Has your period been painful today? Yes No

6. If yes, please circle the number that best reflects the intensity of the pain:

0	1	2	3	4	5	6	7	8	9	1 0

No pain **Intense pain**

7. Please score the intensity of pain according to location.

Abdomen

0	1	2	3	4	5	6	7	8	9	10

Lower back

0	1	2	3	4	5	6	7	8	9	10

Inner side of the thighs

0	1	2	3	4	5	6	7	8	9	10

Tension in breasts

0	1	2	3	4	5	6	7	8	9	10

Other - please explain:

0	1	2	3	4	5	6	7	8	9	10

8. Please circle the symptoms you have had today

Bad temper	Low mood	Swollen belly	Tension in breasts

Intestinal problems (diarrhoea, nausea, vomit…)	Headache

Swollen legs/arms	Dizziness

Other (please specify)_____

9. Did you have the need to stop your activities? Yes No

10. If so, for how long?

Less than 1 hour	Between 1 - 6 hours	Whole day

11. Has you take medication for pain relief today? Yes No

What medication? _____ How many tablets? _____ How many grams? _____

12. Have you relieved by the medication?

No relief □ Slightly relieved □ Fairly relieved □ Very relieved □

DAY 5 of menstruation

1. What was the colour of your menstrual blood today?

Pale (Pink, red, lilac)	**Vivid red**	**Dark** (Brown, blackish, purple)

2. How much did you bleed today?

Scant (1 sanitary towel/tampon every 6h or more)	**Normal** (1 st/t every 3h)	**Abundant** (1 st/t every 1h or less or having to change it during the night)

3. How was your menstrual blood today?

Fluid	**Thick**	**With clots**

4. If you had clots, how were they?

Pale	**Red**	**Dark**

Small (like lentils or rice grains)	**Medium size** (like chickpeas)	**Large** (like a date)

5. Has your period been painful today? Yes No

6. If yes, please circle the number that best reflects the intensity of the pain:

0	1	2	3	4	5	6	7	8	9	1 0

No pain **Intense pain**

7. Please score the intensity of pain according to location.

Abdomen

0	1	2	3	4	5	6	7	8	9	10

Lower back

0	1	2	3	4	5	6	7	8	9	10

Inner side of the thighs

0	1	2	3	4	5	6	7	8	9	10

Tension in breasts

0	1	2	3	4	5	6	7	8	9	10

Other - please explain:

0	1	2	3	4	5	6	7	8	9	10

8. Please circle the symptoms you have had today

Bad temper	Low mood	Swollen belly	Tension in breasts

Intestinal problems (diarrhoea, nausea, vomit…)	Headache

Swollen legs/arms	Dizziness

Other (please specify)_____

9. Did you have the need to stop your activities? Yes No

10. If so, for how long?

Less than 1 hour	Between 1 - 6 hours	Whole day

11. Has you take medication for pain relief today? Yes No

What medication? _____ How many tablets? _____ How many grams? _____

12. Have you relieved by the medication?

No relief □ Slightly relieved □ Fairly relieved □ Very relieved □

DAY 6 of menstruation

1. What was the colour of your menstrual blood today?

Pale	**Vivid red**	**Dark**
(Pink, red, lilac)		(Brown, blackish, purple)

2. How much did you bleed today?

Scant	**Normal**	**Abundant**
(1 sanitary towel/tampon every 6h or more)	(1 st/t every 3h)	(1 st/t every 1h or less or having to change it during the night)

3. How was your menstrual blood today?

Fluid	**Thick**	**With clots**

4. If you had clots, how were they?

Pale	**Red**	**Dark**

Small	**Medium size**	**Large**
(like lentils or rice grains)	(like chickpeas)	(like a date)

5. Has your period been painful today? Yes No

6. If yes, please circle the number that best reflects the intensity of the pain:

0	1	2	3	4	5	6	7	8	9	1 0
No pain										**Intense pain**

7. Please score the intensity of pain according to location.

Abdomen

0	1	2	3	4	5	6	7	8	9	10

Lower back

0	1	2	3	4	5	6	7	8	9	10

Inner side of the thighs

0	1	2	3	4	5	6	7	8	9	10

Tension in breasts

0	1	2	3	4	5	6	7	8	9	10

Other - please explain:

0	1	2	3	4	5	6	7	8	9	10

8. Please circle the symptoms you have had today

Bad temper	Low mood	Swollen belly	Tension in breasts

Intestinal problems (diarrhoea, nausea, vomit…)	Headache

Swollen legs/arms	Dizziness

Other (please specify)_____

9. Did you have the need to stop your activities? Yes No

10. If so, for how long?

Less than 1 hour	Between 1 - 6 hours	Whole day

11. Has you take medication for pain relief today? Yes No

What medication? _____ How many tablets? _____ How many grams? _____

12. Have you relieved by the medication?

No relief □ Slightly relieved □ Fairly relieved □ Very relieved □

DAY 7 of menstruation

1. What was the colour of your menstrual blood today?

Pale (Pink, red, lilac)	**Vivid red**	**Dark** (Brown, blackish, purple)

2. How much did you bleed today?

Scant (1 sanitary towel/tampon every 6h or more)	**Normal** (1 st/t every 3h)	**Abundant** (1 st/t every 1h or less or having to change it during the night)

3. How was your menstrual blood today?

Fluid	**Thick**	**With clots**

4. If you had clots, how were they?

Pale	**Red**	**Dark**

Small (like lentils or rice grains)	**Medium size** (like chickpeas)	**Large** (like a date)

