

# BUPLEURUM & TANG KUEI FORMULA XIAO YAO WAN

# FREE & EASY WANDERER PLUS FORMULA JIA WEI XIAO YAO SAN

**Bupleurum & Tang Kuei Formula** (*Xiao Yao Wan*), and its most popular modification, **Free & Easy Wanderer Plus** (*Jia Wei Xiao Yao San*), are the most commonly prescribed herbal formulas in the United States and Taiwan. The 900 year old classical formula, **Bupleurum & Tang Kuei Formula** (*Xiao Yao Wan*), comes from *The Formulary of the Pharmacy Service for Benefiting the People in the Tai Ping Era* (*Tai Ping Hui Min He Ji Ju Fang*) published in 1107. Both formulas are a modification of the *Shang Han Lun* formula, Frigid Extremities Powder (*Si Ni San*), published nearly 900 years earlier. As is evident from the **Modern Applications** section below, these two formulas are among the most studied and versatile formulas in all of modern Chinese herbal medicine.

## GENERAL INDICATIONS

Generally speaking, both these formulas are used to treat stress with an underlying spleen qi and blood deficiency. Because of the deficiency component, the stress is likely to become emphasized around menstruation, when less blood is available for circulation and for carrying the qi. Dysmenorrhea, PMS, and stress in general (for men and women alike) are the most common reasons for prescribing these formulas today. Children too, especially those who are under pressure to perform/produce, benefit from taking these formulas. Stress will affect any areas of weakness, but particularly those ruled by the liver or middle burner. These include the chest, the abdomen, the entire digestive tract, and, of course, the blood, which is made in the middle burner and ruled by the liver. Altogether, the central role played by blood and digestion for the rest of the body accounts for the wide range of indications for which these two formulas are used. The chief difference between them is that **Free & Easy Wanderer Plus** (*Jia Wei Xiao Yao San*) is preferred when there are heat signs such as irritability or redness of the eyes or tongue, or where chronic stress in the form of qi stagnation has developed into fire. Both formulas are well-balanced and can be taken for acute situations as well as long-term.

## CHINESE MEDICAL ACTIONS

### Bupleurum & Tang Kuei Formula

1. Harmonizes liver and spleen
2. Strengthens spleen and smooths liver qi
3. Nourishes liver blood
4. Frees constraint

### Free and Easy Wanderer Plus

1. Harmonizes liver and spleen
2. Clears heat and cools blood
3. Invigorates blood and breaks up stasis
4. Strengthens spleen and smooths liver qi
5. Nourishes liver blood
6. Calms *shen*

## BUPLEURUM AND TANG KUEI FORMULA INGREDIENTS

PINYIN	LATIN	ENGLISH	PERCENT OF FORMULA
<i>Chai Hu</i> (chief)	Bupleuri Radix	Bupleurum Root	16.1%
<i>Dang Gui</i> (deputy)	Angelicae Sinensis Radix	Dong Quai, Tang Kuei Root	16.1%
<i>Bai Shao</i> (deputy)	Paeoniae Radix, alba	Chinese White Peony	16.1%
<i>Bai Zhu</i> (assistant)	Atractylodis Macrocephalae Rhizoma	White Atractylodes Rhizome	16.1%
<i>Fu Ling</i> (assistant)	Poria	Poria, Hoelen, Tuckahoe	16.1%
<i>Zhi Gan Cao</i> (assistant)	Glycyrrhizae Radix Preparata	Chinese Licorice Root, honey-fried	8.1%
<i>Gan Jiang</i> (envoy)	Zingiberis Rhizoma	Dried Ginger	8.1%
<i>Bo He</i> (envoy)	Menthae Haplocalysis Herba	Chinese Mint	3.3%

## BUPLEURUM AND TANG KUEI GENERAL INDICATIONS / MODERN APPLICATIONS

- |                                    |                             |  |                                    |
|------------------------------------|-----------------------------|--|------------------------------------|
| • Abdominal distension or bloating | • Bi-polar disorder         | • Climacteric states                     | • Cold extremities with warm torso |
| • Allergies, food                  | • Bitter taste in mouth     | • Chest fullness (not from phlegm- heat) | • Colitis                          |
| • Anemia, various types            | • Breast distension         | • Cholecystitis, chronic                 | • Complexion, sallow               |
| • Anxiety, stress-induced          | • Breast hyperplasia        | • Chronic Fatigue Syndrome               | • Constipation                     |
| • Appetite, poor                   | • Breast lumps, fibrocystic |  | (continued)                        |

### BTK FORMULA ACTIONS

- Harmonizes liver and spleen
- Strengthens spleen and smooths liver qi
- Nourishes liver blood
- Frees constraint

### TONGUE

Pale body, slightly red, especially on the sides.

### PULSE

Wiry or tight, thin or weak, may be rapid.

### CONTRAINDICATIONS

When strong heat signs are present, use **Free & Easy Wanderer Plus** (*Jia Wei Xiao Yao San*) instead. Reduce dose if irritability or digestive disturbance increase while taking this formula.

### DOSAGE

The standard dosage is 2 tablets, 3 times daily to gently correct a chronic issue, but this can be increased at practitioner's discretion up to 5 tabs in a single dose for acute conditions.

### FEW PLUS FORMULA ACTIONS

- Harmonizes liver and spleen
- Clears heat and cools blood
- Invigorates blood and breaks up stasis
- Strengthens spleen and smooths liver qi
- Nourishes liver blood
- Calms *shen*

### TONGUE

Red sides, body may be red or pale.

### PULSE

Wiry or tight, thin or weak, rapid.

### CONTRAINDICATIONS

Use with caution during pregnancy. In cases without signs of heat, use **Bupleurum & Tang Kuei Formula** (*Xiao Yao Wan*) instead.

### DOSAGE

The standard dosage is 2 tablets, 3 times daily to gently correct a chronic issue, but this can be increased at practitioner's discretion up to 5 tabs in a single dose for acute conditions.

## BUPLEURUM & TANG KUEI GENERAL INDICATIONS / MODERN APPLICATIONS (CONTINUED)

- Cough, variant asthma
- Cramping, menstrual
- Depression
- Diarrhea
- Dizziness
- Dry mouth/ throat
- Dysmenorrhea
- Edema
- Emotional instability
- Fatigue, esp. after menstruation
- Hay fever, chronic
- Headache, dull
- Hot flashes
- Hypertension, stress-induced
- Hypochondriac pain
- Impotence
- Infertility
- Insomnia
- Irritability
- Lactation, insufficient
- Libido, low
- Lumbar pain, menstrual
- Menopausal symptoms
- Menstrual pain
- Menstruation, irregular
- Mood swings
- Nausea
- Nervous disposition
- Neurasthenia
- Ovarian cysts
- Palpitations
- Polycystic Ovarian Disorder (PCOD)
- Premenstrual Syndrome (PMS)
- PTSD
- Social interaction, no interest in
- Stools, erratic
- Stress
- Urinary difficulty
- Uterine bleeding, dysfunctional
- Weight loss, unintended

## FREE & EASY WANDERER PLUS INGREDIENTS

PINYIN	LATIN	ENGLISH	% OF FORMULA
<i>Chai Hu</i> (chief)	Bupleuri Radix	Bupleurum Root	12.5%
<i>Dang Gui</i> (deputy)	Angelicae Sinensis Radix	Dong Quai, Tang Kuei Root	12.5%
<i>Bai Shao</i> (deputy)	Paeoniae Radix, alba	Chinese White Peony	12.5%
<i>Bai Zhu</i> (assistant)	Atractylodis Macrocephalae Rhizoma	White Atractylodes Rhizome	12.5%
<i>Fu Ling</i> (assistant)	Poria	Poria, Hoelen, Tuckahoe	12.5%
<i>Zhi Gan Cao</i> (assistant)	Glycyrrhizae Radix Preparata	Chinese Licorice Root, honey-fried	6.25%
Chi Shao (deputy)	Paeoniae Radix, Rubra	Chinese Red Peony	6.25%
<i>Mu Dan Pi</i> (deputy)	Moutan Cortex	Tree Peony Root Bark	6.25%
<i>Zhi Zi</i> (deputy)	Gardeniae Fructus	Gardenia Fruit	6.25%
<i>Yu Jin</i> (deputy)	Curcuma Radix	Turmeric, Curcuma Tuber	6.25%
<i>Yi Mu Cao</i> (deputy)	Leonuri Herba	Chinese Motherwort	6.25%

