

Herbal treatment of insomnia

失眠的草藥治療

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Insomnia is a common problem requiring appropriate recognition and management. Despite recent advances in the development of newer hypnotics in western medicine, a significant proportion of patients with insomnia, both locally and internationally, consume herbal hypnotics regularly. The safety and efficacy of these herbal remedies remains uncertain. In this paper, details of different herbs used in western and traditional Chinese medicine for the treatment of insomnia are reviewed. Although current data suggests the use of some herbal treatments in insomnia may be efficacious, further laboratory and clinical studies are required.

失眠是一種常見的問題，它需要得到適當重視和處理。儘管西醫在研製新的安眠藥物方面取得了新進展，但仍有相當多失眠患者，包括本地和國外患者，定期服用草藥安眠劑以治療失眠，但這些草藥療法的安全性和有效性卻值得商榷。本文總覽了西方和傳統中醫用於治療失眠的不同草藥的資料。雖然目前的資料認為使用某些草藥治療失眠可能有效，但仍需要進一步的實驗室和臨床研究。

Insomnia is very common

The majority of studies indicate that insomnia affects between 10% and 30% of the population. In the clinical setting, one fifth of patients attending general practitioners have been reported to be suffering from insomnia.¹

Definition of insomnia

Patients with insomnia report difficulty in initiating sleep, difficulty in maintaining sleep, (ie waking intermittently during the night), or early morning waking (ie waking in the early morning and being unable to fall asleep again).² Insomnia lasting only a few days is often a result of acute and transient stress and is usually regarded as a normal phenomenon. Insomnia lasting more than a few weeks, however, is considered significant. According to the International Classification of Sleep Disorders, persistent insomnia of more than 4 weeks' duration is regarded as significant insomnia.^{3,4} The causes of insomnia include psychiatric disorders, physical problems such as cardiopulmonary failure and chronic pain, drugs and foods such as caffeine, nicotine, alcohol, and amphetamines, and an irregular sleep-wake cycle. A significant proportion of patients with insomnia (approximately 20% to 25%), however, do not have a definite underlying cause for their insomnia.⁵

Consequences of insomnia

When longstanding and severe, insomnia profoundly affects patients' lives. Insomniacs show a higher level of absenteeism,⁶ and poorer performance

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at work. Insomnia also increases the rate of both work-related⁷ and vehicle accidents.⁸ As a result, insomnia has a huge impact on health care costs, either through direct treatment costs, or indirectly through lost productivity and accidents.⁹ The relationship between insomnia and psychiatric disorders is interactive and intriguing. Psychiatric disorders, such as depression and anxiety, can be both the underlying causes, as well as the consequences of longstanding insomnia.¹⁰

Insomnia in the Hong Kong Chinese population

There are relatively few studies of insomnia among the Chinese population. One such study revealed that a high percentage (38.2%) of elderly were suffering from insomnia.¹¹ A population-wide telephone survey of Hong Kong adults about sleep patterns and disorders reported that the insomnia prevalence rate in Hong Kong Chinese adults during the preceding month was nearly 12%.¹²

Principles of management of insomnia

Adequate assessment including a detailed history of psychiatric, physical, and sleep aspects is essential. Those patients with syndromal psychiatric disorders should be treated accordingly. For example, depressed patients with insomnia should be adequately treated with antidepressants. Moreover, improvement of the irregular sleep-wake cycle, sleep hygiene education, and appropriate cognitive-behavioural approach are often necessary and useful adjuncts.

Various hypnotics have been developed over the years for the symptomatic treatment of insomnia. The dependence potential of benzodiazepines has aroused much concern, leading to guidelines and regulations for the restriction of benzodiazepine use to time-limited symptomatic treatment of insomnia.¹³ Other pharmacological compounds, such as tricyclic antidepressants and neuroleptics, have also been used to treat insomnia.¹³ Inconclusive evidence, combined with their poor tolerability and sometimes irreversible adverse effects (eg anticholinergic effects of tricyclic antidepressants, tardive dyskinesia related to neuroleptics), however, have limited their application.¹⁴ Although newly developed hypnotics, including zolpidem and zopiclone, have proven safer with lesser psychomotor impairment and memory deficit, the long-term safety of these agents remains a concern.¹³ In general, the recommended duration of hypnotic treatment for insomnia should be brief and not exceed a few weeks. Recent research, however, has shown that approximately 10% to 15% of insomniac patients,

especially the elderly, regularly use their hypnotic medication for more than a year.^{15,16} Thus, the continuing search for newer, better, and safer hypnotic agents for the treatment of insomnia is needed.

