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Aqueous Extract of Valerian Root (*Valeriana officinalis L.*) Improves Sleep Quality in Man

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LEATHWOOD, P. D., F. CHAUFFARD, E. HECK AND R. MUNOZ-BOX. *Aqueous extract of valerian root (*Valeriana officinalis L.*) improves sleep quality in man.* PHARMAC. BIOCHEM. BEHAV. 17(1) 65–71, 1982.—The effect of an aqueous extract of valerian (*Valeriana officinalis L.*) root on subjectively rated sleep measures was studied on 128 people. Each person received 9 samples to test (3 containing placebo, 3 containing 400 mg valerian extract and 3 containing a proprietary over-the-counter valerian preparation). The samples, identified only by a code number, and presented in random order, were taken on non-consecutive nights. Valerian produced a significant decrease in subjectively evaluated sleep latency scores and a significant improvement in sleep quality; the latter was most notable among people who considered themselves poor or irregular sleepers, smokers, and people who thought they normally had long sleep latencies. Night awakenings, dream recall and somnolence the next morning were relatively unaffected by valerian. With the proprietary valerian-containing preparation, the only change was a significant increase in reports of feeling more sleepy than normal the next morning. Thus the questionnaire, simple to use and non-invasive, provides a sensitive means for detecting the effects of mild sedatives on different aspects of sleep in man. It also allows identification within the test population of the subgroups most affected.

Valerian Human studies Sleep latency Sleep quality

IN traditional herbal folklore a number of plants are reputed to have sedative properties. The list includes almonds, camomile, catmint, fennel, hops, indian hemp, lettuce, lime, marjolaine, may blossom, melissa, mullein, oats, orange flower, passion flower, poppy seed, rosemary, willow and valerian [7]. Although there is no doubt that some plants have real and potent psychoactive properties (opium poppy and Indian hemp are good examples), most of the other herbal remedies are of more doubtful value and have fallen out of favour. All the above (except cannabis and opium) disappeared from the U.S. and British Pharmacopoeias many years ago, but valerian can still be found in the French German and Swiss Pharmacopoeias.

Valerian is the common name given to the genus *Valeriana*, herbaceous perennial plants widely distributed in the temperate regions of North American, Europe and Asia. Of the 170 or so known species, common valerian (*Valeriana offinicalis L.*) is the one most often cultivated for medicinal uses. The dried rhizome has a distinctive odour which is now regarded as offensive but which was, in the 16th century, considered to be fragrant, the root being placed among the clothes as a perfume.

In the U.S. and in Britain, valerian is practically unknown, while in France, Germany and Switzerland, valerian is commonly considered to have sedative properties. A few studies on the composition and pharmacology of valerian have been published. Hauschild [10], and Schultz and Muller [19], studied Indian valerian (*Valeriana wallichii*) and Paris and Moury [15,16] the root of red valerian (*Centranthus ruber*). They showed that extracts of both species, in doses of 5–15 g/kg administered IP, lowered spontaneous locomotor activity in mice. Common valerian, the species most widely used in over-the-counter pharmaceutical preparations, has rarely been studied. Desvaux [8] found that 2 g/kg of an aqueous extract of valerian root lowered locomotor activity in mice, while Torrent *et al.* [22] showed that an alcoholic extract decreased locomotor activity in mice more than did an equivalent dose of alcohol.

Von Eickstedt and Rahman [23] have isolated some polyhydroxypenta(c)pyran esters (valepotriates) from valerian roots and have shown them to be sedative in mice. These compounds, however, are water insoluble and, according to von Eickstedt [24], are not present in aqueous or alcoholic extracts of valerian root.

Research on valerian is in a curious situation. Aqueous extracts of the root reportedly have sedative effects on

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TABLE 1
PRELIMINARY QUESTIONNAIRE (TRANSLATED FROM FRENCH)

(1) Sex:		
(2) Age: <25 □; 26–40 □; 41–55 □; >55 □		
(3) Are you:	—a good sleeper	□
	—an irregular sleeper	□
	—a poor sleeper	□
(4) Do you usually go to sleep:	—quickly	□
	—slowly	□
(5) During the night, do you awake:	—0–2 times	□
	—more than 2 times	□
(6) During the day, how many cups of coffee do you drink:	—none	□
	—1–3	□
	—>3	□
(7) Do you also drink coffee in the evening:	yes □; no □	
(8) Do you smoke:	yes □; no □	

This questionnaire was filled in by each volunteer beginning the sleep study.

animals but only in huge doses [8]. Some chemicals found in valerian roots do seem to calm or sedate man, but these are apparently not present in aqueous or alcoholic extracts. The evidence that valerian is a sedative in man is almost entirely anecdotal and yet valerian is a popular over-the-counter sedative with at least 50 tons being sold each year in France [7].