## FREE & EASY WANDERER PLUS GENERAL INDICATIONS / MODERN APPLICATIONS

Same as *Bupleurum & Tang Kuei Formula* above, with the addition of:

- Acid reflux
- Acne
- Bitter taste (more intense than for BTK)
- Dizziness, visual
- Eyes, red
- Fibromyalgia
- Gastritis, chronic
- Hepatitis, chronic
- Herpes, genital
- Irritable Bowel Syndrome (IBS)
- Indigestion
- Irritability (more intense than for BTK)
- Pelvic inflammatory disease
- Prostatitis, chronic
- Shingles
- Skin rash, red
- Tremors
- Ulcers, peptic or oral

## FORMULA DISCUSSION

The origin formula, Frigid Extremities Powder (*Si Ni San*), is a *Shang Han Lun* formula for treating cold limbs when the qi is stuck in the torso, especially in the chest. Because this is representative of one of the many patterns associated with a liver-spleen disharmony, and because women are especially susceptible to such disharmonies, *Si Ni San*, as well as its many variants, are commonly used to treat disorders marked by qi stagnation or blood deficiency associated with menstruation. The two formulas under discussion in this paper represent the two most popular modifications in modern times. But, as is evident from the **Indications** and **Modern Applications** sections in this monograph, the scope of both these formulas reaches far beyond the gynecological realm.

All liver-spleen disharmonies involve some degree of deficiency (usually in the spleen)

with some degree of excess (usually in the liver). On the continuum of liver-spleen disharmonies, *Si Ni San* addresses a pattern that is primarily excess, but the emphasis of **Bupleurum & Tang Kuei Formula** (*Xiao Yao Wan*) is upon the underlying deficiency, which sets up the issues to become chronic or to repeat month after month. The emphasis of **Free & Easy Wanderer Plus** (*Jia Wei Xiao Yao San*) is more balanced between excess and deficiency, and it includes herbs that address a transformation into fire that can develop from the qi stagnation, as well as herbs that break up stasis where there is a tendency to congeal. Besides applications relating to menses, these 2 formulas were originally used to treat pain in the flanks or hypochondrium, dry mouth and throat, fatigue and poor appetite. Free & Easy Wanderer Plus was a modification specifically to address the liver-spleen disharmony where irritability or other heat signs had developed.

As with any formula that is defined by its ability to “harmonize” any two organs, the strategy of these two formulas is based in *wu xing*/ Five Phase theory. The *ko* cycle (also written as “*ke*” cycle) is the grandmother-grandson or “Control Cycle”. The relationship between spleen and liver is one in which the liver is supposed to control and help regulate the spleen, to keep it running smoothly, the way that gardening tools help keep the soil free from debris, aerated, fresh and fertile. When they are in the right relationship, the regulating function of the liver keeps a smooth flow of qi and blood into the spleen, allowing it to perform its transformation and transportation functions efficiently.

At one end of the liver-spleen disharmony continuum is a liver in extreme excess. The excess of the liver overtakes the spleen or the middle burner in general, causing chest fullness, flank pain, and/or acute digestive distress. The formulas that address the etiology of excess liver are *Si Ni San* (Frigid Extremities Powder), as mentioned above, but also **Shu Gan Formula** (*Shu Gan Wan*) when the excess in the liver is taxing the entire middle burner, or **Chai Hu Shu Gan Formula** (*Chai Hu Shu Gan Tang*) when the liver excess is afflicting the chest or breasts. At the other end of the continuum is a spleen that is so delicate that even normal liver function can prove to be too much for it. The strategy in this case would be simply to strengthen the spleen with formulas such as **Earth-Harmonizing Formula** (*He Tu Pian*), **Astragalus Formula** (*Huang Qi Jian Zhong Tang*) or **Six Gentlemen Formula** (*Liu Jun Zi Tang*).

The two formulas at the center of the present discussion are characterized on this continuum by an underlying weakness of spleen qi as well as a tendency to be blood deficient. In this pattern, under normal circumstances the spleen will still function well enough that the presentation will be subclinical, but when stress causes the liver qi to become stagnant, or when the blood deficiency is intensified by menstruation, the relative state of excess qi stuck in the liver interferes with its support of the spleen and the relationship becomes disharmonious. If this situation repeats enough, or if the stress is severe enough, the qi stagnation can develop into fire, much like the temperature inside a pressure cooker is more intense than in an ordinary pot with the same intensity of flame underneath. If the fire persists,

the situation can further deteriorate into wind, qi clumping (qi nodules), or blood stasis in the abdomen. **Bupleurum & Tang Kuei Formula** (*Xiao Yao Wan*) is for the stage before fire has developed; **Free & Easy Wanderer Plus** (*Jia Wei Xiao Yao San*) addresses the stage when the qi stagnation has turned to fire on up through the initial formation of qi nodules and blood stasis.

### SYNERGY OF INGREDIENTS

Traditionally, the chief herb in these two formulas is thought to be bupleurum (*chai hu*). This is because the acute situation is emerging due to stagnation of liver qi. But there are those who contend that white peony (*bai shao*) and angelica root (*dang gui*) are co-chiefs, since they address the requisite underlying deficiency more directly. During the Han Dynasty, the main function of bupleurum (*chai hu*) was to release constraint in the chest and flanks. This area of the body is governed by the liver, thus, bupleurum (*chai hu*) was classified as a substance for freeing the liver channel. The action of bupleurum (*chai hu*) in this formula is directed specifically upon releasing the diaphragm, a parachute-shaped muscle that attaches to the flanks and the lower ribcage, and articulates on its inferior border with both the spleen and the liver. When the liver qi is stagnant, it is common for the diaphragm to tense up, causing shallow breathing, flank pain, and chest oppression. Interestingly, other herbs in these formulas used to be utilized for chest oppression and flank pain too, but in the last few centuries, these actions have been largely de-emphasized in light of their proven actions in other formulas. Herba menthe (*bo he*) (appearing in **Bupleurum & Tang Kuei Formula** but not in **Free and Easy Wanderer Plus**), has an affinity for the liver, and when prescribed in smaller doses as it is here, was traditionally used to release the diaphragm, while larger doses would take the herba menthe (*bo he*) upward to treat headaches or open the throat. Poria (*fu ling*), back when the *Shen Nong Ben Cao* was written, was commonly used in large doses to release constraint below the heart and in the chest and was often utilized along with bupleurum (*chai hu*) for this purpose. Nowadays, poria (*fu ling*) is primarily seen as a substance that strengthens the spleen and drains dampness. Its inclusion in the formula is therefore doubly justified as an herb that can both free constraint in the liver and support the spleen.

