

# The Use of Supplements, Herbs, and Alternative Therapies in the Treatment of Insomnia

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Insomnia, one of the most common complaints seen in the primary care office, affects at least 30% of the U.S. adult population at an estimated cost to the healthcare system of \$241 billion annually. A number of medications—both over-the-counter (OTC) and prescription—are used to treat insomnia, yet all have varying degrees of unwanted side effects. Antihistamines are the most widely used OTC medications and can have side effects ranging from dizziness to urinary retention. Benzodiazepines, one of the most-used classes of prescription medications for insomnia, can also have deleterious side effects, including daytime sedation and memory impairment.

Due to both the real and perceived side effect profiles of these OTC and prescription medications, more patients are turning to alternative and non-pharmacological therapies to treat their insomnia. Some popular herb and dietary supplements used to treat insomnia include melatonin, tryptophan, valerian, chamomile, lemon balm, and kava. Non-herbal treatments for insomnia include osteopathic cranial manipulation and acupuncture.

With the continuing widespread use and acceptance of complementary and alternative therapies for a wide range of medical conditions, family medicine physicians need to be aware of what alternative therapies their patients may be using for sleep disturbances. While many patients believe that alternative or “natural” products are completely safe, herbs and other supplements can have unwanted side effects and interactions with prescription medications of which both physicians and patients need to be aware.

## INTRODUCTION

Insomnia is one of the most common complaints seen by family medicine physicians. The National Institutes of Health have estimated that at least 30% of the U.S. adult population suffers from insomnia.<sup>1</sup> Sleep disturbances can lead to a number of patient complaints, including fatigue, depression, difficulty concentrating, and an overall decrease in quality of life. The economic cost of insomnia is also significant due to increased healthcare utilization, decreased work performance and productivity, and an increase in work-related accidents. A recent review article estimated that the total economic burden of insomnia is approximately \$241 billion annually in the United States.<sup>2</sup>

There are a number of over-the-counter (OTC) and prescription medications that are used to treat insomnia; however, they all carry, to one degree or another, some form of undesirable side effects. All OTC medications approved by the U.S. Food and Drug Administration (FDA) are antihistamines, such as diphenhydramine or doxylamine. Both agents are

sedating, although, most patients develop tolerance to these effects, which therefore decreases their long-term potential as sleep-inducing agents.<sup>3</sup> Other side effects, including next-day grogginess and anticholinergic side effects (dry mouth, urinary retention, constipation, and mental confusion), may deter patients from taking these medications for any length of time.

A number of prescription medications are also available to treat insomnia, with the majority of those being benzodiazepine (BZD) receptor agonists. The first BZD, introduced in 1960, was Chlordiazepoxide. It was soon followed by a number of other BZD agonists. As their name implies, BZD agonists are believed to treat insomnia by binding to the GABA complex in the brain with resulting inhibitory effects on arousal and alertness. All BZDs shorten sleep latency, decrease nocturnal awakenings, and generally increase total sleep time. Most BZDs are only recommended for treating short-term (2-4 weeks) insomnia because they can disrupt sleep architecture and produce other undesirable side effects, including daytime sedation, rebound insomnia, and amnesia. Newer, more selective BZD receptor agonists, such as zolpidem, zaleplon, and eszopiclone, do not deleteriously affect sleep architecture and one, eszopiclone, has been given FDA approval to be used for up to six continuous months. Side effects of these

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newer medications can include memory impairment, sensory disturbances, and psychotic symptoms.