In preliminary studies, we screened several putative herbal sedatives for their effects on behaviour in mice. Most (hops, lime, mint, melissa and orange leaves) gave negative results, while two (orange flower and valerian extracts) tended to lower spontaneous locomotor activity (Leathwood and Arimanana, unpublished results). Because valerian is the more popular folk remedy, we carried out the large-scale questionnaire study of its effects on sleep in man which is reported here. An electroencephalographic study is reported elsewhere [4].

The specific hypotheses being tested were (1) valerian should decrease sleep latency, decrease night awakenings and improve sleep quality when compared to placebo; (2) these effects should be more evident with habitually poor sleepers than with people who usually sleep well. A secondary aim of the study was to examine patterns of sleep quality and responses to valerian as related to age, sex, coffee drinking, and smoking habits.

METHOD

Three different samples were tested: an aqueous extract of valerian; a commercial preparation containing valerian (Hova,® Zyma S.A., Nyon, Switzerland) and a placebo. The dose level used, 400 mg, was that recommended in the Swiss pharmacopoeia.

Test Samples

Air-dried, coarse-ground valerian root (*Rhizoma valeriana officinalis L.*, Dixa S.A., St.-Gallen, Switzerland) was ground, mixed with deionised water, heated to 60°C, homogenised and centrifuged. After re-extraction of the sediment, the combined supernatant fluids were concentrated and freeze-dried. From 6 kg of starting material we obtained 2.14 kg of freeze-dried powder.

Several "over-the-counter" sedatives containing valerian are sold in Switzerland but none consist of valerian alone. The commercial preparation we tested (Hova®) is made from valerian extract (60 mg/tablet) and hop flower extract (30 mg/tablet). It is advertised as a sedative suitable for treating insomnia, nervousness, over-excitement and night terrors. The hop extract is supposed to improve appetite. Hova® can be used by children and adults. The placebo was finely-ground brown sugar.

The valerian, Hova® and placebo powders were sealed into capsules (Parke-Davis snap-fit bicolor opaque #0, Schaller, Renens, Switzerland) such that each of the test samples contained 400 mg of valerian (2 capsules of 200 mg each) while the placebo contained an equivalent amount of brown sugar.

Volunteers

One hundred sixty-six volunteers were recruited. A detailed analysis of the characteristics of the volunteers is presented in the results section.

Before being enrolled into the experiment, each volunteer was given a short letter explaining the aim of the study. Having agreed to take part, he or she then filled in a preliminary questionnaire (Table 1) describing his or her habitual sleep characteristics, and was then given 9 sachets (3 placebo, 3 valerian and 3 Hova®) of 2 capsules each, identified only by a code number, and 9 post-sleep questionnaires (Table 2). Each volunteer was asked to take one sachet of pills one hour before retiring to bed on non-consecutive nights and, the following morning, to number and fill in the post-sleep questionnaire. Each volunteer was instructed to avoid taking the pills on evenings following abnormal or excessive food intake, drinking, exercise, etc. Attribution of the code number for each sample was based on a set of random number tables.

Statistics

The raw data were tabulated as frequencies for each re-

TABLE 2

SLEEP QUESTIONNAIRE (TRANSLATED FROM FRENCH)

(1) If you refer to the way you usually go to sleep, do you have the impression that you fell asleep:
—with greater difficulty than usual ☐
—more easily than usual ☐
—as usual ☐
(2) Relative to your usual sleep, do you think you:
—slept better ☐
—slept worse ☐
—slept as usual ☐
(3) During the night, did you awake:
—more often than usual ☐
—less often than usual ☐
—as usual ☐
(4) Do you remember dreaming:
—more than usual ☐
—less than usual ☐
—as usual ☐
(5) Referring always to how you usually feel in the morning, do you feel:
—sleepier than usual ☐
—less sleepy than usual ☐
—as usual ☐
(6) Any other remarks?