White peony (*bai shao*) is arguably the most important herb in the *materia medica* for freeing liver qi constraint. This may seem to run contrary to its modern classification as a blood-supplementing substance, but the two actions are inseparable when contemplating white peony (*bai shao*). White peony (*bai shao*) has a sour and bitter taste and strongly nourishes liver blood. Like the heart, the liver is a yin organ with a yang function. But whereas the heart's yang function is intimately bound up with the heavenly charge of housing the shen, the liver's yang function is more like a worker bee, just keeping things moving. It courses the qi for the whole body and directs and dispatches blood according to the requirements of the moment. The liver also has the task of detoxifying blood. This process, as with all processes, has a byproduct. The byproduct of blood detoxification is the discharge of this waste material

into the intestines where some substances will be re-absorbed (bile) and others will be defecated. The waste material of any detoxification process, by definition, is toxin; and the form toxin takes when discharged by the liver into the intestines is damp-heat. In order for the liver to perform any of these functions it needs, above all, to remain supple, with ample yin. The yin of the liver is blood.<sup>i</sup> But it is not synonymous with liver blood. “Liver blood” refers to the blood sent by the liver to other areas of the body to nourish and support function. When discussing the blood that nourishes the liver *zang* itself, we call it liver yin. It is blood that nourishes the liver and allows it to function smoothly. When the liver loses some of its intrinsic suppleness, either due to congestion with toxin or from insufficient blood, it can no longer function smoothly and its coursing/regulating action is interrupted: stagnation develops. This is why white peony (*bai shao*) is so important to the liver. As a sour flavored blood tonic, it has an affinity for the liver and is the taste intrinsic to the wood element. It restores the suppleness to the liver by drenching it with blood, thus recovering for it the ability to course the qi smoothly.

Before the *Shang Han Lun*, angelica root (*dang gui*) was primarily used to rectify rebellious qi, especially cough. Later periods noticed that when women took angelica root (*dang gui*) for qi rebellion, their menses became easier and more regular. (Ever since, angelica root (*dang gui*) has been thought of primarily as a gynecological herb, but it can still be found in many formulas that treat cough.) Eventually, herbalists realized that the common denominator between the ability of angelica root (*dang gui*) to rectify rebellion and regulate menses lay in its ability to nourish and move blood in the liver. It is therefore utilized in the two formulas under discussion here to work with white peony (*bai shao*) to keep the liver supple (by nourishing it with blood) and to invigorate the flow of liver blood as it is dispersed throughout the body.

Atractylodes (*bai zhu*) is seen to serve chiefly as working with poria (*fu ling*) to strengthen the spleen. Normally sweetness has the ability to engender fluids, but atractylodes (*bai zhu*) is bitter as well as sweet. It therefore “rescues the spleen” by drying up the dampness that has encumbered it, restricting its function. The other assistant, prepared licorice root (*zhi gan cao*), is very sweet. It functions in these two formulas to fortify the spleen and to engender fluids in order to preserve the liver and other areas from the drying properties of bupleurum (*chai hu*) and atractylodes (*bai zhu*). And since one of the actions of these formulas is to alleviate pain (especially cramps), prepared licorice root (*zhi gan cao*), along with white peony (*bai shao*), can also be seen here as the famous herb duo that relieves spasm.

The fact that dried ginger (*gan jiang*) is considered to act as an envoy in **Bupleurum and Tang Kuei Formula** (*Xiao Yao Wan*) points to the fact that this pattern emphasizes the underlying weakness in the middle burner. But dried ginger is too warm to be included in **Free and Easy Wanderer Plus** (*Jia Wei Xiao Yao San*), which assumes that the qi constraint has already transformed into fire.

The only two ingredients in **Bupleurum and Tang Kuei**

**Formula** (*Xiao Yao Wan*) that do not appear in **Free and Easy Wanderer Plus** (*Jia Wei Xiao Yao San*) are the dried ginger (*gan jiang*) and the mint (*bo he*). There are, however, five ingredients included in the version of **Free and Easy Wanderer Plus** (*Jia Wei Xiao Yao San*) under discussion here which do not appear in **Bupleurum and Tang Kuei Formula** (*Xiao Yao Wan*), all of them deputies and all of them playing a role with the blood and heat components addressed by **Free and Easy Wanderer Plus** (*Jia Wei Xiao Yao San*). Red peony (*chi shao*) clears heat and cools blood, drains liver fire, and helps to break up the clumping that can begin to occur at this advancing stage of the pattern. Mouton (*mu dan pi*) is the root cortex of the peony tree, making three parts of the peony tree utilized in **Free and Easy Wanderer Plus** (*Jia Wei Xiao Yao San*). It reduces swellings, settles liver fire, cools blood, and drains deficiency heat. Curcuma tuber (*yu jin*) brings the heart and gallbladder into the action. It helps to course qi and blood, clears heat, and even opens the heart orifice to quiet *shen* that may have become unsettled from the liver fire. Gardenia (*zhi zi*) clears heat and cools blood. It also drains damp-heat and calms *shen*. Finally, Chinese motherwort (*yi mu cao*) was included to further assist in the invigoration of blood and to augment the formula’s ability to disperse clumps and reduce masses. It is commonly used to simultaneously regulate menses and drain excess dampness through the urine.

## MODERN APPLICATIONS

### Emotional

*Depression*—A meta-analysis was conducted assessing the overall effectiveness of *Jia Wei Xiao Yao San* treating depressive disorders. 14 randomized controlled trials were included in the meta-analysis. Results stated that *Jia Wei Xiao Yao San* is an effective herbal formulation in treating the symptoms of depression. The study stated that it was more effective compared to placebo, and that when combined with western anti-depressant medications, was more effective than the pharmaceuticals alone. Also noted, when Western anti-depressant medications were combined with *Jia Wei Xiao Yao San* versus Western medications alone there were fewer associated side effects like dizziness, headache, dry mouth, constipation, or nausea.<sup>ii</sup>

Another systematic review was conducted to assess the effects of *Xiao Yao Wan* for depression. Electronic databases were searched including *Xiao Yao Wan* against placebos, antidepressants, and combined with antidepressants versus antidepressants alone. Results show that overall *Xiao Yao Wan* appears to be effective at improving the signs and symptoms of depression. *Xiao Yao Wan* had better results than antidepressants using the Hamilton Depression Rating Scale BCX.<sup>iii</sup>

*Anxiety*—*Xiao Yao Wan* and *Jia Wei Xiao Yao San* have anti-anxiety actions according to one study. A study was conducted to investigate the anti-anxiety actions of *Xiao Yao Wan* and *Jia Wei Xiao Yao San* in rats. The study carried out social interaction tests and field tests to observe the effects of the herbal formulations. Results of both *Xiao Yao Wan* and *Jia Wei Xiao Yao San* showed prolonged social interaction time and increased self-care. *Jia Wei Xiao Yao San* displayed better results compared to *Xiao Yao Wan*.<sup>iv</sup>

Another study compared *Jia Wei Xiao Yao San* with the antidepressant / anti-anxiety drug Mirtazaprine. The study lasted five weeks, dividing 87 patients into two groups. Several sleep quality tests were performed to show efficacy of treating generalized anxiety and improved sleep quality. The total effectiveness rate with both groups showing significant improvement was 83.27% for the Mirtazaprine group and 79.54% for the *Jia Wei Xiao Yao San* group. *Jia Wei Xiao Yao San* had fewer adverse events and the events that did occur were milder, while having a similar efficacy to Mirtazaprine.<sup>v</sup>

**Bi-polar Disorder**—A clinical trial was conducted in the treatment of bipolar disorders using *Xiao Yao Wan* in conjunction with Carbamazepine (Tegretol). This combination may be a useful therapy for bipolar patients. The results showed that when treating bipolar-mania and bipolar-depression the clinical response was significantly higher than carbamazepine alone or placebo. While *Xiao Yao Wan* did not cause additional adverse reactions, it was noted that there was increased incidence of dizziness, blurry vision, rash, and nausea with the co-treatment compared to Carbamazepine alone. **Caution:** Close monitoring and dosage adjustment by a Western physician should be used when combining herbs and/or Western medications with Carbamazepine (Tegretol) as they can increase or decrease Carbamazepine levels.<sup>vi</sup>