Alternative medicine in the treatment of insomnia

In recent years, there has been a resurgence of interest in alternative or complementary medicine, both locally and internationally. As many as 40% of Americans reported that they utilised various types of alternative medicines in 1996. Contrary to belief, this use was prevalent across all ethnic, income, and age groups, with higher educational level and chronic ill-health, especially psychiatric problems, the predictors of frequent use.¹⁷ In a survey of the aids used to facilitate sleep in the US in 1996, 10% of respondents reported consumption of over the counter (OTC) medications regularly.¹⁶ In a recent local telephone survey of 180 Chinese patients with insomnia, approximately 15% consumed OTC medications (Personal communication, S Bartlett, 2001). Thus, the use of OTC medications, of which the majority are herbal products, is relatively common among patients with insomnia in Hong Kong. There remain questions and doubts about the safety and efficacy of such herbal products, however.¹⁸⁻²²

Principles of traditional Chinese medicine applied to insomnia

The underlying principles of traditional Chinese medicine (TCM) in relation to insomnia will be only briefly mentioned in this review. Insomnia appears in the earliest TCM records, such as the *Ling Shu* (circa 200 AD) and the *Golden Chest* (circa 300 AD).²³⁻²⁵ Briefly, insomnia is recognised by TCM practitioners or theory as a symptom of underlying disturbance in the balance between Yin and Yang, as well as in the interaction of five basic elements and the vital organs according to the Wu Hsing theory.²² In other words, insomnia is a symptom which may be related to differing patterns of imbalance in various components, such as 'Yin vacuity and fire effulgence'.²⁶ Thus, treatment should be individualised according to the specific pattern of disturbance.

In the modern practice of evidence-based medicine, however, proof of the effectiveness of specific TCM treatments or herbal products depends on whether they have been rigorously studied with well-controlled clinical trials, disregarding the underlying theoretical assumptions. Such a scientifically based approach will be adopted by this review.

Herbal treatment of insomnia

The use of herbs in the treatment of psychiatric problems including insomnia is not exclusive to orientals. Thus, this review will cover both western and oriental herbs used in the treatment of insomnia. The review is based on Medline searches (1966-2000), frequently cited articles, TCM textbooks and dictionaries, and relevant publications in Chinese journals, books, and electronic media. It is apparent that both western and oriental practitioners have preferred herbs that are claimed to be effective in the treatment of insomnia. Most of these herbs have multiple indications and therapeutic effects. The major difference between the western and oriental use of herbs is that western herbs are more often used in an isolated form, while herb use in TCM is usually within a composite formula. The theory underlying the combination of different herbal ingredients in TCM is based on the belief that different herbs serve different purposes, namely 'Master', 'Soldier', and 'Adviser', in order to restore the body to its premorbid state of balance.²²

Commonly available herbs for the treatment of insomnia in the West

A summary of herbal therapies developed in the West for the treatment of insomnia is contained in Table 1.

St John's wort

The most popular and well-studied herbal treatment for psychiatric problems in the West in recent years is SJW. St John's wort (*Hypericum perforatum*) has long been used as a remedy for wound healing, mild sedation, and pain relief.^{20,27,28} A meta-analysis reviewing 23 randomised trials involving 1757 patients, concluded that it was more effective than placebo and had similar efficacy to conventional antidepressants for treating mild-to-moderate depression.²⁸ Two recent large-scale randomised controlled studies, however, have reported conflicting results on the efficacy of SJW in treating depression.^{29,30}

The use of SJW as a hypnotic has not been studied systematically. One study reported an increase in rapid eye movement (REM) sleep latency with the consumption of a single dose of SJW in 21 healthy subjects.³¹ Another cross-over double-blind placebo-controlled study of high dose hypericum extract in 12 elderly healthy volunteers, suggested that SJW induced an increase in deep sleep but had no effect on other sleep parameters.³² Based on the results of SJW in treating depression and the suggestion that it may modulate REM and deep sleep, however, further study of the potential hypnotic properties of SJW is indicated. A number of active ingredients, especially hypericin and pseudohypericin, are postulated as the main active ingredients of SJW. The crude extract has significant in vitro receptor affinity for γ -aminobutyric acid (GABA)-A,B, benzodiazepine, inositol triphosphate, and monoamine oxidase A and B. Chronic treatment with hypericum may also downregulate β_1 -adrenoceptors, and upregulate post-synaptic 5-HT_{1a} receptors and 5-HT₂ receptors.³³

In general, SJW is well tolerated with minimal side-effects, including sedation, dry mouth, dizziness, gastrointestinal upset, restlessness, and hypersensitivity.^{28,29} Potential drug interactions with serotonin-reuptake inhibitors and monoamine oxidase inhibitors have been reported.^{20,34}

In China, related species of hypericum—*Hypericum japonicum* and *Hypericum sampsonii*—are found.^{35,36} The *Hypericum japonicum* is found locally in Hong Kong, and has been mainly used as an anti-inflammatory, and for wound healing and pain relief.³⁵ It would be interesting to see whether these Asian hypericums share similar psychotropic properties with those reported for SJW.