Due to both the real and perceived undesirable side effects of OTC and prescription medications for insomnia, there is a growing interest among patients in more “natural” or holistic remedies for sleep disturbances. The use of complementary or alternative medicine (CAM) has been steadily increasing in the United States in the past 30 years, with studies showing that more than 50% of the adult population uses some type of medical therapy classified as alternative.<sup>4</sup> CAM modalities have a long history in the use of treating insomnia; historical texts indicate the Greek physician Galen prescribed the herb valerian to his patients to help them sleep. A survey study done in 2006 among 2,000 adults reported that 15% of them admitted to using at least one herbal/dietary supplement to help them sleep in the previous year, compared to 11% who reported using a prescription sleep medication.<sup>5</sup>

Many physicians—both osteopathic and allopathic—are uncomfortable recommending alternative remedies to their patients due to a lack of knowledge regarding CAM therapies or the idea that alternative methods are not scientifically valid. However, a search in the literature reveals there are a number of studies on alternative modalities for insomnia that show patients and their physicians do have a number of choices with which to treat this very common, and at times debilitating, condition.

## NON-PHARMACOLOGICAL ALTERNATIVE MODALITIES FOR THE TREATMENT OF INSOMNIA

### Osteopathic Cranial Manipulation

Cranial manipulation is a technique of manual medicine used by a growing number of osteopathic family medicine physicians.<sup>6</sup> A widely used cranial manipulative technique is compression of the fourth ventricle (CV4), a technique used to influence the rate of the cranial rhythmic impulse. Some limited studies have shown that the CV4 technique can decrease sympathetic tone, and by doing so, can induce a state of relaxation and perhaps treat insomnia. Operating off this idea, Cutler et. al. did a pilot study on 20 healthy men and women, aged 22-35, to see if cranial manipulation could sympathetic nerve activity and sleep latency.<sup>7</sup> The subjects were randomized into three groups: those receiving cranial manipulation; those receiving sham manipulation (simple touching of the scalp); and those having neither (as controls). Results showed that subjects receiving CV4 manipulation had decreased sleep latency when compared with the sham and control groups, leaving the authors to conclude “...cranial manipulation, specifically the CV4 technique, can alter sleep latency and directly measured MSNA [muscle sympathetic nerve activity] in healthy humans.”

### Acupuncture

Acupuncture is used commonly in Asia for a variety of medical complaints, including insomnia. There have been a number of studies conducted on the efficacy of acupuncture in treating insomnia, with some of these studies being randomized controlled trials. Two recent review articles that have examined the validity of these studies have concluded that acupuncture can play a role in the non-pharmacological treatment of insomnia.<sup>8,9</sup>

In a 2009 systematic review of randomized controlled trials of acupuncture treatment of insomnia, the authors examined 46 randomized trials involving 3,811 women and men.<sup>9</sup> Meta-analysis studies of these trials showed a statistically significant and beneficial effect of acupuncture on insomnia. In addition, two randomized trials showed acupuncture use along with BZDs was more efficacious in treating insomnia than BZDs alone.<sup>10,11</sup> Due to the number of statistically significant positive studies on acupuncture treatment of insomnia, the authors of the 2009 meta-analysis concluded, “Acupuncture appears to be effective in the treatment of insomnia.”

## DIETARY & HERBAL SUPPLEMENTS FOR THE TREATMENT OF INSOMNIA

**Table 1: Dietary & herbal supplements for the treatment of insomnia**

Name	Dose	Possible side effects and/or interactions
Melatonin	1-10mg	Daytime sleepiness, dizziness, headaches, possible interactions with anticoagulants, BZDs, OCPs, antidiabetic medications
Tryptophan	2-5 grams	Heartburn, nausea, daytime sleepiness, possible interactions with SSRIs, MAOIs, BZDs
Valerian	200-600 mg	Daytime sleepiness, headaches, possible interactions with BZDs
Chamomile	200-300 mg	Daytime sleepiness, possible interactions with BZDs
Lemon Balm	500-1000 mg	Daytime sleepiness, dizziness, possible interactions with BZDs
Kava	100-300 mg	Daytime sleepiness, dizziness, liver damage, possible interactions with TCAs, SSRIs, BZDs, Levo dopa

### Melatonin

Melatonin, a hormone produced in the pineal gland, is the end product of an enzyme-catalyzed biosynthetic pathway that begins with the amino acid tryptophan. Melatonin is secreted by the pineal gland in a circadian (from Latin: “about one day”) rhythm. In the daytime, via signaling of the suprachiasmatic nucleus (SCN) of the hypothalamus, melatonin production and release are suppressed. At nighttime with fading light,

melatonin production and secretion is increased many times over and is a prime signal of sleep in all mammals, including humans.