**Stress**—*Jia Wei Xiao Yao San* was studied to determine its effectiveness to reduce stress-associated behavior. The study was conducted using rats that were exposed to an enhanced single prolonged stress paradigm; after which they were observed in open field test, elevated maze test, and Morris water maze test. The animals marked cognitive impairments and anxious behavior. The tests were repeated again after the administration of high doses of *Jia Wei Xiao Yao San*. The results showed reversed behavior patterns similar to that of unexposed animals.<sup>vii</sup>

**PTSD**—According to one study, *Jia Wei Xiao Yao San* possesses anxiolytic and cognition-improving effects and may be useful for the treatment of post-traumatic stress disorder (PTSD). This study was conducted to determine whether *Jia Wei Xiao Yao San* could relieve stress-associated behavior in rats. The animals were exposed to various enhanced single prolonged stress paradigms creating pronounced anxiety-like behavior and marked cognitive impairment. Repeated treatments of *Jia Wei Xiao Yao San* at high doses reversed behavioral symptoms similar to that of unexposed animals.<sup>viii</sup>

### Gynecological / Menstruation

**Premenstrual Syndrome (PMS)**—A review of Chinese herbal medicine in Taiwan during 1998-2011 showed that *Jia Wei Xiao Yao San* was the most commonly prescribed herbal formula (37.5% of all herbal prescriptions) for premenstrual syndrome (PMS).<sup>ix</sup> A study, with the aim of examining the efficacy of *Jia Wei Xiao Yao San* for treating PMS was administered to 45 patients for three months. Two evaluating methods were used: Vascular age evaluation was measured prior to treatment and at the one and three month markers. The second evaluation was a self-assessment questionnaire.

Results showed that vascular age decreased significantly after the first month, and continued throughout the three months. Significant improvement of PMS signs and symptoms were noted as a result of using *Jia Wei Xiao Yao San*.<sup>x</sup>

**Premenstrual dysphoric disorder**—Premenstrual dysphoric disorder (PMDD) appears as severe depression, irritability, and tension, in women prior to menstruation. Symptoms are more severe than those seen with premenstrual syndrome (PMS). Research was conducted to see the efficacy of *Jia Wei Xiao Yao San*'s ability to treat the symptoms associated with PMDD. 30 patients were treated with the herbal formula for six menstrual cycles. Hamilton depression rating scale and global assessment of functions tests were done before and after to determine effectiveness. The results showed good efficacy for the treatment of PMDD with 46.7% reporting complete remission, 16.7% showing improvement, and 23.3% having no change; an effectiveness rate of 63.4%.<sup>xi</sup>

**Dysmenorrhea**—Dysmenorrhea is a common gynecological condition. A database search showed that *Jia Wei Xiao Yao San* was the second most common herbal prescription used to treat dysmenorrhea.<sup>xii</sup> 58 patients with dysmenorrhea were given modified *Xiao Yao Wan* in a clinical observation study. Of the 58 cases, 28 were between the ages of 13 and 18, 25 were between the ages of 19 and 24, and 5 cases were between the ages of 25 and 30. All cases had dysmenorrhea for a minimum of six months. Herbs were administered starting two to three days prior to menstruation. Herbs were stopped two to three days after pain disappeared. Treatment course was for three consecutive menstrual cycles. Results showed 27 cases cured with no recurrence of pain, 29 cases improved with pain relief, but with recurrence of pain, and 2 cases showed no pain improvement. Total effectiveness rate was 96.55%.<sup>xiii</sup>

**Irregular Menstruation**—*Xiao Yao Wan* was used in a study to treat 50 cases of irregular menstruation. Of the 50 patients, 22 cases were diagnosed as delayed menstruation, 18 cases were diagnosed as early menstruation, and 10 cases were diagnosed as irregular menstruation. Modifications were added for blood stasis, pain, qi deficiency, and liver stagnation. Results showed 31 cases deemed cured, 15 cases showed improvement, and 4 cases showed no effect, with a total effectiveness rate of 92%.<sup>xiv</sup>

**Menopause**—An analysis was conducted encompassing over 54,000 prescriptions for 15,000+ patients to determine the most commonly prescribed Chinese herbal products used to treat menopause in Taiwan. *Jia Wei Xiao Yao San* was the most commonly prescribed herbal formula and considered the core formula for this condition. The most common co-prescription of two herbal formulas included *Jia Wei Xiao Yao San* with *Zhi Bai Di Huang Wan* and the most common addition included *Jia Wei Xiao Yao San* with *dan shen*.<sup>xv</sup>

During the menopausal transition, climacteric syndrome is quite common, presenting as hot flashes, night sweats, headaches, insomnia, depression, anxiety, irritability, etc. A study was conducted to analyze alternative therapies to manage menopausal signs and symptoms. The study compared *Jia Wei Xiao Yao San* with Premelle.<sup>xvi</sup> The results noted that there

was no significant difference between *Jia Wei Xiao Yao San* and Premelle, as both effectively alleviated most menopausal symptoms. *Jia Wei Xiao Yao San*, however, had a lower discontinuation rate due to the adverse effects associated with Premelle. Another study was conducted with 45 patients taking *Jia Wei Xiao Yao San* for four weeks. The results showed that it was effective for 33 patients, decreasing both physical and emotional symptoms. The authors noted that it was especially beneficial for patients with marked psychological symptoms.<sup>xvii</sup>

**Pelvic Inflammatory Disease**—Pelvic Inflammatory Disease (PID), an infection of the female reproductive organs, can be a serious condition resulting in irreversible damage to the uterus, ovaries, fallopian tubes, etc. A clinical observation study was conducted on 98 patients who were randomly divided into a treatment group of 50 patients treated with *Jia Wei Xiao Yao San* and a control group of 48 patients treated with antibiotics. The results showed a total effectiveness rate of 98% for the treatment group and 83.3% for the control group.<sup>xviii</sup>

**Polycystic Ovary Syndrome**—Modified *Jia Wei Xiao Yao San* was used in a recent study to address polycystic ovary syndrome (PCOS) when there was a Traditional Chinese Medicine (TCM) diagnosis of liver stagnation and blood heat. The study observed 73 cases of PCOS broken down into two groups: 37 cases in the treatment group and 36 cases in the control group. The treatment group was prescribed modified *Jia Wei Xiao Yao San* and the control group was prescribed Diane-35, a pharmaceutical. Treatment course consisted of three menstrual cycles. After treatment, regulation of menstrual cycle was roughly equal between the treatment group and control group at 54.05% and 58.33% respectively. Observing three cycles after stopping treatment, normalized menstrual cycles remained at 43.24% of the cases for the treatment group and only 19.44% of the cases for control group, noting the long term effects of using modified *Jia Wei Xiao Yao San* for the treatment of PCOS.<sup>xix</sup>

**Chloasma**—Chloasma (melisma) is a temporary skin condition that occurs due to a hormonal change, as seen in pregnancy, and manifests as large brown patchy pigmentation changes, usually on the face. A clinical efficacy study was conducted on 60 patients with chloasma diagnosed with liver qi stagnation pattern. The patients were divided into a treatment group and control group. Both groups were given oral administration of vitamin E and C. The treatment group was given a *Jia Wei Xiao Yao San* topical mask. The control group was given hydroquinone ointment. 15 days was one course of treatment, with a total of five courses prescribed. The total effectiveness rate was 93.3% for the treatment group and 86.7% for the control group.<sup>xx</sup>