Valerian

Valerian (*Valeriana officinalis*), from the plant family *Valerianaceae*, has been widely used in the West as a folk remedy for its hypnotic properties. A limited

Table 1. Commonly available herbs for insomnia/depression in the West

Name	Functions	Constituent or active ingredients
St John's wort (<i>Hypericum perforatum</i>) 貫葉金絲桃	<ul style="list-style-type: none"> • antidepressant • anti-inflammatory • sedative 	<ul style="list-style-type: none"> • hypericin • pseudohypericin
Valerian (<i>Valeriana officinalis</i>) 纈草	<ul style="list-style-type: none"> • sedative, tranquilising properties 	<ul style="list-style-type: none"> • γ-aminobutyric acid • benzodiazepines
Hops (<i>Humulus lupulus</i>) 啤酒花	<ul style="list-style-type: none"> • to produce beer • sedative 	<ul style="list-style-type: none"> • volatile oils (eg 2-methyl-3-butene-2-ol)
Skullcap (<i>Scutellaria laterifolia</i>) 美洲黃芩	<ul style="list-style-type: none"> • sedative 	<ul style="list-style-type: none"> • unclear

number of human studies with double-blind, cross-over design, suggest that valerian could be used as a mild hypnotic with minimal psychomotor impairment or residual side-effects.^{19,20,37-39} Objective sleep measurements using polysomnographic recordings have suggested improvements in sleep efficiency and slow wave sleep as well as reductions in stage 1 sleep, with repeated rather than single-dose administration.^{40,41} Animal studies suggest valerian administration has a similar behavioural effect to that of benzodiazepine, and possible antidepressant properties.^{42,43} The exact biochemical action of valerian remains unclear but effects on GABA metabolism and reuptake, 5HT_{1a} and adenosine receptors have been postulated.²⁰ Hepatotoxicity, cardiac complications, and delirium have been reported sporadically.⁴⁴⁻⁴⁶

A closely related species of the *Valerianaceae* family, Baijianggen (*Patriniae rhizoma et radix*), is distributed over most parts of China and has been widely used as an ingredient for treating insomnia and neurasthenia.⁴⁷

Hops

Hops (*Humulus lupulus*) are traditionally used to brew beer and to date there have been few studies of their use, usually in combination with valerian. Improvements in subjective sleep quality and quality of life equivalent to that with benzodiazepine use, but with fewer side-effects and without a withdrawal reaction, have been reported.⁴⁸ The exact biochemical substance is unknown but a volatile oil, such as 2-methyl-3-butene-2-ol, may be a likely candidate.⁴⁹ Possible adverse reactions include allergy, menstrual disturbances, and the potentiation of other sedatives and alcohol.⁴⁴

Skullcap

The leaves and blue flowers of the skullcap (*Scutellaria laterifolia*) are used as an ingredient in many OTC sleep remedies in the West. Some related species are common ingredients in some Chinese herbal formulas for inflammation and hepatitis.⁵⁰ Clinical studies of their use are currently lacking. Adverse effects include dizziness, confusion and seizures, and hepatotoxicity.⁵¹

Common traditional Chinese medicine herbs/ingredients for insomnia

According to TCM, a variety of natural products are effective in the treatment of insomnia. Most of these products are herbal in origin, but the use of fungal and mineral products is also common. In this review, herbal products are classified according to their anatomical origins within the plant. A total of 16 botanical

products (Table 2), two fungal products (Table 3), and one mineral product (Table 4) will be discussed. Most support for the effectiveness of such herbal treatments comes from clinical experience. Clinical trials using randomised, double-blind and placebo-controlled designs were the exception. The majority of these studies were published in Chinese journals.

According to the criteria developed by the 1994 Canadian Guide to Clinical Preventive Health Care,⁵² the quality of evidence for use of a drug or treatment can be assessed as being from level I (evidence obtained from at least one properly randomised controlled trial) to level III (descriptive studies and case reports, or reports from expert committees). Most western herbal products, with the notable exception of the antidepressant effects of SJW, would be classified as having level III or insufficient evidence.²⁰ Similarly, most evidence for the use of oriental herbs and formulas for insomnia constitutes level III or insufficient evidence.

Fruit

Suanzaoren (Semen ziziphi spinosae, Zizyphi acidojubarbae semen)

Perhaps the most well-known herb for the treatment of insomnia in TCM is Suanzaoren. The herb is the dried ripe seed of the *Zizyphus acidojubarba* (family *Rhamnaceae*).⁴⁷ Animal studies suggest that it may protect cerebral ischaemic injuries,⁵³ has hypnotic effects in rats,⁵⁴ modulates stress-induced sleep changes in mice,⁵⁵ and enhances total sleep time and slow wave sleep in rabbits.⁵⁶ It is a common ingredient of the traditional herbal formulas used in treating insomnia, such as Suanzaoren Tang.²⁴ The exact biochemical action of Suanzaoren is unknown. However, it contains jujuboside A and B, betulinic acid, betulin, spinosin, and feruloyl spinosin.⁴⁷ In vitro analysis suggests an affinity for 5HT_{1a}, 5HT₂, and GABA receptors.⁵⁷

Dazao (Fructus jubarbae)

This herb is the dried ripe fruit of *Zizyphus jubarba* (family *Rhamnaceae*).⁴⁷ The use of dazao has a long tradition and a traditional herbal formula, 'Liquorice, wheat and jubarba soup' was first recorded during the Han dynasty.²⁴ It has been a common prescription for treating mental problems including neurasthenia, insomnia, and even schizophrenia.⁵⁸ The active biochemical ingredient of the herbal formula is unknown. Jujube contains stepharine, N-nor-nuciferine, asimilobine, and two kinds of *Zizyphus* saponin.⁴⁷

Longyanrou (Arillus longan)

This commonly consumed fruit is the dried aril of the

Table 2. Common traditional Chinese medicine herbs/ingredients available in Hong Kong for insomnia: botanical products^{47,59,60}