5. Has your period been painful today? Yes No

6. If yes, please circle the number that best reflects the intensity of the pain:

0	1	2	3	4	5	6	7	8	9	1 0

No pain **Intense pain**

7. Please score the intensity of pain according to location.

Abdomen

0	1	2	3	4	5	6	7	8	9	10

Lower back

0	1	2	3	4	5	6	7	8	9	10

Inner side of the thighs

0	1	2	3	4	5	6	7	8	9	10

Tension in breasts

0	1	2	3	4	5	6	7	8	9	10

Other - please explain:

0	1	2	3	4	5	6	7	8	9	10

8. Please circle the symptoms you have had today

Bad temper	Low mood	Swollen belly	Tension in breasts

Intestinal problems (diarrhoea, nausea, vomit…)	Headache

Swollen legs/arms	Dizziness

Other (please specify)_____

9. Did you have the need to stop your activities? Yes No

10. If so, for how long?

Less than 1 hour	Between 1 - 6 hours	Whole day

11. Has you take medication for pain relief today? Yes No

What medication? _____ How many tablets? _____ How many grams? _____

12. Have you relieved by the medication?

No relief □ Slightly relieved □ Fairly relieved □ Very relieved □

APPENDIX XIXc – Proposal for final assessment of menstrual pain in PD in TCM questionnaire

Thank you for completing this questionnaire. The information provided by you will remain confidential. Nobody except Cindy Méndez and her assistant will have access to it. Your name and identity will not be disclosed at any time. However, the data may be published in a scientific journal and elsewhere without giving your name or disclosing your identity.

Your collaboration will be very helpful for this study about pain during menstruation.

Score the characteristics of your menstruation after the treatment

1. Score in the following scale the intensity of the pain in the last period (circle one)

0	1	2	3	4	5	6	7	8	9	1 0

No pain **Intense pain**

2. Can the pain be relieved with local application of heat? □ No □ Yes

3. During menstruation, the pain is located in (mark an X in the correct alternatives):

Belly □ Lower back □ Thighs (internal side) □

Tension in breasts □ Other places (specify) _____

4. What is the colour of your menstrual blood today?

Pale	**Vivid red**	**Dark**
(Pink, red, lilac)		(Brown, blackish, purple)

5. How much do you normally bleed?

Scant	**Normal**	**Abundant**
(1 sanitary towel/tampon every 6h or more)	(1 st/t every 3h)	(1 st/t every 1h or less or having to change it during the night)

6. How is your menstrual blood?

Fluid	**Thick**	**With clots**

7. If you had clots, how were they?

Pale	**Red**	**Dark**

Small	**Medium size**	**Large**
(like lentils or rice grains)	(like chickpeas)	(like a date)

8. Before or during menstruation, do you have any of these symptoms? (Mark with X)

Bad temper □ Sadness □

Swollen belly □ Swollen, painful breasts □

Intestinal problems □ (e.g. diarrhoea, dizziness, vomiting . . .)

Other (specify) _____

9. Pain or menstrual cramps usually begin:

Two days before menstruation □ One day before menstruation □

On the same day of menstruation □

Sometimes the day before and sometimes the same day □

10. Do you take medication for pain relief?

□ N o □ Yes what? :

11. Are you relieved by the medication?

No relief □ Slightly relieved □ Fairly relieved □ Very relieved □

12. Do you need to stop what you are doing because of the pain? □ N o □ Yes

13. How long do you abandon what you are doing? (Mark with X)

Less than one hour □ One to 6 hours □ Whole day □

14. When you are not menstruating, do you suffer from any of these? (Mark all that are present)

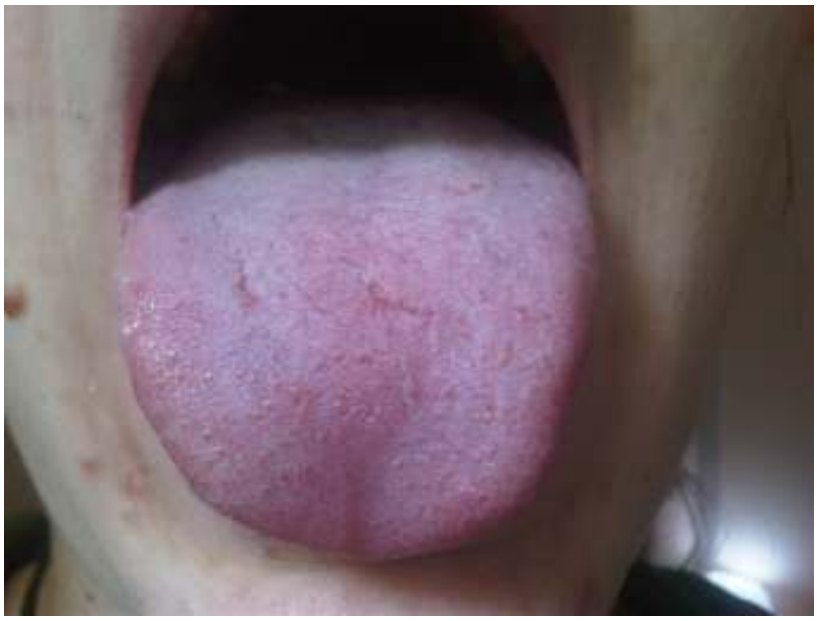
Cold hands or feet □ Headache □ High blood pressure □