Due to the known connection between melatonin and sleep, there have been a number of studies examining the use of melatonin to treat insomnia. An early randomized, placebo-controlled double-blind study done in 2001 examined the effects of different doses of melatonin (0.1, 0.3, and 3.0 mg) on insomnia in patients over 50 years of age.<sup>12</sup> All doses, taken 30 minutes before bedtime, restored sleep efficiency, with the 0.3 mg dose elevating melatonin levels to normal and the 3.0 mg dose inducing hypothermia and causing plasma melatonin levels to remain elevated into daylight hours.

More recent studies have also confirmed the use of melatonin to treat insomnia.<sup>13,14,15</sup> A randomized, double-blind placebo-controlled trial of 2 mg prolonged release melatonin was done in 2010 on 791 men and women, aged 18-80 years, with primary insomnia.<sup>14</sup> Over an eight-month period, the authors showed that elderly patients receiving melatonin had a statistically significant decrease in their sleep latency, which was maintained over the treatment period.

### **Tryptophan**

Since melatonin is synthesized in the body from tryptophan, there have been a number of studies examining the effects of supplementation of this amino acid on insomnia and sleep parameters.<sup>16,17,18,19</sup> A small, double-blind placebo-controlled trial examined the effects of 2 grams of tryptophan administration in eight middle-aged men and women.<sup>17</sup> Patients taking tryptophan showed a decrease in their sleep latency with no undesirable side effects. Another similar study examined the effects of the supplementation of 5 grams of tryptophan on patients with insomnia.<sup>18</sup> As in earlier studies, patients taking tryptophan showed a decrease in their sleep latency times as well as an improvement on sleep period time and total sleep time.

### **Valerian**

Valerian (*Valeriana officinalis*) is a perennial herb native to both Europe and Asia. Its roots and stems have been used by herbal medicine practitioners for at least 2,000 years to treat insomnia and is the most commonly used herbal product to treat insomnia in both Europe and the United States.<sup>20,21,22</sup> Due to its long use in traditional medicine, numerous studies and review articles have examined the scientific validity of valerian to treat insomnia.<sup>23-28</sup>

An early randomized, double-blind placebo-controlled crossover study published in 2000 assessed the effects of

valerian extract on both objective and subjective sleep parameters in 16 male and female patients, aged 22-55, with subjective complaints of insomnia.<sup>23</sup> During the two-week study, patients underwent eight polysomnographic recordings during which both the short- and long-term effects of valerian, compared with placebo, were examined. No effects of valerian were noted after a single dose. However, multiple doses of valerian produced statistically significant reductions in sleep latency as well as other improvements in sleep architecture, such as an increase in REM sleep percentage. The authors concluded, "...treatment with a herbal extract of radix valerian demonstrated positive effects on sleep structure and sleep perception of insomnia patients, and can therefore be recommended for the treatment of patients with mild psychophysiological insomnia."

Other, newer studies have confirmed the efficacy of valerian in treating insomnia. A randomized, double-blind study published in 2002 compared the effects of 600 mg valerian root extract versus 10 mg of oxazepam among 202 male and female patients, aged 18-73, who suffered from insomnia.<sup>28</sup> At the end of this six-week study, both valerian and oxazepam reduced time to sleep and increased sleep length. In addition, according to multiple subscales (refreshment after sleep, exhaustion in the evening, dream recall, and duration of sleep), both agents showed essentially the same efficacy.

