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Valerian for Sleep: A Systematic Review and Meta-Analysis

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Abstract

Insomnia affects approximately one-third of the adult population and contributes to increased rates of absenteeism, health care use, and social disability. Extracts of the roots of valerian (*Valeriana officinalis*) are widely used for inducing sleep and improving sleep quality. A systematic review of randomized, placebo-controlled trials of valerian for improving sleep quality is presented. An extensive literature search identified 16 eligible studies examining a total of 1093 patients. Most studies had significant methodologic problems, and the valerian doses, preparations, and length of treatment varied considerably. A dichotomous outcome of sleep quality (improved or not) was reported by 6 studies and showed a statistically significant benefit (relative risk of improved sleep = 1.8, 95% confidence interval, 1.2-2.9), but there was evidence of publication bias in this summary measure. The available evidence suggests that valerian might improve sleep quality without producing side effects. Future studies should assess a range of doses of standardized preparations of valerian and include standard measures of sleep quality and safety.

Keywords: Herb, Alternative medicine, Insomnia, Sleep, Meta-analysis, Systematic review

Insomnia is one of the most common complaints among adults. Numerous surveys conducted in countries around the world report that approximately 30% to 40% of adults have problems initiating or maintaining sleep.[1-3] A smaller percentage of adults report severe problems (10%-15%), but the prevalence of severe, chronic sleep problems increases to 25% in the elderly.[2] Insomnia is also more common in patients with chronic medical problems and is found in up to 69% of patients enrolled in primary care clinics.[4]

Approximately 40% of adults with insomnia have used either over-the-counter medication or alcohol to

help induce sleep, and approximately one-quarter have used prescription medications at least once.[1] There is only limited evidence to support the efficacy of many of the commonly used medications for insomnia, including antihistamines, chloral hydrate, barbiturates, tryptophan, and melatonin.[5] Although benzodiazepines are known to be effective for insomnia, the clinical benefit is small (<1 hour of increased sleep) and similar to that found with exercise therapy alone.[6] Moreover, chronic benzodiazepine therapy for sleep is associated with several negative side effects, including cognitive impairment and an increased risk of motor vehicle accidents, falls, and fractures.[5]

The extract of the root of valerian (*Valeriana officinalis*), a flowering plant, has been widely used to treat sleeping disorders in Europe for decades.[7] Valerian is becoming increasingly popular in the United States as a self-prescribed treatment for insomnia. In a national survey conducted in 2002, 1.1% of the adult population in the United States, or approximately 2 million adults, reported using valerian in the past week.[8] If valerian is an effective treatment for insomnia, it may be an important treatment alternative because it is relatively inexpensive and without known side effects. We sought to clarify the efficacy of valerian for improving sleep quality by conducting a systematic review and meta-analysis of all prior randomized, controlled trials.

Methods

We conducted a search of PUBMED, EMBASE, IBIDS, BIOSIS, and the Cochrane Library (through June 2005) using the keywords “valerian,” “valeriana,” and “baldrian” and retrieved and screened all relevant publications in all languages. Studies were included if they were randomized, placebo-controlled trials of valerian reporting some measure of sleep quality.

Two authors independently abstracted all relevant data including study quality, which was assessed with a commonly used scale (the Jadad scale; range: 0-5, higher scores indicate better quality).[9] No single measure of sleep quality was reported in all studies. The most commonly reported outcome of sleep quality was a simple dichotomous measure (sleep quality improved or not), and studies reporting this outcome were combined using both a fixed-effects (Mantel-Haenszel method) and a random-effects (DerSimonian and Laird method) model. Heterogeneity of pooled studies was assessed with the Q statistic.[10] A funnel plot was used to examine the correlation between study outcome (relative risk) and standard error, and a statistical test of this relationship was performed using Kendall's tau.[11]

Results

Our search yielded a total of 370 articles. Sixteen randomized, controlled trials, examining a total of 1093 patients, satisfied all inclusion criteria. The characteristics of the individual studies are shown in Table 1. (Studies are arranged in order of decreasing sample size). The sample size for most of the studies was small, with 8 of the studies examining fewer than 25 patients.[12-19] The severity of insomnia in study participants was generally not well defined, although most studies included otherwise healthy patients with some self-reported sleep problems. Two studies were limited to elderly patients,[13,20] and 1 study enrolled only children with intellectual deficits.[16] One study was a combination of multiple n-of-1 studies, rather than a traditional randomized, controlled trial.[17] One study was a randomized, controlled trial that recruited and enrolled all patients entirely over the Internet.[21]

Table 1

Randomized, Controlled Trials of Valerian for Sleep

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NR = not reported.