Low back pain □ Neck pain □ Stomach or abdomen pain □

Allergy □ Changes in your cardiac rhythm □

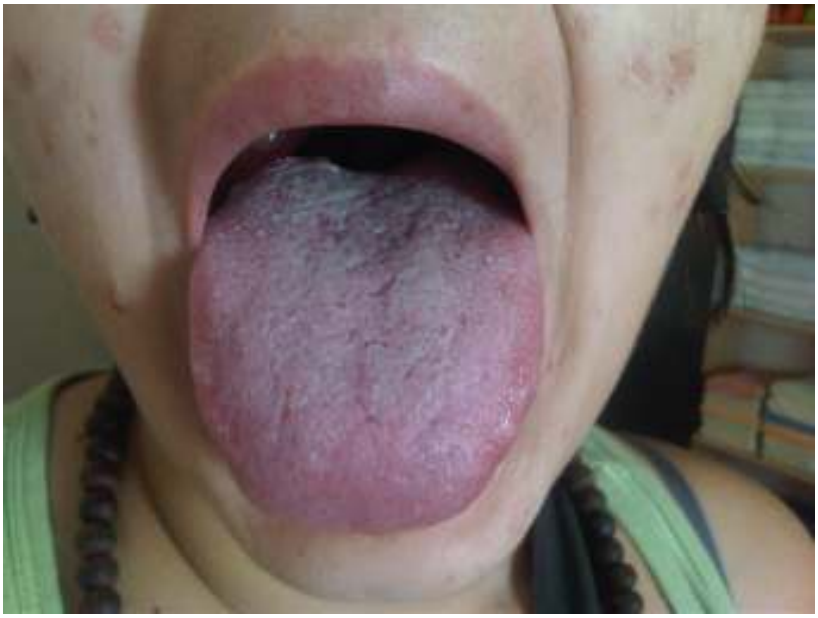
We've finished. Thank you very much for your cooperation. Remember, your data is anonymous and will be treated confidentially.

APPENDIX XX – Tongues and radial pulses of the participants at the beginning and at the end of the study



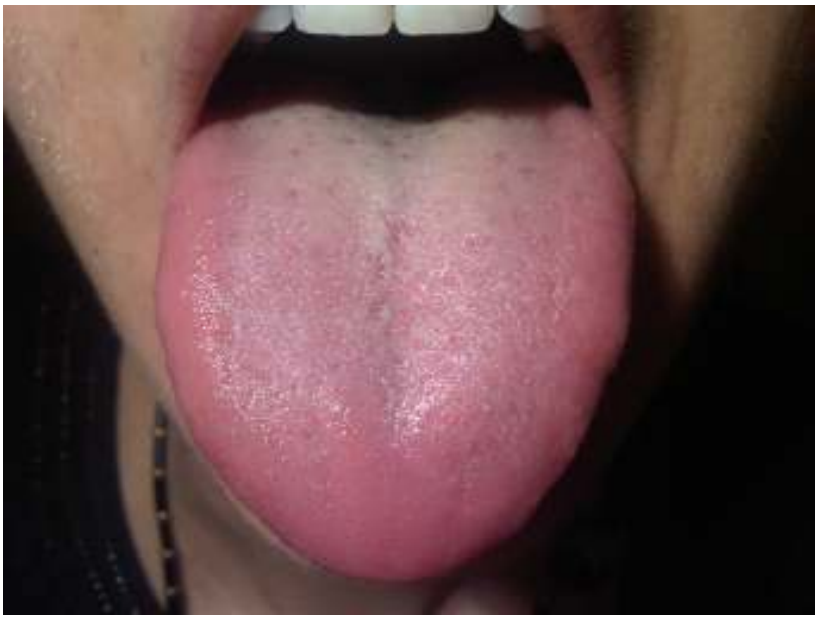
ED-10JN01 First interview

Tongue	Swollen, red, red edges, studded top, red spots on roots, small crack in the tip, thick dry and cracked in the center
Radial Pulse	Little thin and taut, fast



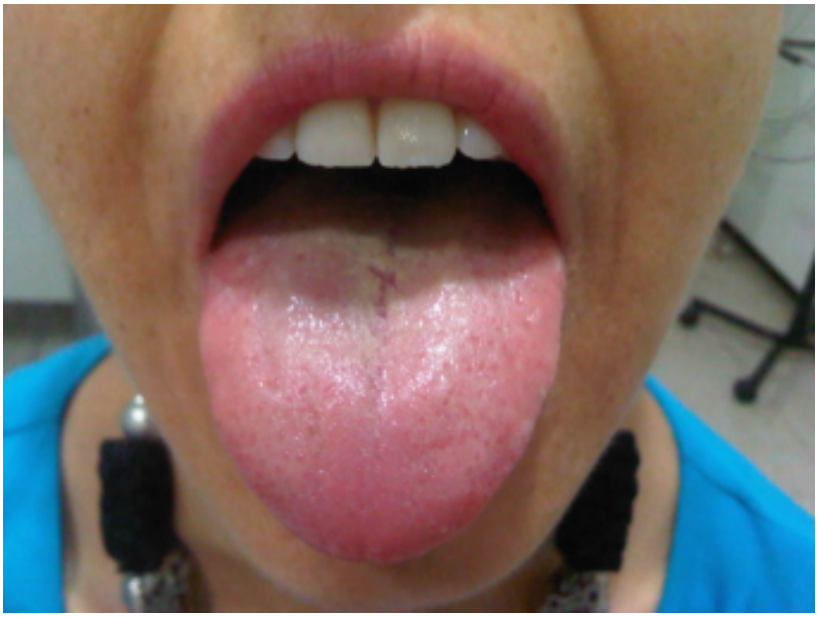
ED-10JN01 Final interview

Tongue	Red, swollen, thick at root, and bristling red tip, red edges
Radial Pulse	Deep, fast, slippery