Botanical product	Name	Traditional Chinese medicine rationale for use/indications	主治
Fruit 果實種子類	Suanzaoren (Semen ziziphi spinosae) 酸棗仁	<ul style="list-style-type: none"> “Nourish the heart, benefit the liver & tranquillise the mind” for vexation, insomnia, severe palpitations, fearfulness, and amnesia stop sweating 	<ul style="list-style-type: none"> 養心益肝，寧心安神 治心煩失眠、驚悸怔忡、健忘 斂汗
	Dazao (Fructus jujubae) 大棗	<ul style="list-style-type: none"> “Revitalise the spleen & stomach” for blood deficiency with insomnia to moderate the potency of drugs 	<ul style="list-style-type: none"> 補益脾胃 養血安神，治血虛失眠 緩和藥性
	Longyanrou (Ariilus longan) 龍眼肉	<ul style="list-style-type: none"> “Revitalise the heart & spleen, nourish blood & calm the mind” for palpitations, insomnia, amnesia, and dizziness 	<ul style="list-style-type: none"> 補益心脾，養血安神 治氣血虛所致驚悸怔忡、失眠、健忘、眩暈
	Baiziren (Platycladi semen) 柏子仁	<ul style="list-style-type: none"> “Nourish the heart & tranquillise the mind” for fearfulness, severe palpitations, lack of concentration, amnesia, and night sweats relax the bowels 	<ul style="list-style-type: none"> 養心安神 治心血不足之驚悸怔忡、失眠、多夢、健忘、虛汗 潤腸通便
	Wuweizi (Schisandrae fructus) 五味子	<ul style="list-style-type: none"> “Benefit vital energy & invigorate kidney, nourish the heart and calm the mind” for palpitations, insomnia, and frequent dreams 	<ul style="list-style-type: none"> 益氣生津，斂肺氣止咳喘，補腎固澀，養心安神 治心虛之心悸、失眠、多夢
	Fuxiaomai (Triticifruetus levis) 浮小麥	<ul style="list-style-type: none"> “Nourish the heart & tranquillise the mind” for palpitations, insomnia, and lack of concentration stop sweating 	<ul style="list-style-type: none"> 養心安神 治心血不足之婦人，臟躁、神志恍惚、失眠、多夢 止汗
Roots and rhizomes 根及根莖類	Banxia (Pinelliae rhizoma) 半夏	<ul style="list-style-type: none"> “Deprive dampness & disperse stagnation” eliminate phlegm, stop vomiting eliminate toxic material, disperse lumps, and relieve carbuncles 	<ul style="list-style-type: none"> 燥濕化痰 降逆止嘔 消痞散結；外敷攻毒散結消癰
	Chuanxiong (Chuanxiong rhizoma) 川芎	<ul style="list-style-type: none"> “Promote the circulation of the blood and vital energy, expel wind” alleviate pain 	<ul style="list-style-type: none"> 活血行氣 祛風止痛
	Danshen (Radix salviae miltiorrhizae) 丹參	<ul style="list-style-type: none"> “Promote blood circulation to remove blood stasis, clear away heat, relieve vexation, nourish blood & tranquillise the mind” for restlessness, ‘frights’, and insomnia to relieve carbuncles 	<ul style="list-style-type: none"> 活血祛瘀，清熱除煩，養血安神 治心熱或心血不足之心神不安、驚悸、失眠 涼血消瘀
	Baijianggen (Patriniae rhizoma et radix) 敗醬草	<ul style="list-style-type: none"> “Clear away heat” relieve abscesses and promote pus drainage remove blood stasis and alleviate pain as a tranquiliser: for vexation, insomnia, and insanity 	<ul style="list-style-type: none"> 清熱解毒 消癰排膿 祛瘀止痛 寧心安神：治心神不安、失眠、癲狂
	Chaihu (Bupleuri radix) 柴胡	<ul style="list-style-type: none"> “Disperse the stagnated liver energy, and increase Yang-energy” 	<ul style="list-style-type: none"> 解表洩熱，清透少陽邪熱，疏肝解鬱，升舉陽氣
	Danggui (Radix angelicae sinensis) 當歸	<ul style="list-style-type: none"> “Enrich blood and promote blood circulation” regulate menstruation and alleviate pain loosen bowels 	<ul style="list-style-type: none"> 補血 活血 潤燥滑腸
	Baizhu (Rhizoma atractylodis macrocephalae) 白朮	<ul style="list-style-type: none"> “Invigorate the spleen and benefit vital energy” promote diuresis and stop sweating soothe the foetus 	<ul style="list-style-type: none"> 補脾益氣 燥濕利水，固表止汗 安胎
	Ganjiang (Zingiberis rhizoma) 乾薑	<ul style="list-style-type: none"> “Recuperate the depleted yang, warm the lung” eliminate sputum 	<ul style="list-style-type: none"> 溫中祛寒，回陽通脈 溫肺化痰
Cortex 皮類	Hehuanpi (Albiziae cortex) 合歡皮	<ul style="list-style-type: none"> “Tranquillise the mind and disperse the depressed vital energy” for emotional upset, depression, insomnia, and amnesia activate blood circulation and relieve carbuncles 	<ul style="list-style-type: none"> 安神解鬱 治七情所致精神忿怒憂鬱、虛煩不眠、健忘 活血消癰
Rattan 藤木類	Shouwuteng (Polygoni caulis) 首烏藤/夜交藤	<ul style="list-style-type: none"> “Nourish the heart and tranquillise the mind” for vexation, insomnia, lack of concentration, and insanity to alleviate itching 	<ul style="list-style-type: none"> 養心安神 治陰虛血少的虛煩、失眠、多夢 祛風通絡，止癢