*Quality was assessed using the Jadad scale (0-5 points).

†Sleep quality improvement indicates a statistically significant benefit in the reported subjective sleep quality measure.

The average study quality was 3.4 (95% confidence interval [CI], 3.0-3.9, 0-5 scale), indicating important methodologic problems in the included studies. There was significant variation in study design, including variations in valerian preparation and dosing, length of treatment, and outcome assessment (Table 1). Valerian doses ranged from 225 to 1215 mg per day, excluding the 1 study involving children whose doses were based on weight.[16] Only 2 of the 16 studies stated that the valerian extract was standardized to a specific percentage of valerenic acids.[17,21]

There was no single sleep quality outcome measure reported by all of the included studies. Seven studies[12-14,16,19,22,23] used a visual analog scale to assess change in sleep quality among participants. Five of these 7 studies[12-14,19,23] reported that there was no statistically significant improvement in the visual analog scales in the valerian group compared with the placebo group. The remaining 2 studies[16,22] noted improvements in the valerian groups but did not present enough information to determine whether the changes were statistically significant compared with the placebo group. The statistical presentation of the data did not allow pooling of this outcome measure.

The most commonly reported outcome measure that could be combined was a dichotomous outcome of sleep quality (sleep improved or not), which was reported in 6 of the 16 studies.[20,21,23-26] With the more conservative random-effects model to pool these data, the use of valerian was found to almost double the chance of sleeping better when compared with placebo (relative risk of improved sleep = 1.8, 95% CI, 1.2-2.9) (Figure 1). The studies were heterogeneous, which is clear from a visual inspection of Figure 1, in which the Jacobs study is the only one showing no effect. Because the Jacobs study used a unique, Internet-based design, we performed a sensitivity analysis and found that there was no significant heterogeneity when this study was excluded from the meta-analysis (relative risk = 1.9, 95% CI, 1.6-2.3, *P* value for heterogeneity = .3).