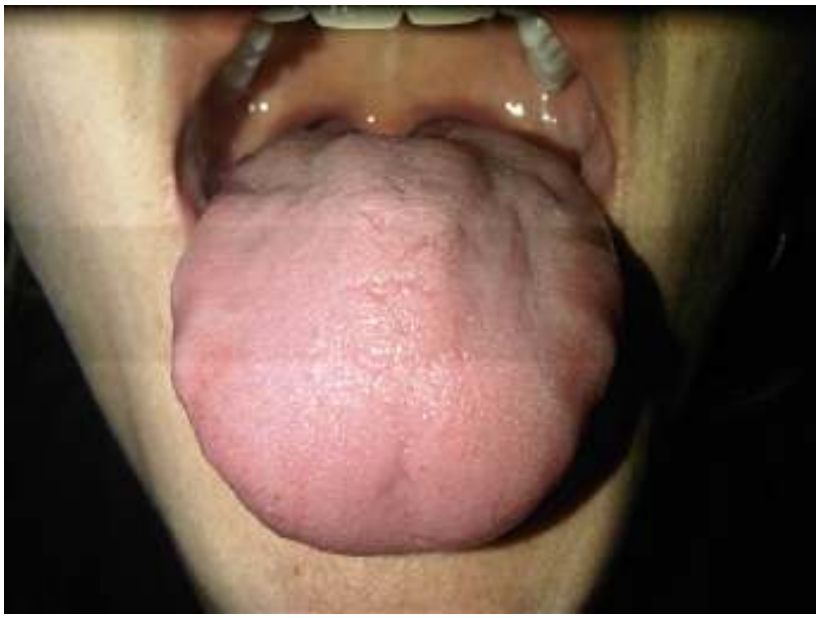
ED-10M01 First interview

Tongue	Swollen, red spots on root, edges red, yellow root layer, strawberry tongue
Radial Pulse	Tense and strongest in the Middle Heater



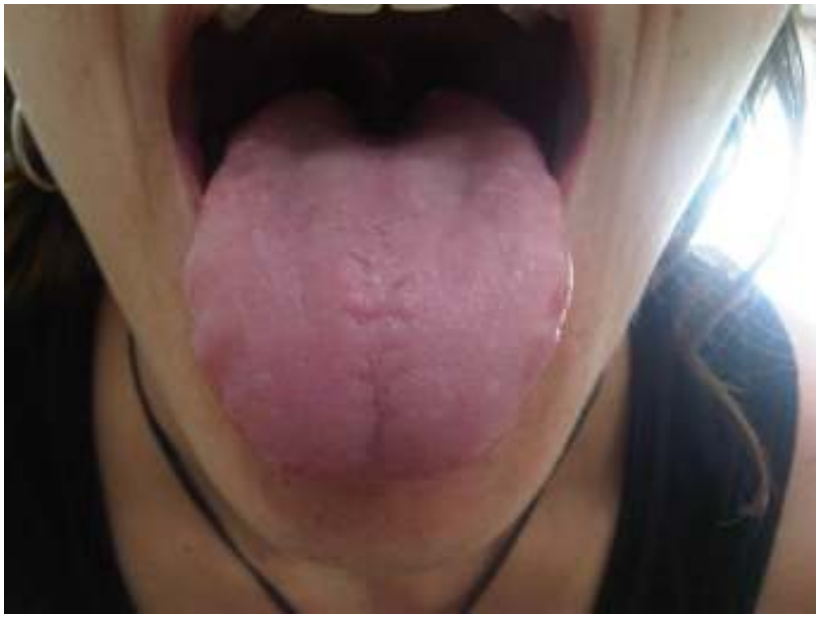
ED-10M01 Final interview

Tongue	Swollen, red edges, red dots across the tongue, thick yellow seborrheic in root
Radial Pulse	Deep on the Right , soft and slightly slippery, slightly tense and tender on the Left