Two meta-analysis of randomized placebo-controlled trials of valerian for sleep (one done in 2006 in the United States and one in 2010 in Europe) showed that valerian was effective for the treatment of insomnia.<sup>26,27</sup> The 2006 report identified 16 studies with a total of 1,093 male and female patients. The authors reported that random effects modeling of the pooled data showed that the use of valerian almost doubled the chances of sleeping better when compared with placebo. The 2010 European study analyzed 18 studies with a total of 1,317 male and female patients and concluded that, "The qualitative dichotomous results suggest that valerian would be effective for a subjective improvement of insomnia, although its effectiveness has not been demonstrated with quantitative or objective measurements."

Finally, a recently published article (2011) reported on the effects of valerian on sleep quality in postmenopausal women.<sup>27</sup> In this randomized, placebo-controlled triple-blind trial of 100 women aged 50-60, subjects took either 530 mg of valerian extract or placebo twice a day for four weeks. The results of the study showed that the women taking valerian had a statistically significant improvement in their quality of sleep when compared with the women taking placebo.

## Chamomile

Chamomile (*Matricaria recutita*) is a herb that has been used for millennia in traditional herbal medicine for a variety of ailments, including insomnia.<sup>29</sup> Scientific studies have shown that the dried flower heads of chamomile contain a compound (apigenin) that is an agonist for central benzodiazepine receptors that can elicit anxiolytic and sedative effects.<sup>30</sup> A recent study published in 2011 examined the effects and efficacy of chamomile extract for insomnia.<sup>31</sup> In this randomized, placebo-controlled double-blind study, 34 men and women, aged 18-65 years, with the diagnosis of insomnia were randomized over a 28-day period to receive either placebo or 270 mg of chamomile extract daily. Those patients randomized to the chamomile group showed a small to moderate decrease in sleep latency, nighttime awakenings and Fatigue Severity Schedule, leading the authors of the study to conclude, “Chamomile could provide benefits of daytime functioning and mixed benefits on sleep diary measures relative to placebo in adults with chronic primary insomnia.”

## Lemon Balm

Lemon Balm (*Melissa officinalis*) is a perennial lemon scented herb that has been used for centuries to treat a variety of health-related disorders. It is often sold and consumed in combination with valerian for insomnia, with studies showing that this combination can improve sleep quality in patients with sleep disorders.<sup>32,33</sup> A recent 2011 study examined the effects of lemon balm extract alone in the treatment of anxiety disorders and insomnia.<sup>34</sup> In this prospective, open-label study, 20 men and women, aged 18-70 years, took 600 mg of a proprietary lemon-balm extract twice daily for 15 days. At the end of the study, 14 out of the 20 patients reported full remission of their anxiety, while 85% (17/20) reported resolution of their insomnia.

## Kava

Kava (*Piper methysticum*) is a perennial plant native to the islands of the Pacific and has been used in traditional ceremonies there for millennia. Kava is known to have sedative properties, and it is hypothesized that this is brought about by GABA-binding activities of some of the plants biochemically active constituents.<sup>35</sup> An early double-blind, placebo-controlled study published in 1991 showed that 100 mg of Kava extract taken three times daily significantly reduced anxiety among 29 subjects.<sup>36</sup> A more recent study examined the effects of a kava extract on insomnia secondary to anxiety.<sup>37,38</sup> In this randomized, placebo-controlled, double-blind clinical trial, 61 men and women received 200 mg of a standardized kava extract (WS 1490) or placebo for four weeks. At the end of the study, those subjects taking the kava extract showed a statistically significant self-reported increase

in quality of sleep when compared with those subjects taking placebo. The authors of the study stated, “We conclude that sleep disturbances associated with non-psychotic anxiety disorders can be effectively and safely treated with kava extract WS 1490.”

## CONCLUSIONS

Insomnia continues to be, and most likely will continue to be, a major complaint of patients seen by osteopathic family physicians. While benzodiazepines will continue to be the mainstay of standard pharmacological treatment, integrative therapies—including cranial manipulation, acupuncture, supplements like melatonin and herbs such as valerian—have the potential to play an important role in the treatment of insomnia.

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