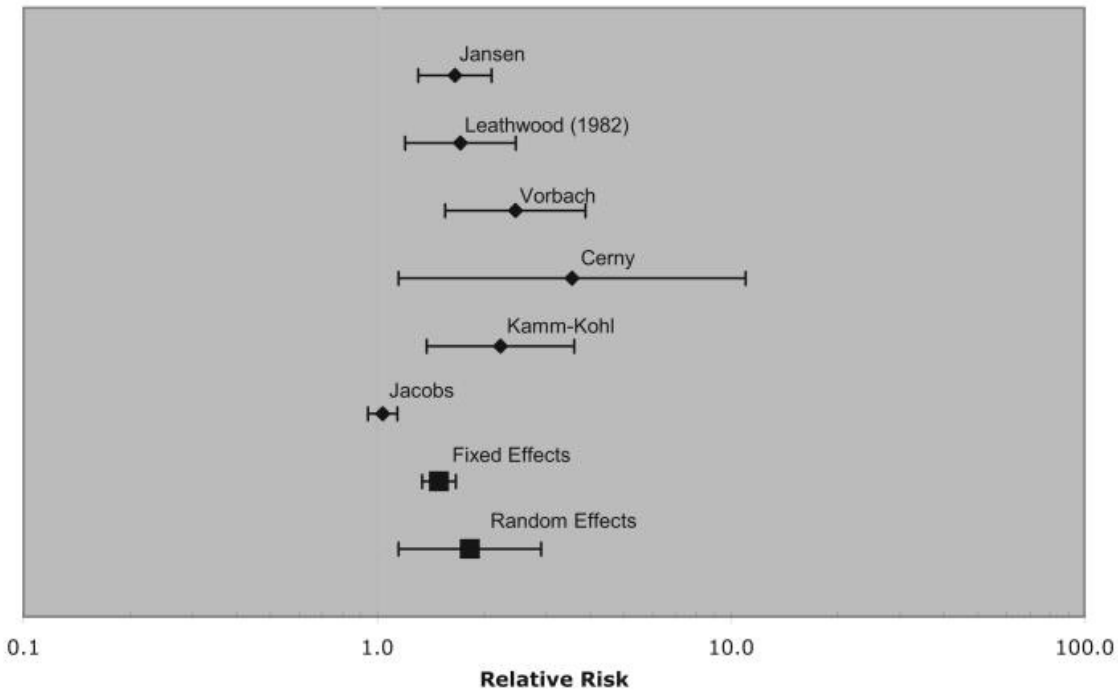

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Figure 1

Meta-analysis of 6 studies reporting dichotomous outcomes for sleep quality (sleep improved or not). The dichotomous outcome (improved sleep or not) is presented as the relative risk for reporting improved sleep in the valerian group. Risk ratios greater than one indicate a benefit in the valerian group. Point estimates are represented by diamonds (with first author names) for individual studies and by squares for the summary estimates. Vertical lines represent 95% confidence intervals [CIs].

An examination of the funnel plot (Figure 2) reveals that there is a relationship between study size (as measured by standard error of the mean) and treatment effect (relative risk of a better sleep), which is confirmed by the statistical test Kendall's tau ($P < .01$). This suggests that publication bias may be present, which occurs when negative studies are less likely to be published than positive studies, often resulting in an absence of small negative studies, as shown in Figure 2. The test for publication bias was still positive even when the Jacobs study was excluded ($P = .03$).

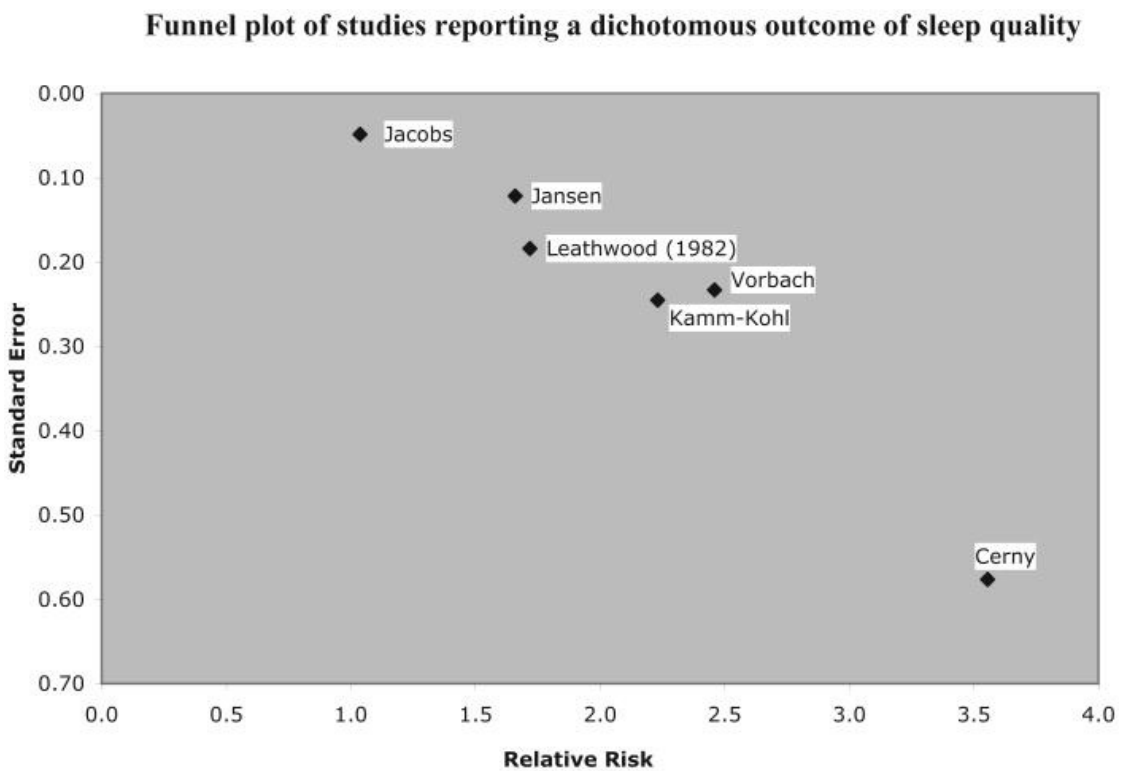

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Figure 2

Funnel plot of studies reporting a dichotomous outcome of sleep quality. The funnel plot shows the relationship between study size (as measured by standard error, with larger standard errors indicating smaller studies) and study outcome (as measured by relative risk). The visual inspection of the graph suggests an absence of small negative studies (low relative risk, bottom left), which is supported by the statistical test for publication bias, Kendall's tau ($P = .03$). The points are labeled with the first author name.