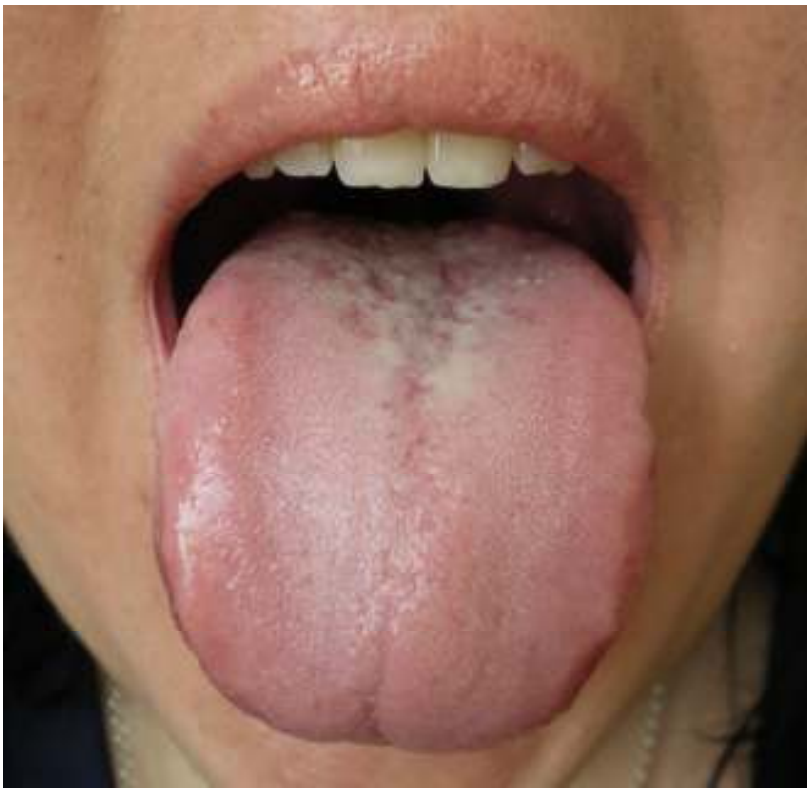
ED-11M01 First interview

Tongue	Pale purple, red edges, teeth marks, swollen, cleft to the tip
Radial Pulse	Tight, thin and fast



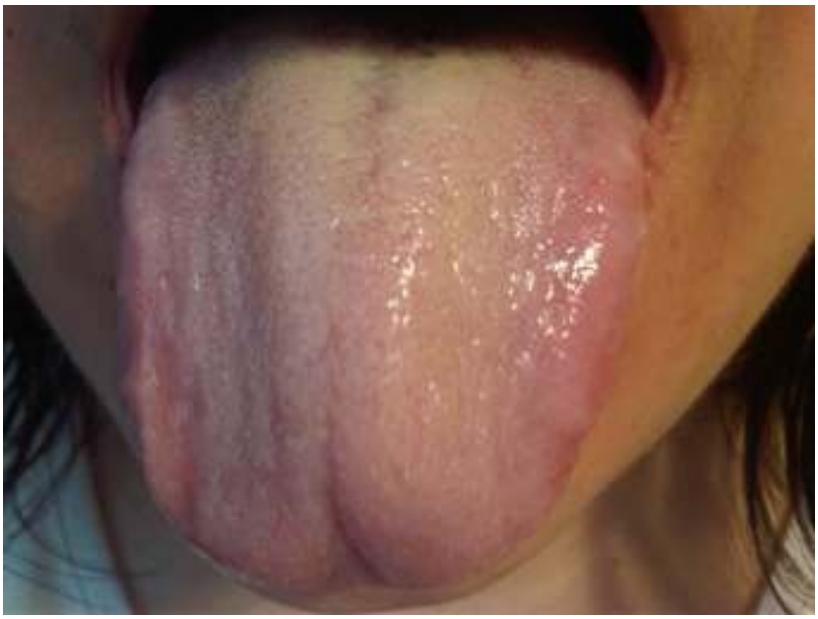
ED-11M01 Final interview

Tongue	Pale-purple, pale edges, teeth marks, swollen edges and anterior portion
Radial Pulse	Thin and slightly tense



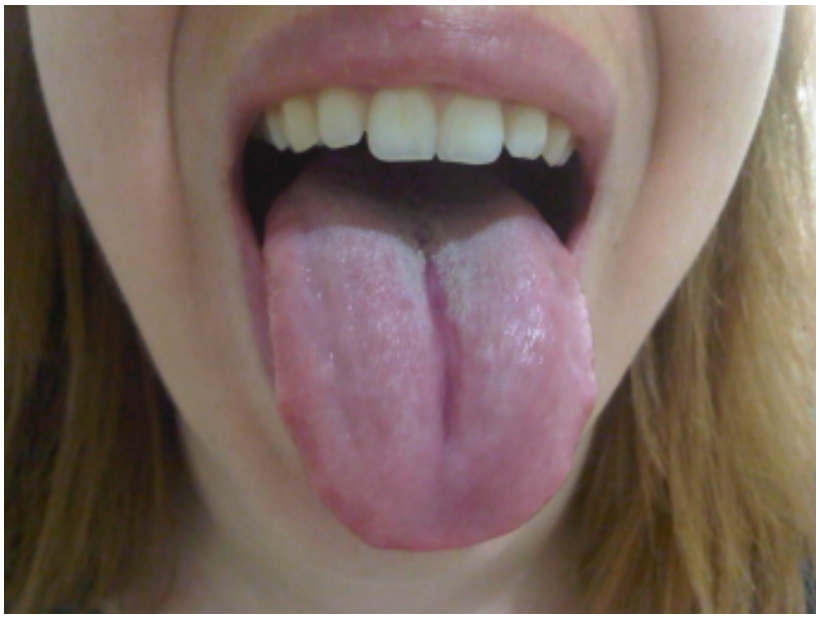
ED-13A01 First interview

Tongue	Swollen, teeth marks, slightly purple, moist, thick at root with red spots
Radial Pulse	Deep, fast, slippery