**Infertility**—Modified *Xiao Yao Wan* was used to treat infertility. 25 patients between the ages of 22 through 39 were treated. 14 cases were diagnosed as primary infertility, defined as unable to conceive for greater than one year, and 11 cases were defined as secondary infertility, defined as having a prior pregnancy, but unable to conceive currently. All women were diagnosed with infertility due to liver stagnation. Accompany-

ing signs and symptoms included: PMS, breast tenderness, abdominal pain, cramps during menstruation, depression, and irritability. Treatment efficacy was defined as: cured- no liver stagnation signs and pregnant, effective- no or little liver stagnation signs, but not pregnant, and invalid- no improvement. In the primary infertility group of 14 patients, eight were deemed cured, five were deemed effective, and one was invalid. In the secondary infertility group of 11, five were deemed cured, four were deemed effective, and two were invalid.<sup>xxi</sup>

**Menstrual Headaches**—96 patients with menstrual headaches were treated with modified *Xiao Yao Wan*. Primary modifications were made for blood deficiency, qi deficiency, liver yang rising, blood stasis, and qi stagnation. Treatment course was 14 days. 42 cases were deemed cured, with resolution of symptoms without recurrence for one year. 35 cases marked improvement with resolution of symptoms, but relapsed during the year, 11 cases had effective results with reduced symptoms and duration of headache, and eight cases had no change.<sup>xxii</sup>

**Ovarian Cysts**—Modified *Xiao Yao Wan* was used to treat 36 cases of ovarian cysts. Patients had a TCM diagnosis of liver qi stagnation. The patients ranged in ages from 21 to 45. The cyst sizes ranged from the smallest of 3.0 x 3.6cm to the largest of 5.2 x 6.8cm. Treatment course was 20 days. The outcome of treatment included 28 cases cured, with disappearance of clinical signs and symptoms and cyst disappeared. Three cases were effective with clinical symptoms relieved and a reduction of cyst. Two cases were deemed invalid. The total efficacy was 94.44%.<sup>xxiii</sup>

## Breast

**Breast Proliferation Disease**—Breast proliferation disease is a non-cancerous condition defined by increased growth of specific cells in the breast and is a risk factor for breast cancer. A three month clinical trial was conducted using *Xiao Yao Wan* in combination with **Citrus and Pinellia Formula** (*Er Chen Tang*) for the treatment of breast proliferation disease. There was an overall effectiveness rate of 96.1%, with x-rays showing absorption of proliferation masses in 21 out of the 51 cases. In addition, saliva estradiol, saliva progesterone, and plasma prolactin concentrations declined significantly. No change was noted on saliva testosterone concentrations.<sup>xxiv</sup>

**Breast Hyperplasia**—Breast hyperplasia describes the accumulation of abnormal breast cells and is considered a precancerous condition. In a recent report, 48 cases of breast hyperplasia were treated with a modified version of *Xiao Yao Wan*. Roughly 80% were diagnosed as atypical lobular hyperplasia. All cases were confirmed by mammogram. Common symptoms included breast pain and tenderness that was worse before and after menstruation, and small, hard, cord-like nodules. After three menstrual cycles 24 cases were deemed cured, 20 cases showed improvement, and 2 cases had little or no improvement; a total effectiveness rate of 95.83%.<sup>xxv</sup>

**Breast Cancer**—An analysis of Chinese herbal products for breast cancer was conducted in Taiwan. The results showed that *Jia Wei Xiao Yao San* was the most frequently prescribed herbal formula for treating breast cancer.<sup>xxvi</sup> *Jia Wei Xiao Yao*

*San* was used in combination with chemotherapy in the treatment of patients with breast cancer. 60 patients were divided into two groups of 30 each. The treatment group used *Jia Wei Xiao Yao San* with fluorouracil, doxorubicin, and cyclophosphamide. The control group only used the western medications. The results showed significant improvement in quality of life with a total effectiveness rate of 97% in the treatment group and 57% in the control group. Adverse reactions were dramatically down in the treatment group at 10% compared to 80% in the control group. The treatment survival rate was 100% for the treatment group and 87% for the control group, and the recurrence rate was 3% for the treatment group compared to 23% for the control group. *Jia Wei Xiao Yao San*, when combined with western chemotherapy, can be effective to address quality of life, improve clinical symptoms, and prolong patient survival.<sup>xxvii</sup> A population-based study was conducted on breast cancer patients in Taiwan that were treated with Tamoxifen with and without Chinese herbal formulas in order to determine the risk factor of developing Tamoxifen-induced endometrial cancer. The group of patients that used the combination of Tamoxifen in conjunction with Chinese herbs had a decreased risk of subsequent endometrial cancer. *Jia Wei Xiao Yao San* was the most commonly prescribed herbal formula in the study.<sup>xxviii</sup>

**Hyperprolactinemia**—30 cases of hyperprolactinemia were observed. Patients were given *Xiao Yao Wan* modified with *dan shen*, *ze lan*, *niu xi*, *sheng di huang*, *xiang fu*, and *shi chang pu* for three months. Treatment results showed significant improvement in the formula's ability to reduce serum prolactin levels as well as improve the clinical signs and symptoms. 22 cases were deemed cured; 5 cases showed improvement; 3 cases had no effect; with a total effectiveness rate of 90%.<sup>xxix</sup>

### Men's Health

**Impotence**—A clinical observation of *Xiao Yao Wan* to treat impotence was conducted. 123 cases of erectile dysfunction used modified *Xiao Yao Wan*. Of the 123 patients, ages ranged from 21-54. 56 cases were under 30, 52 cases were from 31-40 years of age, and 15 cases were over 41 years old. A TCM diagnosis of liver qi stagnation with kidney deficiency was given. "Recovery" was defined as satisfactory penile erections and a normal sex life. "Marked improvement" was defined as improved erectile stiffness with difficulty having sex. "Improvement" was defined as penile erections, but unable to perform sexual activity. "Invalid" marks no significant change. Results showed 87 cured/"recovery", 20 with "marked improvement", seven showing "improvement", and 9 "invalid."<sup>xxx</sup>

**Retrograde Ejaculation**—98 cases of retrograde ejaculation were treated with modified *Xiao Yao Wan*. Patients were aged 22 to 47. Clinical symptoms include ejaculation with no sperm and first urination after intercourse was cloudy. All cases were confirmed with lab tests. The formula was a modified version of *Xiao Yao Wan*, with additions for qi deficiency, heat, and blood stasis. The treatment course was 1-4 months. 85 cases were deemed cured. Of the 85 cases, 38 cases were cured in the first month, 32 cases were cured in the second month, and the remaining in the following two months. 11 cases showed im-

provement. Two cases showed no significant improvement.<sup>xxxi</sup>

**Chronic Prostatitis**—*Jia Wei Xiao Yao San* was used in the treatment of 60 cases of chronic prostatitis. Patient ages ranged from 21-73 and were diagnosed with chronic prostatitis. 17 cases were deemed cured, 21 cases showed marked improvement, 19 cases showed some improvement, and three cases had no effect. There was a total effectiveness rate of 95%, showing *Jia Wei Xiao Yao San* to be effective for chronic prostatitis with improvement of clinical symptoms and prostatic fluid examination after treatment.<sup>xxxii</sup>

### Liver

**Fatty Liver Disease**—Modified *Xiao Yao Wan* was used to treat fatty liver disease in a research study of 86 patients. Observation of symptoms, liver function, blood lipid levels, and liver imaging was performed. The results showed a total effectiveness rate of 95.35%. Symptom and liver function improved, showing *Xiao Yao Wan* can be an effective treatment strategy for fatty liver.<sup>xxxiii</sup>

**Hepatitis B**—A study was conducted to observe the clinical efficacy of *Jia Wei Xiao Yao San* to treat hepatitis B. 32 patients with chronic hepatitis B were treated with modified *Jia Wei Xiao Yao San*. Main symptoms included fatigue, abdominal pain and distention, poor appetite, and hypochondriac pain. Liver function tests were also conducted before and after treatment. Treatment course was one month. One to two courses were given. Of the 32 patients, 13 were deemed cured, nine cases improved, and no change in one case; a total effectiveness rate of 96.9%. ALT normalization rate was 90.6%, with 29 of the 32 cases normalizing.<sup>xxxiv</sup>