Nine of the included studies reported the effect of valerian on "subjective sleep onset latency," which is defined as the self-reported time it takes to fall asleep (Table 2).[12,14-20,25] The methods used to examine this outcome varied considerably, and only 4 studies reported the actual difference in minutes that it took participants to fall asleep. Of these 4 studies, 2 reported a nonsignificant improvement in subjective sleep-onset latency of 17.7 minutes[16] and 15 minutes,[12] and 2 reported significant improvements of 16.7 minutes[18] and 14 minutes.[14] Because of the limited statistical presentation of data in the individual studies, this outcome could not be pooled to create a summary measure.

Table 2

Studies Reporting the Effect of Valerian on Sleep-Onset Latency

First Author, Year	No. of Participants	Subjective Sleep Latency Outcome	Sleep Latency Result	Statistical Significance
Leathwood, 1982[25]	128	No. who went to sleep more rapidly/total No. of participants	Placebo: 29/128 Valerian: 47/128	Yes $P = .01$
Kamm-Kohl, 1984[20]	80	No. with improved falling asleep/total No. of participants	Placebo: 10/39 Valerian: 33/39	Yes $P < .001$
Farag, 2003[18]*	25	Mean No. of minutes to fall asleep (SD)	Placebo: 74.1 min (69) Valerian: 57.4 min (51) Mean decrease: 16.7 min (44.8)	Yes $P = .003$
Coxeter, 2003[17]	21	Proportion of success (95% CI)	43% (29-57)	No
Diaper, 2004[19]	16	Visual analog score from 0-100 (100 = best) (SD)	Placebo: 49.7 (11.1) Valerian 300 mg: 47.0 (10.8) Valerian 600 mg: 49.5 (8.3)	No
Donath, 2000[12]*	16	Median No. of minutes to fall asleep (1st-3rd quartiles)	Baseline: 60.0 min (30.0-90.0) Placebo: 60.0 min (30.0-105.0) Valerian: 45.0 min (17.5-75.0)	No
Balderer, 1985[14]*	10	Mean No. of minutes to fall asleep (SEM)	Placebo: 23 min (5) Valerian 450 mg: 18.5 min (8) Valerian 900 mg: 9 min (3)	Yes $P < .01$
Leathwood, 1985[15]	8	9-point scale, 9 is best score (SD)	Placebo: 4.9 points (0.4) Valerian 450 mg: 4.3 points (0.4) Valerian 900 mg: 4.9 points (0.3)	No
Francis, 2002[16]*	5	Mean No. of minutes to fall asleep, reported by parents (SD)	Baseline: 41.1 min (21.0) Placebo: 39.1 min (34.7) Valerian: 23.4 min (13.4)	No

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SD = standard deviation; CI = confidence interval; SEM = standard error of mean.

*Of four studies reporting subjective sleep-onset latency in minutes, two reported statistically significant benefits.

Eight of the trials included a measurement of hangover effect the morning after study medication was given,[12,13,15,17,19,22,24,25] and 6 of those studies reported results.[12,15,17,19,22,25] All showed no difference between the valerian and placebo groups in terms of sleepiness the next morning. The variation in assessment and presentation of this outcome measure also prevented statistical pooling of

the results.

Five of the included studies used polysomnographic sleep recordings to evaluate the effects of valerian on sleep.[12-15,19] There were no consistent, statistically significant changes in any of these outcome measures, which included sleep efficiency index, sleep period time, time in each of the stages of sleep, measured sleep-onset latency, rapid eye movement sleep-onset latency, and number of arousals.

Adverse events were not consistently assessed or reported. Of the 16 studies, 5 reported that there were no adverse events,[15,16,18,26,27] and 8 reported various side effects in both groups with no statistically significant difference in the frequency of adverse events between the valerian and placebo groups.[12,17,19,20,22-25] Two studies did not report any results on adverse events.[13,14] Only 1 study[21] reported a statistically significant increase in any adverse event (diarrhea), which occurred in 18% of patients in the valerian group compared with 8% of patients in the placebo group ($P = .02$).