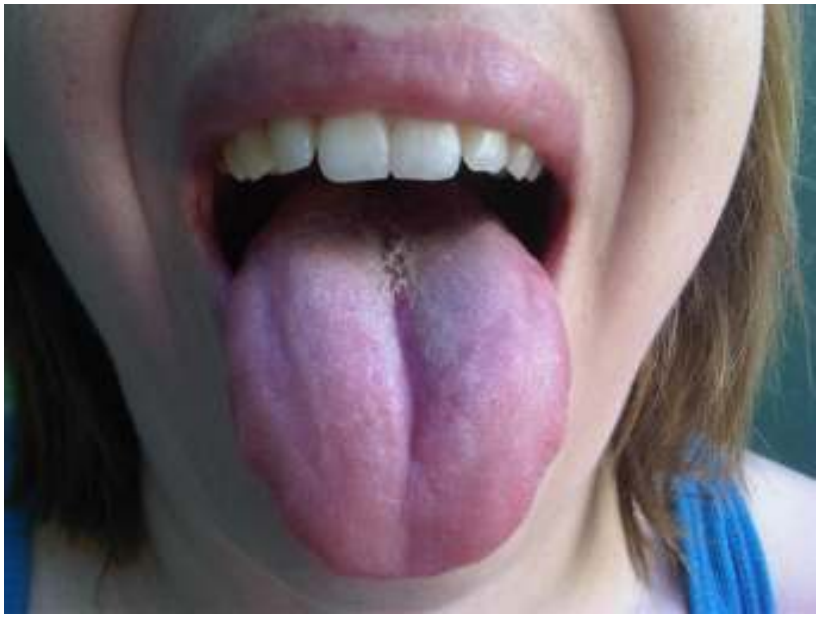
ED-13A01 Final interview

Tongue	Red spots on root, swollen, yellowish thick, teeth marks
Radial Pulse	Deep, fast, slippery



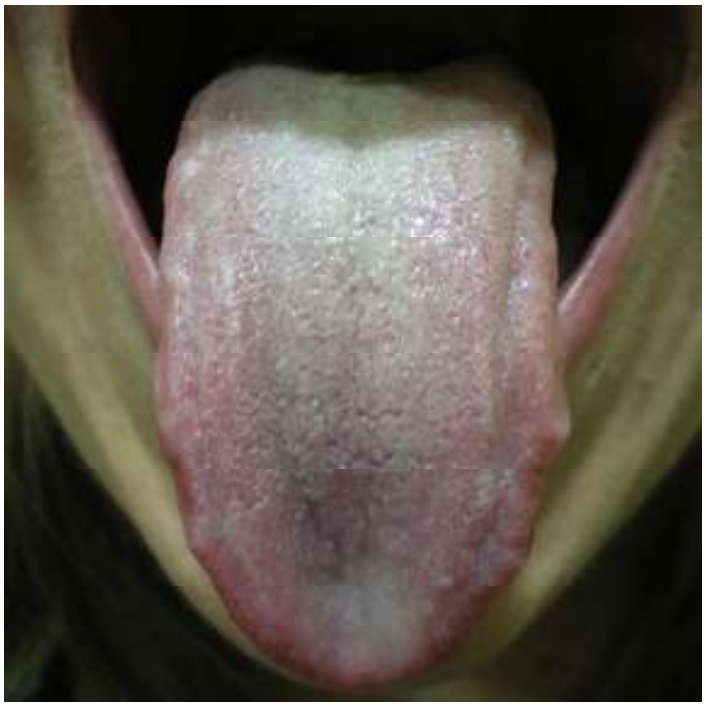
ED-16M01 First interview

Tongue	Red, red spots on root, thick in root, deep central fissure, swollen, teeth marks, red edges
Radial Pulse	Deep, weak, rapid, weak in left Kidney



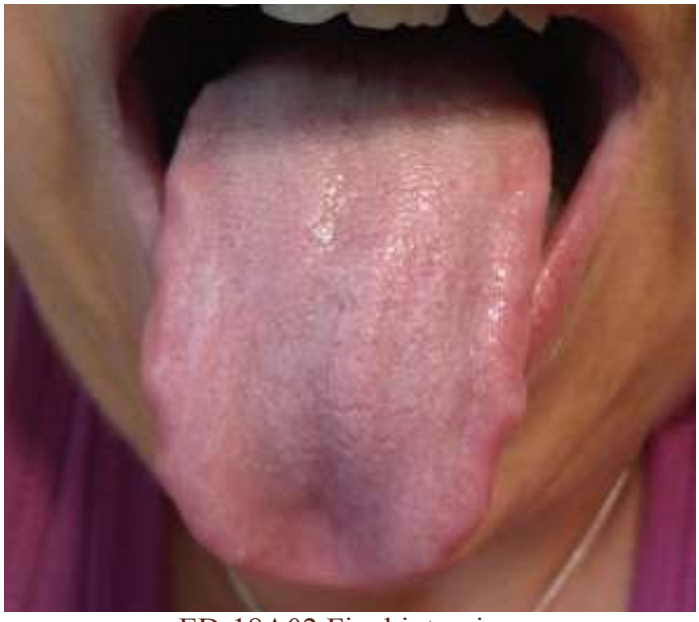
ED-16M01 Final interview

Tongue	Red, red spots on root, thick in root, deep central fissure
Radial Pulse	Deep, soft