**Liver Cancer**—A retrospective cohort study was conducted on liver cancer patients to determine whether the combination of TCM with conventional cancer treatment affected survival rate. Close to 25% of the 127,237 patients used TCM. The study showed that patients who used TCM were associated with a decreased risk of death and that TCM may improve survival in liver cancer patients. *Jia Wei Xiao Yao San*, followed closely by *Chai Hu Shu Gan Tang*, were the most effective formulas associated with improved survival.<sup>xxxv</sup>

**Liver Support**—*Jia Wei Xiao Yao San* was used to in a study to investigate its hepatoprotective effects. Rats were given dimethylnitrosamine, inducing chronic hepatitis and hepatic fibrosis. *Jia Wei Xiao Yao San* was shown to inhibit liver fibrosis. These anti-fibrotic effects are partially attributed to the Chinese formulas ability to inhibit lipid peroxidation.<sup>xxxvi</sup>

Hepatoprotective effects of *Xiao Yao Wan* on chronic liver injury were investigated. Rat models of chronic liver injury were given *Xiao Yao Wan* for 45 days. General activity, ALT, AST, TP, ALB, A/G, T-BIL, HyP serum levels, and SOD, MDA, ChE, GSH-PX activities in liver homogenate, were observed. The results found *Xiao Yao Wan* rats to have improved behavior and activity, reduced ALT, AST, TP, ALB, A/G, T-BIL, HyP serum levels, and increased activity of SOD, MDA, ChE, GSH-PX, concluding that *Xiao Yao Wan* shows significant protective action on chronic liver injury.<sup>xxxvii</sup>

**Digestion**

*Functional Dyspepsia*—The effect of *Jia Wei Xiao Yao San* on patients with functional dyspepsia was studied. Functional dyspepsia is defined as indigestion, mild pain in the abdomen or upper epigastric area that occurs during or right after eating. The study used 20 patients with functional dyspepsia who were assessed by EGG (electrogastrography) and symptom evaluation. The outcome showed improvement of symptoms and adjustment of the abnormal gastric motility and gastric myoelectrical activity of the patients.<sup>xxxviii</sup>

*Irritable Bowel Syndrome*—A meta-analysis was performed to evaluate the efficacy and safety of *Jia Wei Xiao Yao San* for the treatment of irritable bowel syndrome (IBS). The study included 17 trials and 1,542 patients. The results showed that *Jia Wei Xiao Yao San* had a lower recurrence rate and was more effective than other medications for treating the signs and symptoms of IBS. Based on the analysis, this formula is effective for IBS. Also noted was that most studies did not report adverse reactions.<sup>xxxix</sup>

One study observed the efficacy of modified *Xiao Yao Wan* for IBS- diarrhea predominant. The study had 36 patients in the treatment group take the herbal formula for four weeks. The control group of 26 patients was given Western anti-diarrheal medications. The results showed a total efficacy of 91.6% for the treatment group and 62.5% for the control group.<sup>xi</sup>

Another study showed the efficacy of *Xiao Yao Wan* in combination with *Si Mo Tang* (Four Milled Decoction) for the treatment of IBS- constipation predominant. 60 patients were split into a treatment group and control group, with the treatment group receiving *Xiao Yao Wan* plus *Si Mo Tang* and the control group receiving a gastroprokinetic pharmaceutical. The course of treatment was eight weeks. The results showed short term total effectiveness rate of 93.33% for the treatment group and 63.33% for the control group. And long term effectiveness rate of 83.33% for the treatment group and 40% for the control group.<sup>xii</sup>

*Chronic Gastritis*—Swelling or inflammation of the stomach lining, known as chronic gastritis, can be treated with Chinese herbal formulas. A study was conducted giving modified *Jia Wei Xiao Yao San* to 48 patients. Chronic gastritis symptoms included abdominal pain, bloating, belching, heartburn, acid reflux, nausea, and vomiting for more than 4 weeks. All cases were confirmed by endoscopy. The study showed that modified *Jia Wei Xiao Yao San* was an effective treatment for chronic gastritis, with the ability to quickly relieve symptoms. 38 patients were deemed cured, with relief from epigastric pain and a normal endoscopy. Eight patients showed improvement of epigastric pain, reduced number of attacks, and improved endoscopy. Two patients showed no change. There was a total effectiveness rate of 96%. The average time for elimination of symptoms was 5 days. The recurrence rate was 6%.<sup>xiii</sup>

*Stomach Ulcers*—A study was conducted using *Jia Wei Xiao Yao San* in combination with *Zuo Jin Wan* to treat stomach ulcers. 114 cases diagnosed with stomach ulcers and an OM diagnosis of liver and stomach heat were treated. Patients were

broken into a treatment group treated with Chinese herbs and a control group treated with omeprazole. Over 90% of the patients were positive for *H. pylori* (Hp). Symptoms included epigastric pain, irritability, acid reflux, fever, yellow urine, dry stool, red tongue with yellow coat, and a wiry pulse. Course of treatment was four weeks. Patients were followed for 12 months. In the treatment group of 57 patients, 40 cases were deemed cured with no clinical symptoms; 16 cases showed marked improvement, and one case showed some improvement. In comparison, the control group had 25 cases deemed cured; 15 cases showed marked improvement; 13 cases showed some improvement, and 4 cases had no effect. Hp eradication was roughly the same between the two groups at 65%. Recurrence rate between the two groups was statistically different: 5.4% after six months and 8.9% after 12 months for the treatment group; and 20.8% after six months and 29.2% after 12 months for the control group.<sup>xliii</sup>

*Ulcerative Colitis*—*Xiao Yao Wan* combined with Mesalazine was used for the treatment of ulcerative colitis in a randomized controlled study. The study used 80 patients broken into two groups of 40, the treatment group using the combination therapy and the control group using only the pharmaceutical. The results indicated a 95% effectiveness rate, with 22 cases cured, 16 cases improved, and not effective for two cases in the treatment group. This was compared to a total effectiveness rate of 67.5% for the control group, which had 15 cases cured, 12 cases improved, and 13 cases deemed not effective.<sup>xliv</sup>

*Chronic Cholecystitis*—Chronic cholecystitis is defined as repeated attacks of the gallbladder, characterized by inflammation, often caused by gall stones. *Xiao Yao Wan*, combined with *Ban Xia Xie Xin Tang*, treated 78 cases of chronic cholecystitis. Course of treatment was four weeks with follow ups at six months and one year. Patients had accompanying signs and symptoms that included abdominal distention, epigastric burning sensation, acid reflux, belching, nausea, and loss of appetite. Of the 78 cases, 28 cases were deemed cured, with remission of symptoms for one year; 23 cases showed to be effective, with remission of symptoms for six months; 22 cases showed improvement in symptoms; and five cases were deemed ineffective, with a total effectiveness rate of 93%.<sup>xlv</sup>

**Other**

*Insomnia*—*Jia Wei Xiao Yao San* was used in a study treating 40 cases of insomnia characterized by a TCM diagnosis of liver qi stagnation with fire. Clinical manifestations included insomnia, irritability, easily upset, thirst, red eyes, and constipation. 19 cases were deemed cured, with a return to normal sleep time; 10 cases had significant improvement, with increased sleep time by at least 3 hours and with increased deep sleep; 7 cases showed some improvement, and 4 cases showed no improvement, with a total effectiveness rate of 90%.<sup>xlvi</sup>