Table 3. Common traditional Chinese medicine herbs/ingredients available in Hong Kong for insomnia: fungus^{47,59,60}

Name	Traditional Chinese medicine rationale for use/indications	主治
Lingzhi (Ganoderma) 靈芝	<ul style="list-style-type: none"> • “Tranquillise the mind, enrich vital energy and blood” • for insomnia, frequent dreams • eliminate phlegm, relieve cough, and dyspnoea 	<ul style="list-style-type: none"> • 養心安神，補益血氣 • 用於心氣虛或心血虛之失眠、多夢 • 止咳祛痰
Fuling (Poria) 茯苓	<ul style="list-style-type: none"> • “Promote diuresis” • invigorate the spleen • tranquillise the mind 	<ul style="list-style-type: none"> • 利水滲濕 • 健脾補中 • 寧心安神：心脾兩虛或痰飲所致心悸、失眠

Table 4. Common traditional Chinese medicine herbs/ingredients available in Hong Kong for insomnia: minerals^{47,59,60}

Name	Traditional Chinese medicine rationale for use/indications	主治
Zhusha (Cinnabaris) 朱砂	<ul style="list-style-type: none"> • “Clear away heart-fire & tranquillise the mind” • for irritability, tightness in the chest, and insomnia • external use for detoxifying and as an antiseptic 	<ul style="list-style-type: none"> • 清心火，定驚安神 • 治心火亢盛之心神不安，胸中煩熱，驚悸不眠 • 好用解毒防腐

Euphoria longan (family *Sapindaceae*).⁵⁹ It is commonly used for the treatment of palpitations, forgetfulness, and insomnia. Clinical studies are lacking, however. Longan aril contains glucose, sucrose, and vitamins.⁵⁹

Baiziren (*Platycladi semen*)

The herb is the dried kernel of the ripe seed of *Platycladus orientalis* (family *Cupressaceae*).⁴⁷ It is commonly used for the treatment of insomnia, palpitations, and night sweats. It has been a main ingredient of the traditional insomnia formula used since the Ming dynasty, Tin Wang Bu Xin Dan. Animal studies suggest a hypnotic effect in rats.⁵⁸ It contains glycosides, steroids, and vitamin A.⁴⁷

Wuweizi (*Schisandrae fructus*)

This herb is the dried ripe fruit of *Schisandra chinensis* or *Schisandra sphenanthera* (family *Magnoliaceae*).⁴⁷ It is commonly used to treat chronic cough and asthma, protracted diarrhoea, and night sweats.⁶⁰ It is also included in herbal formulas such as Tian Wang Bu Xin Dan for the treatment of insomnia. More clinical studies are required. This herb contains deoxyschizandrin, γ -schizandrin, wuweizisu (五味子素), and wuweiziester (五味子醇).⁴⁷

Fuxiaomai (*Triticum fructus levis*)

This herb is the light grains of *Triticum aestivum* (family *Gramineae*).⁴⁷ It is used for hectic fever and sweating.⁶⁰ It is an integral component of the traditional formula ‘Liquorice, wheat and jujuba soup’ used in the treatment of insomnia.⁵⁸ Light wheats contain saccharides, sitosterol, vitamins, and enzymes.

Roots and rhizomes

Banxia (*Pinelliae rhizoma*)

The herb is the dried tuber of the *Pinellia ternata* (family *Araceae*).⁴⁷ Used as a diuretic, expectorant, and anti-emetic, it is included in the traditional formula, ‘Pinellia

and millet soup’ for the treatment of insomnia.²⁵ It requires a special preparation of banxia in order to minimise toxicity.⁶¹ A study in mice suggests that it might have sedative and anti-convulsive effects.⁶² It contains glutamic acid, arginine, aminotuburic acid, choline, β -sitosterol, and homogentisic acid.⁴⁷

Chuanxiong (*Chuanxiong rhizoma*)

This herb is the dried rhizome of the *Ligusticum chuanxiong* (family *Umbelliferae*).⁴⁷ It is used as an anti-rheumatic, an analgesic, and a blood activator. It is also included in some herbal formulas such as Suanzaoren Tang for treatment of insomnia.⁵⁸ Extracts have demonstrated affinity to GABA and 5HT_{1a} receptors.⁵⁷ This herb contains butylidenephthalide, butylphthalide, tetramethylpyrazine, and indole.⁴⁷

Danshen (*Radix salviae miltiorrhizae*)