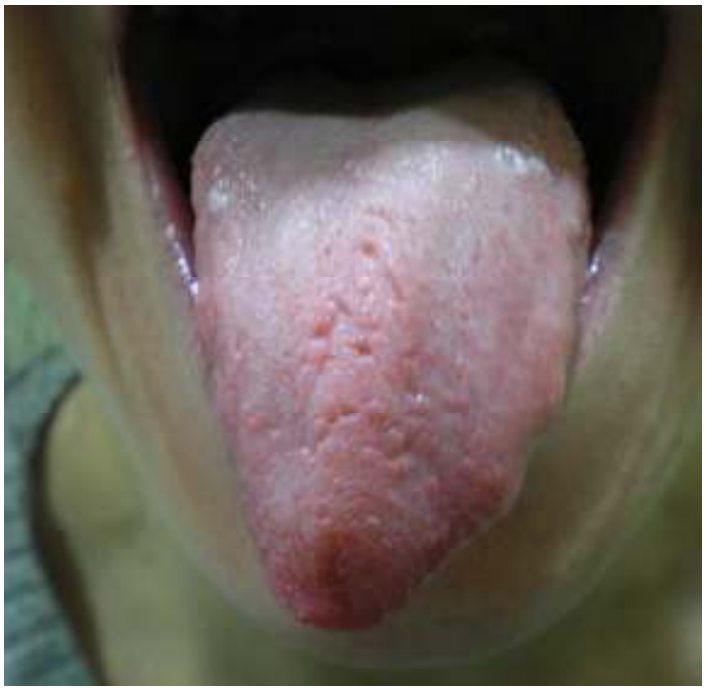
ED-18A02 First interview

Tongue	Red, slightly purple, teeth marks, red edges, depression in tip
Radial Pulse	Weak, deep, short (no Chi barrier)



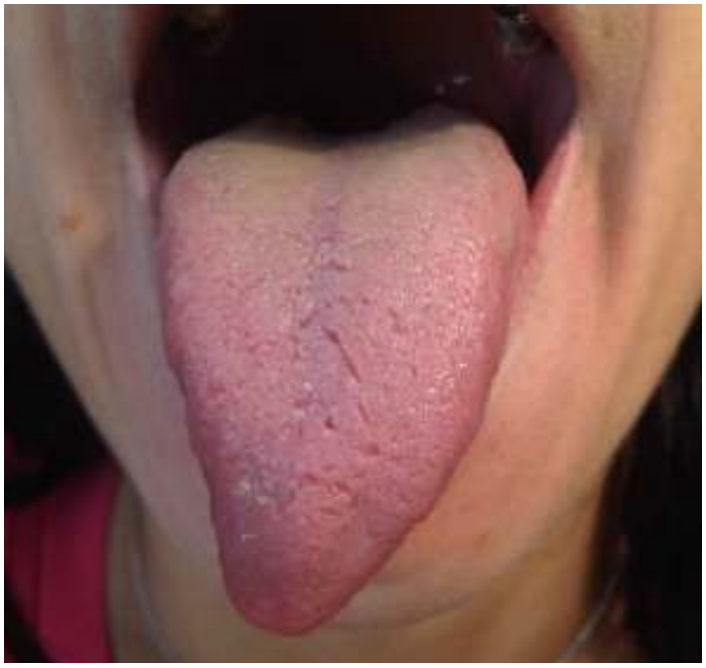
ED-18A02 Final interview

Tongue	Normal color, teeth marks and depression in anterior portion
Radial Pulse	Weak, short (no barrier Chi)



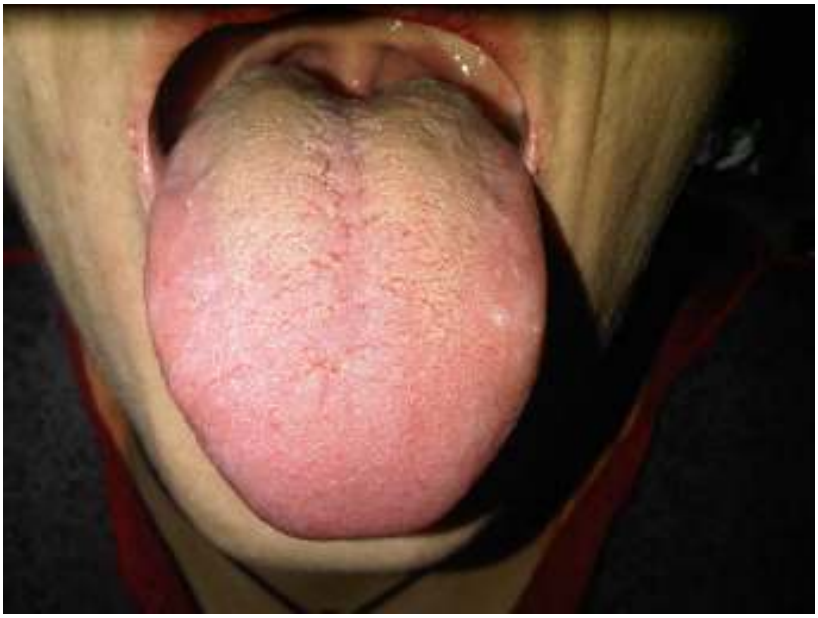
ED-18A03 First interview

Tongue	Normal color, low layer in middle and Upper Heater, swollen, teeth marks, cracks in the center, bristling red tip, root layer with red dots
Radial Pulse	Thin and weak