*Tremors*—A study was conducted to evaluate *Jia Wei Xiao Yao San's* ability to reduce tremors due to antipsychotic medication-induced Parkinsonism. The herbal formula was given to eight patients exhibiting tremors. The results showed significant reduction of tremors after administration of *Jia Wei Xiao*



*Yao San*. Five of the eight patients, 62.5%, showed improvement. Additionally, no adverse events were noted.<sup>xlvi</sup>

**Diabetes**—52 patients with type 2 diabetes were treated with modified *Xiao Yao Wan* taken in conjunction with Metformin. Exercise and dietary advice was also given. TCM differential diagnosis was defined as liver qi stagnation with stagnant heat. Treatment course was 45 days. Efficacy of the treatment was determined by blood glucose levels and accompanying signs and symptoms. The results showed 32 cases were deemed cured, with blood glucose levels in normal range and accompanying signs and symptoms disappeared. 17 cases showed improvement with reduction of both blood glucose levels and accompanying signs and symptoms; 3 cases were deemed ineffective with no changes.<sup>xlviii</sup>

**Persistent dentoalveolar pain disorder (PDAP)**—PDAP is defined as pain in the teeth. The effects of *Jia Wei Xiao Yao San* as a treatment for PDAP were studied. The formula was taken for two weeks. The results show there to be improvement in pain for 14 of the 15 participants in the study. Jaw exercise therapy was used in conjunction with the formula. Also noted, the exercise therapy was practiced for two months prior to the administration of *Jia Wei Xiao Yao San* with no effect.<sup>xlviix</sup>

**Cough Variant Asthma**—A clinical study using *Xiao Yao Wan* to treat cough variant asthma was conducted. Cough variant asthma is a form of asthma with the only symptom being a dry, non-productive cough, usually without the wheezing associated with traditional asthma. The study showed *Xiao Yao Wan* to have a total effectiveness rate of 90%. A 73.33% rate was deemed markedly effective with significant improvement in symptoms and shortened time between onset and disappearance of cough, indicating this formula to have significant therapeutic effect for treating cough variant asthma.<sup>l</sup>

**Herpes Zoster**—A study in the treatment of herpes zoster was conducted in which 302 patients were divided into two groups: a treatment group, who were prescribed *Jia Wei Xiao Yao San*, and the control group who were prescribed acyclovir. Patients were observed for blistering stop time, crusting time, length of time for pain relief, and recovery time. After 1 week the cure rate was 52.5% for the treatment group and 37.8% for the control group. After the second and third weeks there was no significant difference in efficacy between the treatment group and control group, with the treatment group leaving 18 patients with significant herpes zoster and the control group with 14 cases. *Jia Wei Xiao Yao San* can effectively shorten the course of herpes zoster.<sup>li</sup>

**Chronic Fatigue Syndrome**—A combination of *Xiao Yao Wan* and *Sheng Mai San* was used to treat 32 cases of chronic fatigue syndrome. Treatment course consisted of two weeks with two courses total. Fatigue Assessment Scale (FAS) was used to determine efficacy. The total effectiveness rate was 87.5% with significant improvement in FAS score from before to after treatment.<sup>lii</sup>

**Fibromyalgia**—27 cases of fibromyalgia were treated with *Jia Wei Xiao Yao San* with satisfactory results. Of the 27 cases, 4 were male and 23 were female. All cases had been suffering

from fibromyalgia for a minimum of five months. The results showed that 16 cases were cured; six cases showed marked improvement in the condition; three cases showed some improvement in the condition, and two cases had no change.<sup>liii</sup>

**Oral Ulcers**—*Jia Wei Xiao Yao San* was used to treat 40 cases of recurrent oral ulcers, also known as recurrent aphthous ulcers. Treatment course was two weeks, with a follow up at six months. The results showed that 34 cases were deemed cured with healed ulcer, no pain, and no recurrence after six months. Four cases showed marked improvement. Relapse occurred; however, the number of recurrences were lessened. Two cases showed no significant changes. There was a 95% total effectiveness rate.<sup>liv</sup>

**Hyperlipidemia**—A study was conducted to investigate the effect of *Xiao Yao Wan* combined with *Tao Hong Si Wu Tang* to treat hyperlipidemia. 64 patients in the treatment group were given this herbal combination. Total cholesterol, triglycerides, and LDL cholesterol levels were significantly decreased, and HDL cholesterol increased. Additionally, accompanying signs and symptoms, like headache, tinnitus, insomnia, and palpitations improved. Of the 64 cases, 87.5% were deemed cured; 9.4% showed improvement; and 3.1% had no effect; with a total effectiveness rate of 96.9%.<sup>lv</sup>

**Chronic Pharyngitis**—A study was conducted to determine the efficacy of modified *Xiao Yao Wan* to treat 92 cases of chronic pharyngitis. 81 cases were diagnosed as simple chronic pharyngitis and 11 cases as chronic hypertrophic pharyngitis. Symptoms included throat pain and itchiness, swelling, and a sensation of a foreign body stuck in the throat. Course of treatment was ten days and a statistical effect follow-up was performed after three months. 43 cases were deemed cured; 47 cases showed improvement, but still had swelling and some pain; and two cases were invalid; the total effectiveness rate was 97.8%.<sup>lvi</sup>

**Acne**—86 cases of acne were treated with modified *Xiao Yao Wan*. Patients were identified by TCM diagnosis of wind-heat, damp-heat, and phlegm and blood stasis. Additions to *Xiao Yao Wan* were made dependent upon diagnosis. For wind-heat, *pi pa ye*, *sang bai pi*, *mu dan pi*, *zhi zi*, and *huang qin* were added. For damp-heat, *yin chen hao*, *huang bai*, *yi yi ren*, and *da haung* were added. For phlegm and blood stasis, *chen pi*, *ban xia*, *xia ku cao*, *dang gui*, *yi mu cao*, and *nu zhen zi* were added. Treatment course was ten days with three courses given. 66 cases had their acne cleared; ten cases showed marked improvement, with 80% improvement of the acne; eight cases were improved with 50% improvement of the acne; and two cases showed no improvement. The total efficacy of the treatment was 97.7%.<sup>lvii</sup>

**Migraine Headaches**—A clinical observation study was conducted using *Jia Wei Xiao Yao San* to treat migraine headaches. 49 patients were administered the herbal formula for 20 days. After the course of treatment 22 cases were cured, with disappearance of headache; 24 cases showed improvement, with some headache relief, duration shortened, and frequency lessened; and three cases showed no change. The total effectiveness rate was 89.3%.<sup>lviii</sup>

**Optic Neuritis**—Optic neuritis is inflammation of the optic nerve causing pain and temporary vision loss. *Xiao Yao Wan* has been used to effectively treat optic neuritis. One study treated 67 cases (125 eyes) of optic neuritis using *Xiao Yao Wan* with modifications dependent on patient presentations. 102 eyes were deemed cured with hyperemia of the optic disk and edema subsided, improvement of visual acuity, and visual field returned to normal. 23 eyes showed improvement with some visual acuity improvement and partial visual field recovery. The total effectiveness rate was 100%.<sup>lvix</sup>

**Hashimoto's Disease**—A research study was conducted to investigate the integrative effects of *Xiao Yao Wan* in conjunction with the Western pharmaceutical Levothyroxine for the treatment of Hashimoto's hypothyroidism. 46 cases were divided into a treatment group of 25 cases and control group of 21 cases. Treatment lasted three months. Thyroid function (TSH, FT3, and FT4) was measured. The integrative approach proved to be more effective than Western medicine alone, improving clinical symptoms and restoring thyroid hormone levels. With the integrative approach, FT3 and FT4 were significantly higher than before treatment and TSH levels were significantly lowered compared to before the treatment.<sup>lx</sup>