This herb is the dried root of the *Salvia miltiorrhiza* or *Salvia przewalskii* (family *Labiatae*).⁴⁷ It is used as a tranquiliser, for the treatment of menstrual disorders, and for insomnia. Combined with wuweizi, it was shown to improve insomnia in a case series of 48 patients (71% cured and 21% improved with treatment).⁶³ A further study compared treatment of insomnia with a 5-day course of danshen plus huangqi (黃芪) in 80 patients, with 76 patients receiving another patent TCM formula. Improvement was seen in 93% of patients with the combination treatment, while 75% improved with the patent formula.⁶⁴ These studies, however, were limited by lack of randomisation, placebo group, and statistical analysis. Extracts of danshen have demonstrated affinity to benzodiazepine receptors.⁵⁸ Danshen contains tanshinone, cryptotanshinone, isotanshinone, miltirone, and danshenxinkun.⁴⁷

Baijianggan (*Patriniae rhizoma et radix*)

The herb is the dried root and rhizome of the *Patrinia scabiosaefolia* (family *Valerianaceae*).⁴⁷ It is used for

the treatment of hepatitis, carbuncles, neurasthenia, and insomnia. As discussed previously, a closely related species, valerian, has long been used in the West as a folk remedy for insomnia. Patrinia root contains mainly triterpenoid saponins, patrinene, isopatrinenone, and isovaleric acid.⁴⁷

Chaihu (*Bupleuri radix*)

The herb is the dried root of *Bupheurum chinense*, *Bupheurum scorzoniferolium* or *Bupheurum marginatum* (family *Umbelliferae*).⁴⁷ It is used for treating fever, and liver complaints, but is also included in some herbal formulas for insomnia, such as Xiao Yao Wan. The water extracts of the herb have an affinity for the dopamine D₂, GABA and 5HT_{1a} receptors.⁵⁷ Chaihu contains saikosaponin, adonitol, α -spinasterol, and volatile oils.⁴⁷

Danggui (*Radix angelicae sinensis*)

The commonly used herb is the dried root of *Angelica sinensis* (family *Umbelliferae*).⁴⁷ It is used as a blood activator, menstruation regulator, analgesic, and aid to digestion, but is also a common ingredient in many herbal formulas for the treatment of insomnia, such as Xiao Yao Wan, Tian Wan Bu Xin Dan, and Zhu Sha An Shen Wan.⁵⁸ The extracts have demonstrated affinity for the GABA and 5HT_{1a} receptors.⁵⁷ Danggui contains monoterpenoids, sesquiterpenoids, β -sitosterol, ferulic acid, and succinic acid.⁴⁷

Baizhu (*Rhizoma atractylodis macrocephalae*)

The herb is the dried rhizome of *Atractylodes macrocephala* (family *Compositae*).⁴⁷ It is used for anorexia, chronic diarrhoea, dizziness, and lethargy, but is also included in herbal formulas such as Xiao Yao Wan.⁵⁸ The rhizome contains atractylon, butenolide, acetoxyatractylon, and hydroxy-butenolide.⁴⁷

Ganjiang (*Zingiberis rhizoma*)

The herb is the dried rhizome of *Zingiber officinalis* (family *Zingiberaceae*).⁴⁷ It is used for the treatment of epigastric pain and faint pulse but is also included in some herbal formulas, such as Xiao Yao Wan. Animal studies suggest it has a hypnotic effect, prolonging the sleep of mice induced by pentobarbitone, and suggesting a synergistic action with banxia.⁶⁵ Ganjiang or dried ginger contains zingiberol, zingiberene, bisabolene, and farnesene.⁴⁷

Cortex

Hehuanpi (*Albizzia cortex*)

This herb is the dried stem bark of *Albizzia julibrissin durazz* (family *Leguminosae*).⁴⁷ It is used as a sedative and blood activator, for the treatment of distractibility, depression, and insomnia.⁶⁰ The stem bark contains

saponins such as julibroside J6, acacigenin B, and tannin.^{47,66}

Rattan

Shouwuteng (*Polygoni caulis*)

The herb is the dried stem of *Polygonum multiflorum* (family *Polygonaceae*).⁴⁷ It is used for the treatment of insomnia and rheumatic diseases. Animal studies with rats suggest it increases slow wave sleep, reduces REM sleep and has a synergistic hypnotic effect with pentobarbital.⁶⁷ It contains anthraquinones.⁴⁷

Fungus

Lingzhi (*Ganoderma*)

The fungus is the dried fructifications of *Ganoderma lucidum* (赤芝) or *Ganoderma sinense* (紫芝) (family *Polyporaceae*).⁴⁷ It is used as a tranquiliser, appetiser, and tonic, as well as for the treatment of neurasthenia, insomnia, loss of appetite, and weakness. *Ganoderma lucidum* contains triterpenes, such as ganoderic acid, lucidenic acid, and ganolucidic acid.^{47,68}

Fuling (*Poria*)

This fungus is the dried sclerotium of *Poria cocos* (family *Polyporaceae*).⁴⁷ It is used for the treatment of oedema, dizziness and palpitations, diarrhoea, restlessness, and insomnia. It is a common ingredient in a number of formulas such as Suanzaoren Tang, Xiao Yao Wan and Tian Wang Bu Xin Dan.⁵⁸ The sclerotium contains a number of chemicals: triterpenic acids, histidine, adenine, choline, β -pachymanase, lecithin, ergosterol, and porin.⁴⁷

Minerals

Zhusha (*Cinnabaris*)