Discussion

Valerian is the most commonly used herbal product to induce sleep in both the United States and Europe.[7,28,29] We identified 16 studies that examined the effect of valerian on sleep quality, but eight of the studies were small (<25 patients)[12-19] and most had significant methodologic problems. In addition to the low average study quality score, which measures problems related to the conduct or description of randomization, blinding, and participant withdrawal,[9] there were numerous other problems that limit the ability to draw conclusions about the safety and efficacy of valerian. These limitations include the lack of use of standard measures of subjective sleep quality,[30,31] inadequate statistical presentation of data, wide variation in the dose and duration of valerian treatment, and limited assessment of side effects. Because of these numerous problems, the summary estimates of this meta-analysis should be interpreted with caution.

By pooling the most commonly reported sleep quality measure, we found that valerian had a statistically significant effect on the relative risk of improved sleep (1.8, 95% CI, 1.2-2.9). Only 6 of the 16 identified studies reported a dichotomous outcome measure of sleep and could be included in the summary measure. However, these studies were all relatively large, accounting for 72% of all patients studied, and therefore may provide a reasonable summary estimate of the effect of valerian in the identified studies. Because both the funnel plot and the accompanying statistical test (Kendall's tau) were positive, there is evidence for publication bias, which suggests that small negative studies may have been unpublished and not located by our review, potentially leading to an overestimate of the effect of valerian.

Although nine studies reported the effect of valerian on subjective sleep-onset latency, a summary measure could not be created because of the variable presentation of data. Overall, 4 of these 9 studies reported a statistically significant benefit, and all four studies reporting the outcome in minutes found at least a trend favoring valerian.

There was a large variation in the dose of valerian used in the identified studies. Doses ranged from 225 mg to 1215 mg per day, and only 2 of the studies specifically stated that the herb was standardized to a specific amount of valerenic acid, which is believed to be one of the most biologically active components of the herb.[32] Although there is clearly not enough evidence to define the optimum amount of valerenic acid that should be present in a given dose of the herb, the use of standardized products in clinical trials of valerian might improve the reproducibility and clinical relevance of the results. The variation in the dose of valerian in these studies is also reflected in products sold in the United States. Thirteen valerian products commonly used in this country were evaluated by a reference laboratory, and the recommended doses ranged from 75 to 3000 mg per day; most of the standardized extracts were

standardized to 0.8% valerenic acids.[33]

The poor overall methodology observed in these studies is a common problem in clinical trials of herbal products.[34] Methodologic problems are also common in randomized, controlled trials of pharmaceutical drugs used to treat insomnia. Many of these studies incompletely report results[35] and use a variety of different outcome measures, making it difficult to compare the efficacy of different agents.[36] It is possible that the methodologic flaws in the studies included in this systematic review led to invalid results in individual studies, and the only way to address this concern is to conduct new, high-quality clinical trials.

In addition to evidence from clinical trials, there is some intriguing historical and basic science evidence regarding the efficacy of valerian. Several different species of *Valeriana* have been used for sedation and sleep in many different cultures throughout the world, including *V. wallichii* in India and *V. angustifolia* in China and Japan.[7] Also, several studies have shown that components of valerian inhibit the breakdown of gamma-aminobutyric acid in the brain and induce sedation and a decrease in central nervous system activity in mice.[7] The presence of this plausible mechanism of action lends support to the limited clinical trial data.

Valerian may be a more attractive option than other sleeping agents because of the lack of hangover effect. Of the six studies that reported a measure of morning feeling, all reported no difference between valerian and placebo.[12,15,17,19,22,25] Similarly, a previous randomized, controlled trial of valerian, which was excluded from this review because a sleep quality outcome was not reported, found that valerian had a hangover effect equal to placebo and less than the benzodiazepine flunitrazepam.[22]

Although only 1 of the included studies[21] identified a statistically significant increase in an adverse event in the valerian group (diarrhea), it is not possible to reach definitive conclusions regarding the safety of valerian on the basis of this review. Most studies did not describe the process of identifying, recording, or analyzing adverse events, as recently recommended.[37] Similarly, because the included studies had small sample sizes and lasted 1 month or less, they do not have sufficient power to rule out even relatively common adverse events.