This questionnaire was completed the morning following ingestion of a test sample.

TABLE 3

CHARACTERISTICS OF THE TEST POPULATION

	Number	% of Total
Total	128	100
Men	72	56
Women	56	44
≤40	76	59
>40	52	41
Good sleepers	67	52
Poor or irregular sleepers	61	48
Quick to fall asleep	93	73
Long to fall asleep	35	27
≤2 Awakenings/night	96	75
>2 Awakenings/night	32	25
0–3 Cups of coffee/day	70	54
>3 Cups of coffee/day	58	46
Smokers	42	33
Non-smokers	86	67

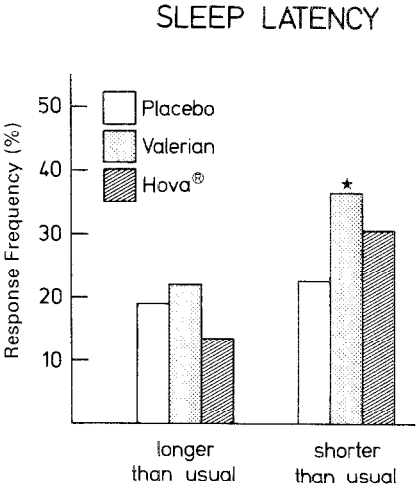

FIG. 1. Percentage of the whole population reporting a mean rating over 3 nights of longer or shorter sleep latency than usual following the different treatments. The frequency of shorter sleep latencies with valerian is significantly higher than for placebo ($p<0.05$).

sponse and for each treatment. The results were then analysed using Friedman's generalised non-parametric analysis of variance [1]. This technique ranks the 9 observations and takes into account within-subject variability as well as the differences between treatments. It can also make allowance for incomplete cells.

For binary comparisons (e.g., did more people report better sleep quality—as opposed to normal or worse—with valerian than with placebo?), Brownlee's [3] test for binary comparisons was used. For each of these tests a probability of 5% was taken as the level of statistical significance.

RESULTS

Characteristics of the Test Population

Before distribution of the pills and test questionnaires, all the volunteers were asked to fill in a preliminary questionnaire on his or her normal sleep characteristics. Table 3 summarises this information for the 128 people who completed the study.

Analysis of these results using Pearson's χ^2 showed that rapidity to fall asleep was similar for men and women, while women recalled more frequent awakenings ($p<0.05$) and remembered more dream episodes than did men ($p<0.05$). Age differences in habitual sleep quality were more marked, with the younger (<40 years old) people reporting higher frequencies of good sleep quality ($p<0.05$), less night awakenings ($p<0.01$) and less dream recall ($p<0.01$) than older people.

Responses to the Test Questionnaires

Failures to complete the study. Samples and test questionnaires were distributed to 166 volunteers of whom 128 (77%) completed the study. The following reasons were given for failing to complete the study: 11 people moved away, 17 changed their minds before taking any pills, 3 lost the pills, 1 person claimed that his response was lost in the post, one thought the pills too big, one would give no reason, 2 stopped because they thought the pills were useless and one stopped because the pills caused nausea. The person who claimed that the pills caused nausea threw the rest of the pills and all the questionnaires away, so we did not discover whether placebo, Hova® or valerian was to blame. In summary, only one person withdrew from the study because of