The drug is in the cinnabar group of minerals of the sulphide class.⁴⁷ It is used as a tranquiliser and anti-inflammatory agent, for the treatment of palpitations, insomnia, epilepsy, and blurred vision. The main caution with its use is the cumulative toxicity of mercury when zhusha is taken for a long time or in large quantity.⁶⁹ Due to this risk of toxicity, a recent case series adapted the external use of zhusha in children as treatment for night terror and sleeping difficulties.⁷⁰ Cinnabar contains mainly mercuric sulphide and other trace elements.⁴⁷

Commonly used traditional Chinese medicine formulas in the treatment of insomnia

As mentioned previously, TCM herbs are rarely used alone but rather in combination formulas. Insomnia and traditional formulas have been noted in Chinese medicine from the earliest records. In Ling Shu (200 AD), the description of 'Pinellia and millet soup' in the

treatment of insomnia is described as follows: “the chi runs against the direction of flow...eyes cannot close... For new occurrence, it suffices to take a drink and one sleeps soon after turning over the cup... for chronic cases, 3 drinks will show effect”.²⁵ Though most of the traditional and modified formulas have survived the passing of time, robust clinical studies are required to confirm their effectiveness in insomnia. Moreover, with composite formulas it is sometimes difficult to determine the main active ingredient, and the possibility of herb-herb interaction cannot be excluded. Nevertheless, these traditional formulas have been widely used for centuries and are therefore a good beginning point for further investigation (Table 5).

‘Pinellia and millet soup’

This formula has a long tradition. The main ingredients are a simple mix of Pinellia rhizoma and Setaria italica.²⁵ The formula can be further mixed with or added to Xiao Yao Wan, or combined with Dan Zhi Xiao Yao Wan (丹樞逍遙丸). A recent study on mice

with a modified formula (including Sclerotium poriae cocos and Zingiberis rhizoma) suggested a similar antidepressant effect to that of Prozac.⁷¹

‘Liquorice, wheat and jujuba soup’

This traditional herbal formula, ‘Liquorice, wheat and jujuba soup’ was first recorded in the ‘Golden Chest’ (300 AD), and contains Radix glycyrrhizae, Triticum aestivum, and Fructus ziziphus.²⁴ It has been a common prescription for treating mental problems including neurasthenia, insomnia and even schizophrenia, and for restoring cardiac rhythm.⁵⁸ Animal studies support a hypnotic effect in rats.^{72,73} Open case series of more than 100 patients with either insomnia or neurasthenia reported an improvement in 80% to 90% of cases with treatment.⁷⁴ These studies, however, were limited by the lack of randomisation and a control group.

Suanzaoren Tang

This famous traditional formula was first recorded in the Han dynasty classical text, the ‘Golden Chest’.²⁴

Table 5. Traditional Chinese medicine preparations/formulas for treating insomnia

Preparation/formula	Ingredients	成分
‘Pinellia and millet soup’ 半夏秫米湯	<ul style="list-style-type: none"> • Pinelliae rhizoma • Setaria italica 	<ul style="list-style-type: none"> • 半夏 • 秫米
‘Liquorice, wheat and jujuba soup’ 甘麥大棗湯	<ul style="list-style-type: none"> • Radix glycyrrhizae • Triticum aestivum • Fructus ziziphus 	<ul style="list-style-type: none"> • 甘草 • 小麥 • 大棗
Suanzaoren Tang 酸棗仁湯	<ul style="list-style-type: none"> • Semen ziziphi spinosae • Poria • Chuanxiong rhizoma • Rhizoma anemarrhenea • Radix glycyrrhizae 	<ul style="list-style-type: none"> • 酸棗仁 • 茯苓 • 川芎 • 知母 • 甘草
Xiao Yao Wan 逍遙丸	<ul style="list-style-type: none"> • Radix bupleuri • Radix angelicae sinensis • Radix albus paeoniae lactiflorae • Rhizoma atractylodis macrocephalae • Poria • Radix glycyrrhizae • Herba menthae haplocalycis • Uncooked Rhizoma zingiberis 	<ul style="list-style-type: none"> • 柴胡 • 當歸 • 白芍 • 白朮 • 茯苓 • 甘草 • 薄荷 • 生乾薑
Tian Wang Bu Xin Dan 天王補心丹	<ul style="list-style-type: none"> • Uncooked Radix rehmanniae • Radix scrophulariae ninpoensis • Fructus schisandrae • Tuber asparagi cochinchinensis • Tuber ophiopogonis japonici • Radix angelicae sinensis • Platycladi semen • Semen ziziphi spinosae • Radix salviae miltiorrhizae • Radix polygalae tenuifoliae • Poria • Radix codonopositis pilosulae 	<ul style="list-style-type: none"> • 生地黃 • 玄參 • 五味子 • 天門冬 • 麥門冬 • 當歸 • 柏子仁 • 酸棗仁 • 丹參 • 遠志 • 茯苓 • 黨參
Zhu Sha An Shen Wan 朱砂安神丸	<ul style="list-style-type: none"> • Radix angelicae sinensis • Uncooked Radix rehmanniae • Rhizoma coptidis chinensis • Rhizoma coptidis • Cinnabaris 	<ul style="list-style-type: none"> • 當歸 • 生地 • 黃蓮 • 甘草 • 朱砂