Conclusion

This systematic review suggests that valerian may improve sleep quality, but methodologic problems of the included studies limit the ability to draw firm conclusions. Because of the significant limitations of the identified studies, we believe that larger randomized, controlled trails that adhere to established quality guidelines[38] and have adequate power to assess changes in standard, subjective measures of sleep quality[30,31,39] and overall quality of life are necessary. These studies should evaluate valerian products that are standardized to specific levels of the suspected active ingredients and should focus on detecting possible adverse effects, including the development of tolerance and withdrawal effects. Given the high prevalence of insomnia worldwide and the associated morbidity and economic costs, future studies of valerian should assume a high priority.

Clinical Significance

- Valerian is commonly used to improve sleep.
- Patients taking valerian had an 80% greater chance of reporting improved sleep compared with patients taking placebo; however, there was evidence of publication bias.

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References

1. Ancoli-Israel S, Roth T. Characteristics of insomnia in the United States: results of the 1991 National Sleep Foundation Survey. I. *Sleep.* 1999;22(Suppl 2):S347–S353. [PubMed] [Google Scholar]

2. Sateia MJ, Doghramji K, Hauri PJ, Morin CM. Evaluation of chronic insomnia. An American Academy of Sleep Medicine review. *Sleep.* 2000;23:243–308. [PubMed] [Google Scholar]

3. Ohayon M. Epidemiology of insomnia: what we know and what we still need to learn. *Sleep Med Rev.* 2002;6:97–111. [PubMed] [Google Scholar]

4. Shochat T, Umphress J, Israel AG, Ancoli-Israel S. Insomnia in primary care patients. *Sleep.* 1999;22(Suppl 2):S359–S365. [PubMed] [Google Scholar]

5. Holbrook AM, Crowther R, Lotter A, Cheng C, King D. The diagnosis and management of insomnia in clinical practice: a practical evidence-based approach. *CMAJ.* 2000;162:216–220. [PMC free article] [PubMed] [Google Scholar]

6. Morin CM, Culbert JP, Schwartz SM. Nonpharmacological interventions for insomnia: a meta-analysis of treatment efficacy. *Am J Psychiatry.* 1994;151:1172–1180. [PubMed] [Google Scholar]

7. Houghton PJ. The scientific basis for the reputed activity of valerian. *J Pharm Pharmacol.* 1999;51:505–512. [PubMed] [Google Scholar]

8. Barnes PM, Powell-Griner E, McFann K, Nahin RL. Complementary and alternative medicine use among adults: United States, 2002. *Adv Data.* 2004:1–19. [PubMed] [Google Scholar]

9. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials.* 1996;17:1–12. [PubMed] [Google Scholar]

10. Egger M, Davey-Smith G, Altman DG. *Systematic Reviews in Health Care.* London: BMJ Publishing Group; 2001. [Google Scholar]

11. Begg D, Berlin JA. Publication bias: a problem in interpreting medical data. *J R Stat Soc Ser A.* 1988;151:419–463. [Google Scholar]

12. Donath F, Quispe S, Diefenbach K, Maurer A, Fietze I, Roots I. Critical evaluation of the effect of valerian extract on sleep structure and sleep quality. *Pharmacopsychiatry.* 2000;33:47–53. [PubMed] [Google Scholar]

13. Schulz H, Stolz C, Müller J. The effect of valerian extract on sleep polygraphy in poor sleepers: a pilot study. *Pharmacopsychiatry.* 1994;27:147–151. [PubMed] [Google Scholar]

14. Balderer G, Borbély AA. Effect of valerian on human sleep. *Psycho-pharmacology.* 1985;87:406–409. [PubMed] [Google Scholar]

15. Leathwood PD, Chauffard F. Aqueous extract of valerian reduces latency to fall asleep in man. *Planta Medica.* 1985;53:144–148. [PubMed] [Google Scholar]

16. Francis AJ, Dempster RJ. Effect of valerian, Valeriana edulis, on sleep difficulties in children with intellectual deficits: randomised trial. *Phytomedicine.* 2002;9:273–279. [PubMed] [Google Scholar]

17. Coxeter PD, Schluter PJ, Eastwood HL, Nikles CJ, Glasziou PP. Valerian does not appear to reduce symptoms for patients with chronic insomnia in general practice using a series of randomised n-of-1 trials. *Complement Ther Med.* 2003;11:215–222. [PubMed] [Google Scholar]

18. Farag NH, Mills PJ. A randomised-controlled trial of the effects of a traditional herbal supplement on sleep onset insomnia. *Complement Ther Med.* 2003;11:223–225. [PubMed] [Google Scholar]