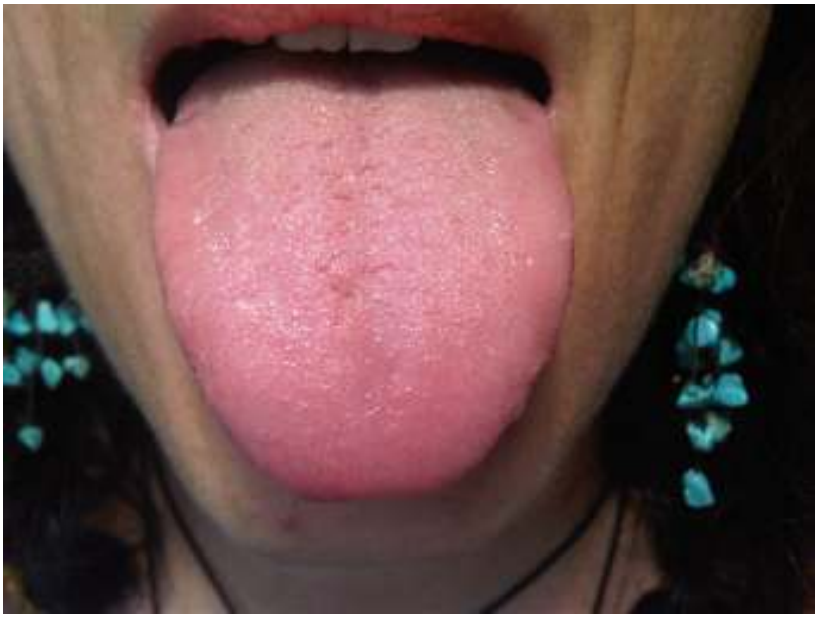
ED-18A03 Final interview

Tongue	Normal color, root layer with red dots, trembling, teeth marks
Radial Pulse	Thin and tight



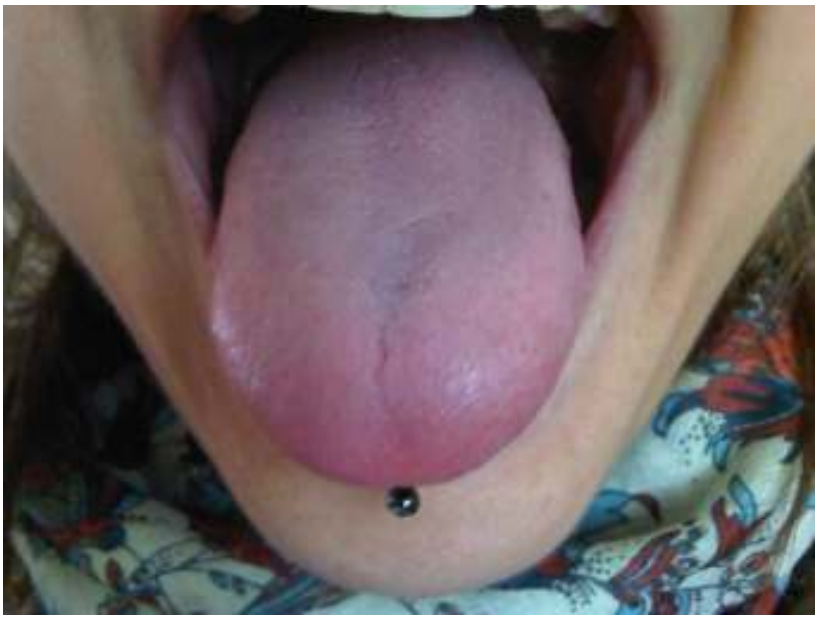
ED-20A01 First interview

Tongue	Red, peeling in Middle and Upper Heater, swollen, puffy edges, root and center cracks
Radial Pulse	Slightly thin, tense



ED-20A01 Final interview

Tongue	Normal color, swollen edges and toe, red spots on root, horizontal fissures, normal layer
Radial Pulse	Fast, tight and thin in Chi barrier

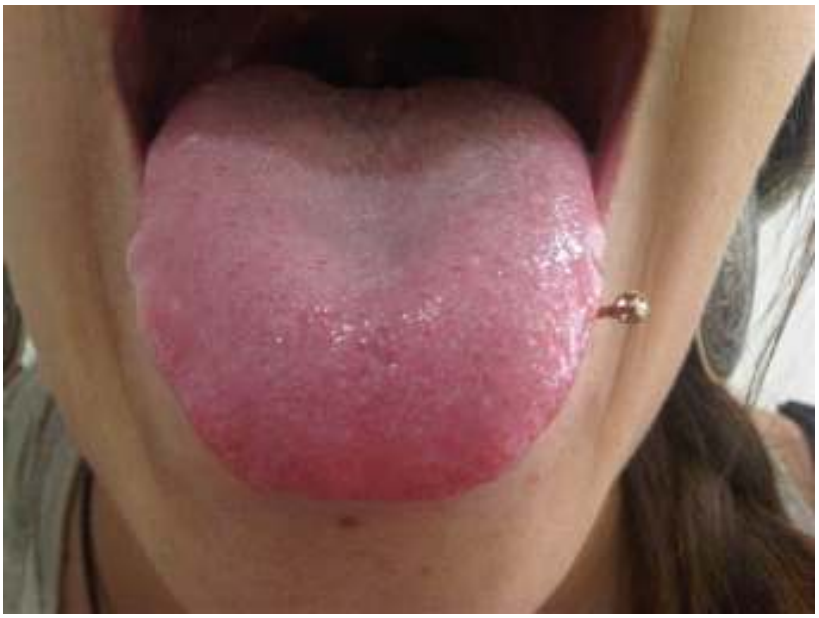


ED-20M01 First interview

Tongue	Normal color, borders and anterior portion more swollen, red spots on edges, tip and anterior
Radial Pulse	Fine and tight, weaker in the left

ED-20M01 Final interview

Tongue	Normal color, borders and anterior portion more swollen, red spots on edges, tip and anterior
Radial Pulse	Fine and tight, weaker on the left



ED-25M01 First interview

Tongue	Slightly pale purple, red edges and tip (especially tip), teeth marks, red spots on root
Radial Pulse	Soft on the Left and fast, tense, deep on the right

ED-25M01 Final interview

Tongue	Pink, thin white layer, thicker in the right, slight teeth marks
Radial Pulse	Fine, slightly faster, rough on the left