Suanzaoren Tang (soup or mixture) contains *Semen zizyphi spinosae*, *Sclerotium poriae cocos*, *Radix ligustici wallichii*, *Rhizoma anemarrhenea aspheloidis*, and mix-fried *Radix glycyrrhizae*. A group of Japanese researchers has suggested that this herbal formula may modulate stress-related sleep changes in mice rather than merely act as a hypnotic.⁵⁵ Clinically, there are different formulations in use with apparently similar effects in treating insomnia.⁷⁵ Most clinical studies of Suanzaoren Tang have been case series.⁵⁸ One large series of 209 patients with neurasthenia and insomnia demonstrated significant improvement in symptoms with Suanzaoren Tang treatment.⁷⁶ A more recent large-scale double-blind case-controlled study of 303 patients with insomnia has been reported. One hundred and fifty-one patients received a combination 'sleep-aid pill' (containing suanzaoren, baishao, *Radix bupleuri*, *Albizziae*, etc), while 152 patients received an 'Anshen pill' (ingredients not revealed). More patients receiving the 'sleep-aid pill' demonstrated improvement (92.7%) than did patients in the 'Anshen pill' group (85.5%).⁷⁷ Although this study used a better research design than earlier studies, the lack of a placebo group, objective assessment, and the unknown ingredients of the 'Anshen pill' limit the interpretation of this study.

Xiao Yao Wan

Xiao Yao Wan has a long tradition and was originally recorded in the Sung dynasty, (太平惠民和劑局).⁷⁸ The literal translation of the name of this formula means 'promotion of a free and relaxed spirit'. The ingredients include *Radix bupleuri*, *Radix angelicae sinensis*, *Radix albus paeoniae lactiflorae*, *Rhizoma atractylodis macrocephalae*, *Sclerotium poriae cocos*, mix-fried *Radix glycyrrhizae*, *Herba menthae haplocalycis*, and uncooked *Rhizoma zingiberis*. This formula has long been used to treat mood-related problems. Case series also suggest it effects an improvement in sleep and mood, as well as reducing chronic fatigue.^{79,80} A further modification of this formula is to add *Cortex radcis moutan* and *Fructus gardeniae jasminoidis*. This modified formula, known as Dan Zhi Xiao Yao Wan, is believed to have a better effect on depression-related anxiety and irritability.

Tian Wang Bu Xin Dan

This traditional formula (攝生秘方) was first recorded in the Ming dynasty.⁸¹ The name of this formula is translated as Heavenly Emperor's Supplement, the Heart Elixir. It is used to treat insomnia, restlessness, fatigue, and palpitations.⁵⁸ The ingredients include: uncooked *Radix rehmanniae*, *Radix scrophulariae ninpoensis*, *Fructus schisandrae chinensis*, *Tuber asparagi cochinchinensis*, *Tuber ophiopogonis japonici*, *Radix angelicae sinensis*, *Semen biotae orientalis*, *Semen*

zizyphi spinosae, *Radix salvia miltiorrhizae*, *Radix polygalae tenuifoliae*, *Sclerotium poriae cocos*, and *Radix codonopositis pilosulae*. As can be seen, some of the ingredients are shared with Suanzaoren Tang. Adverse reactions of skin rash, oedema, diarrhoea, and dyspepsia have been reported.⁵⁸

Zhu Sha An Shen Wan

This traditional formulation was first recorded in the Ming dynasty.⁵⁸ The ingredients include *Radix angelicae sinensis*, uncooked *Radix rehmanniae*, *Rhizoma coptidis chinensis*, *Radix glycyrrhizae*, and cinnabar. Studies in cats have demonstrated a decrease in awake time, an increase in sleep duration and slow wave sleep, and a shortening of sleep latency with use.⁸² Cinnabar, however, is a mercuric compound and the toxic effect of mercury is cumulative. Thus, this formula should be used very cautiously and only for a very short period, if at all. It is contraindicated in children and pregnant woman.

Future directions in the herbal treatment of insomnia

The importance of herbal/TCM treatment in the management of illness is increasingly being recognised. There has been a long tradition in TCM of using specific herbs, fungal, animal, and mineral ingredients, mostly in composite formulas, for treating insomnia. While both western and oriental herbal treatment equally have not been subjected to rigorous study, it is apparent that TCM has a greater variety of herbs and formulations available for the treatment of insomnia. More basic and clinical studies are required however, to demonstrate their safety and efficacy.

The application of the modern scientific approach to research, using randomised controlled studies, with standardised dosages and measurements (both subjective and objective), as well as careful monitoring of any adverse effects and potential drug interactions, is essential. Some individual TCM herbal and fungal ingredients, such as *Semen zizyphi spinosae*, *Fructus zizyphi jujubae*, *Semen biotae*, *Radix salviae miltiorrhizae*, *Cortex albizziae*, *Caulis polygoni multiflori*, *Poria* and *Ganoderma lucidum*, appear promising for the treatment of insomnia. Composite formulas such as 'Pinellia and millet soup', 'Liquorice, wheat and jujuba soup', Suanzaoren Tang, and Xiao Yao Wan also appear to have therapeutic potential.

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