19. Diaper A, Hindmarch I. A double-blind, placebo-controlled investigation of the effects of two doses of a valerian preparation on the sleep, cognitive and psychomotor function of sleep-disturbed older adults. *Phytother Res.* 2004;18:831–836. [PubMed] [Google Scholar]

20. Kamm-Kohl AV, Jansen W, Brockmann P. Moderne Baldriantherapie gegen nervose storungen im senium. *Medwelt.* 1984;35:1450–1454. [Google Scholar]

21. Jacobs BP, Bent S, Tice JA, Blackwell T, Cummings SR. An internet-based randomized, placebo-controlled trial of kava and valerian for anxiety and insomnia. *Medicine (Baltimore)* 2005;84:197–207. [PubMed] [Google Scholar]

22. Kuhlmann J, Berger W, Podzuweit H, Schmidt U. The influence of valerian treatment on “reaction time, alertness and concentration” in volunteers. *Pharmacopsychiatry.* 1999;32:235–241. [PubMed] [Google Scholar]

23. Cerny A, Schmid K. Tolerability and efficacy of valerian/lemon balm in healthy volunteers (a double-blind, placebo-controlled, multicentre study) *Fitotherapia.* 1999;70:221–228. [Google Scholar]

24. Vorbach EU. Therapie von insomnien: wirksamkeit und vertraglichkeit eines Baldrianpraparats. *Psychopharmakotherapie.* 1996;3:109–115. [Google Scholar]

25. Leathwood PD, Chauffard F, Heck E, Munoz-Box R. Aqueous extract of valerian root (Valeriana officinalis L.) improves sleep quality in man. *Pharmacol Biochem Behav.* 1982;17:65–71. [PubMed] [Google Scholar]

26. Jansen W. Doppelblindstudie mit Baldrisedon. *Therapiewoche.* 1977;27:2779–2786. [Google Scholar]

27. Delsignore R, Orlando S, Costi D, Baroni M, Butturini U. Avaliacao clinica comparativa com placebo de um extrato estabilizado de valeriana. *Farmacologia Clinica.* 1992;104:191–196. [Google Scholar]

28. Richman A, Witkowski JP. 4th Annual Herbal Products Sales Survey. *Whole Foods.* 1998;21:19–26. [Google Scholar]

29. Richman A, Witkowski JP. 5th Annual Herbal Product Sales Survey. *Whole Foods.* 1999;22:49–56. [Google Scholar]

30. Buysse DJ, Reynolds CF, 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res.* 1989;28:193–213. [PubMed] [Google Scholar]

31. Bastien CH, Vallieres A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep Med.* 2001;2:297–307. [PubMed] [Google Scholar]

32. Rotblatt M, Ziment I. *Evidenced-Based Herbal Medicine.* Philadelphia: Hanley & Belfus Inc; 2002. pp. 355–359. [Google Scholar]

33. [Accessed February 16, 2006];*Product Review: Valerian Supplements: ConsumerLab, 2004.*

Available at: www.consumerlab.com.

34. Linde K, Jonas WB, Melchart D, Willich S. The methodological quality of randomized controlled trials of homeopathy, herbal medicine, and acupuncture. *Int J Epidemiol.* 2001;30:526–531. [PubMed] [Google Scholar]

35. McCall WV, D'Agostino R, Jr, Dunn A. A meta-analysis of sleep changes associated with placebo in hypnotic clinical trials. *Sleep Med.* 2003;4:57–62. [PubMed] [Google Scholar]

36. Dundar Y, Boland A, Strobl J, et al. Newer hypnotic drugs for the short-term management of insomnia: a systematic review and economic evaluation. *Health Technol Assess.* 2004;8:iii–x. 1–125. [PubMed] [Google Scholar]

37. Ioannidis JP, Evans SJ, Gotzsche PC, et al. Better reporting of harms in randomized trials: an extension of the CONSORT statement. *Ann Intern Med.* 2004;141:781–788. [PubMed] [Google Scholar]

38. Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. *Clin Oral Investig.* 2003;7:2–7. [PubMed] [Google Scholar]

39. Weaver TE, Laizner AM, Evans LK, et al. An instrument to measure functional status outcomes for disorders of excessive sleepiness. *Sleep.* 1997;20:835–843. [PubMed] [Google Scholar]