**Alzheimer's Disease**—Research was conducted on the effect of *Xiao Yao Wan* on Alzheimer's Disease. Male rats with Alzheimer disease induced by intraperitoneal injection of D-gal and A-β1 ~ 42 peptide bilateral hippocampal injection were used. *Xiao Yao Wan* was administered for 28 days. The results showed that *Xiao Yao Wan* inhibited expression of GSK-3β animal hippocampus and increased expression of PP-2A positive cells, reversing the induced condition, and having a positive effect on memory and improving cognitive impairment.<sup>lxi</sup>

### FORMULA COMPARISONS

**Bupleurum & Tang Kuei Formula** (*Xiao Yao Wan*) and **Chai Hu Shu Gan Formula** (*Chai Hu Shu Gan Tang*) both treat liver qi stagnation. **Chai Hu Shu Gan Formula** (*Chai Hu Shu Gan Tang*) focuses primarily on the excess condition of liver qi stagnation and can be used for severe qi stagnation situations. This formula has the added actions to invigorate and move blood, making it an effective choice for conditions where qi stagnation is accompanied with blood stasis. **Bupleurum & Tang Kuei Formula** (*Xiao Yao Wan*) is more suitable for patients with chronic spleen qi and blood deficiency who are adversely affected by stress. It is more suitable for long term use than **Chai Hu Shu Gan Formula**.

**Bupleurum & Tang Kuei Formula** (*Xiao Yao Wan*) is a variation of **Bupleurum and Aurantium Immaturus Formula** (*Si Ni San*). Both formulas harmonize the liver and spleen and treat liver qi stagnation. **Bupleurum and Aurantium Immaturus Formula** (*Si Ni San*), one of the first formulas ever created for qi stagnation, is more for excess conditions and is most noted for addressing cold extremities due to qi stagnation in the torso. Using *chai hu* and *zhi shi*, the formula moves qi stagnation, improving circulation to the extremities. **Bupleurum and Aurantium Immaturus Formula** (*Si Ni San*) is stronger to course liver qi than **Bupleurum & Tang Kuei Formula** (*Xiao*

*Yao Wan*), but is weaker to nourish qi and blood. **Bupleurum & Tang Kuei Formula** (*Xiao Yao Wan*) addresses the excess condition and also treats deficiency by nourishing spleen qi and liver blood.

**Bupleurum Formula** (*Yi Gan San*) is similar to **Bupleurum & Tang Kuei Formula** (*Xiao Yao Wan*). Both formulas treat excess and deficiency at the same time. Both formulas address wood overacting on earth. Both formulas support spleen qi, liver blood, and regulate liver qi. **Bupleurum Formula** (*Yi Gan San*)'s primary function, and main difference between the two formulas, is to address wind and liver ascent due to excess in the liver, manifesting as spasms, seizures, dizziness, headaches, nervousness, irritability, and insomnia.

Classically, **Minor Bupleurum Formula** (*Xiao Chai Hu Tang*) was formulated to treat *shaoyang* syndrome, but has never been restricted to simply treating this pattern. **Minor Bupleurum Formula** (*Xiao Chai Hu Tang*) has often been used to treat wood / earth disharmonies, much like **Bupleurum & Tang Kuei Formula** (*Xiao Yao Wan*) and **Free & Easy Wanderer Plus** (*Jia Wei Xiao Yao San*). These formulas address very similar signs and symptoms. From this understanding of liver overacting on spleen, choosing between these two formulas can be broken down as follows. If the presentation of symptoms appears to be more physical in nature, use **Minor Bupleurum Formula** (*Xiao Chai Hu Tang*). If psycho-emotional symptoms are more pronounced, use **Bupleurum & Tang Kuei Formula** (*Xiao Yao Wan*) or **Free & Easy Wanderer Plus** (*Jia Wei Xiao Yao San*). An example of this would be if hypochondriac pain is the primary reason for treatment, using **Minor Bupleurum Formula** (*Xiao Chai Hu Tang*) is most suitable, even if it is accompanied by other symptoms like depression, mood swings, etc. Alternatively, if the primary reason for treatment is depression, the use of **Bupleurum & Tang Kuei Formula** (*Xiao Yao Wan*) or **Free & Easy Wanderer Plus** (*Jia Wei Xiao Yao San*) will be most appropriate.

**Free & Easy Wanderer Plus** (*Jia Wei Xiao Yao San*) and **Linking Formula** (*Yi Guan Jian*). Both treat similar conditions caused by liver qi stagnation, like hypochondriac pain, abdominal or epigastric pain, acid reflux, nausea or vomiting. Both formulas address deficiency as well as liver qi stagnation, but the underlying deficiencies between these two formulas are very different. **Linking Formula** (*Yi Guan Jian*) treats liver and kidney yin deficiency. **Free & Easy Wanderer Plus** (*Jia Wei Xiao Yao San*) treats spleen qi and liver blood deficiency.

### Formula Combinations

**Bupleurum & Tang Kuei** (*Xiao Yao Wan*) and **Free & Easy Wanderer Formula** (*Jia Wei Xiao Yao San*) are very good base formulas for many disorders. Much of the modern research currently being done uses additions to these formulas for the specific person and/or condition being treated. This can be achieved with herbal formula combinations as well.

**See next page for useful combinations.**

## USEFUL COMBINATIONS

For acne	Combine with <b>Margarita Complexion Formula</b>
For breast hyperplasia	Combine with <b>Two Immortals Formula</b>
For cardiac neurosis	Combine with <b>Blood Palace Formula</b> or <i>Gan Mai Da Zao Tang</i>
For chronic fatigue syndrome or hyperthyroidism	Combine with <b>Sheng Mai Formula</b>
For depression after stroke	Combine with <i>Bu Yang Huan Wu Tang</i>
For painful diarrhea	Combine with <b>Peony and Atractylodes Formula</b>
For functional dyspepsia	Combine with <b>Ease Digestion Formula</b>
For epigastric pain or chronic cholecystitis	Combine with <i>Ban Xia Xie Xin Tang</i>
For H-pylori ulcer	Combine with <i>Zuo Jin Wan</i>
For Herpes Zoster	Combine with <b>Viola Clear Fire Formula</b>
For hepatitis	Combine with <b>Capillaris Formula</b>
For hyperlipidemia	Combine with <b>Chong Release Formula</b>
For IBS constipation	Combine with <b>Ginseng and Longan Formula</b> or <b>Persica and Cistanches Formula</b>
For IBS diarrhea	Combine with <i>Shen Ling Bai Zhu San</i>
For jaundice or hepatitis	Combine with <b>Lysmachia GB Formula</b>
For Pelvic Inflammatory Disease	Combine with <b>Stasis-Transforming Formula</b>
For Polycystic Ovary Syndrome (PCOS)	Combine with <b>Phlegm-Transforming Formula</b>

### ENDNOTES

<sup>i</sup> We often separate liver yin and liver blood in TCM. But if one examines the *materia medica*, it will be discovered that every substance listed as supplementing/ tonifying/ nourishing liver yin never has only that action. All of the liver-yin nourishing herbs fall into one of three categories: 1) nourish kidney and liver yin, 2) nourish liver yin and blood, or 3) nourish liver yin and anchor yang. The third category is made up of heavy substances, usually minerals, that by their very density have an anchoring action upon the yang and are therefore adding yin to the body. The first category are really kidney yin supplements that also nourish the liver, that is to say, they nourish the kidney yin in such a way that the liver receives some of the benefit. Other kidney yin supplements direct the yin nourishment to the heart. The second category can be seen in these categorizations as equating liver blood and liver yin.

<sup>ii</sup> Feng Qin, et al., "Meta-analysis of Randomized Controlled Trials to Assess the Effectiveness and Safety of Free & Easy Wanderer Plus, a Polyherbal Preparation for Depressive Disorders," *Journal of Psychiatric Research*, 2011, Vol 45, No 11.

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