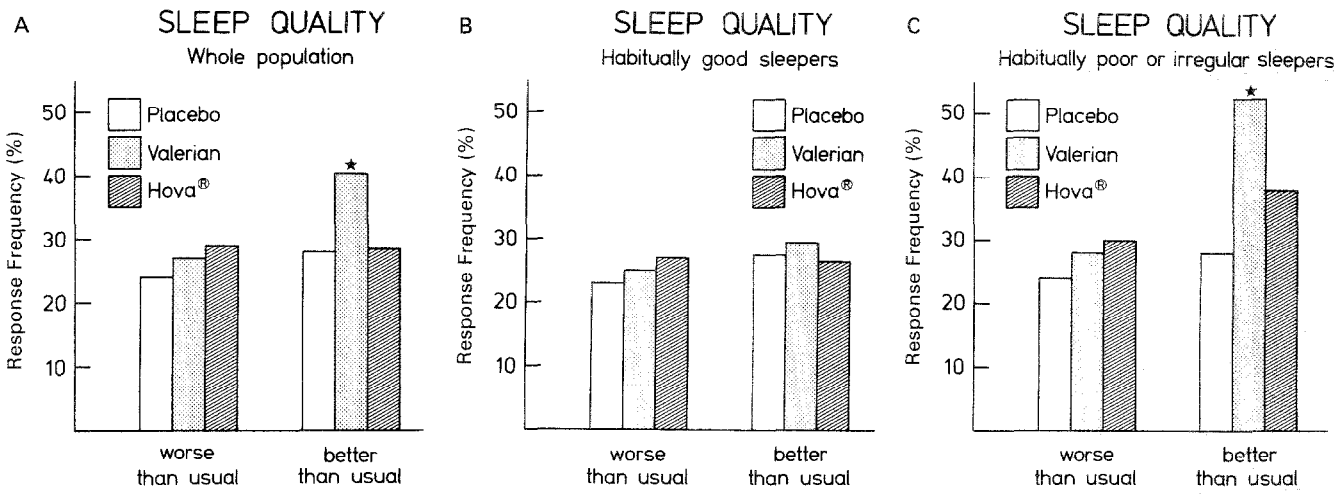

FIG. 2. (a) Percentage of the whole population reporting a mean rating over 3 nights of better or worse sleep quality than usual following the different treatments. The frequency of better sleep quality reports with valerian is significantly higher than for placebo ($p<0.05$). (b) and (c) Separate analyses of sleep quality ratings for good and poor sleepers. With valerian, the poor or irregular sleepers show a marked increase in reports of better sleep quality. Good sleepers show no change.

adverse side effects, and even then, we are not sure that valerian caused the symptoms.

Errors and non-responses. As 128 volunteers completed the study, there should have been 1152 questionnaires to analyse (9×128). In fact, 8 were missing or improperly identified and 2 were in excess (because two people received 4 samples of one product and only 2 of another). Some volunteers failed to answer individual questions; the mean rate of such failures was less than 1.5%, so for statistical analysis, these were left as empty cells.

Sleep latency. The volunteers were asked if they thought they went to sleep more rapidly than usual, as usual or more slowly than usual. With placebo 23% of the people reported shorter sleep latency than usual; 19%, longer than usual and the majority (58%) experienced normal sleep latency. The percentage of people reporting reduced sleep latency was 37% with valerian and 31% with Hova® (Fig. 1). The difference between placebo and valerian was statistically significant ($p=0.01$, Brownlee). Separate analyses on the different subgroups defined in Table 1 showed that the most marked effects of valerian were to be found among the older people, men, and those who considered themselves to be habitually poor or irregular sleepers, where 49%, 44% and 43%, respectively, reported reduced sleep latency with valerian.

None of the subgroups showed any significant change in sleep latency with Hova®.

Sleep quality. Volunteers were asked the following question: "Par rapport à votre sommeil habituel, pensez-vous avoir: —mieux dormi; —moins bien dormi; —dormi comme d'habitude (relative to your usual sleep, do you think you: —slept better; —slept worse; —slept as usual)?"

With placebo, about 50% of the people reported that they slept "as usual", about 25% reported better sleep than usual and 25% worse sleep than usual. With valerian, 31% slept "as usual", 26% worse than usual and 43% better than usual (Fig. 2a). This distribution is different from placebo ($p<0.05$, Friedman generalised non-parametric analysis of variance) and represents a significant rise in the proportion of responses reporting better sleep quality than usual ($p<0.01$, Brownlee binary test). With Hova® there was no significant change in the response pattern.

TABLE 4

PERCENTAGE OF POPULATION REPORTING BETTER SLEEP QUALITY THAN USUAL* AFTER TAKING PLACEBO, VALERIAN OR HOVA®: ANALYSIS OF DIFFERENT SUBGROUPS

Group	Number	% Reporting better sleep quality than usual		
		Placebo	Valerian	Hova®
Young,† good sleepers	45	27	31	22
Young, poor sleepers	31	16	45§	32
Old, good sleepers	22	32	36	45
Old, poor sleepers	30	43	63	43
Women, good sleepers	42	33	33	31
Women, poor sleepers	30	23	50‡	27
Men, good sleepers	25	20	32	28
Men, poor sleepers	31	35	58	48

*Mean score for the 3 nights.
†Young=<40 year-old.
‡Different from placebo $p<0.05$.
§Different from placebo $p<0.01$.

Separate analyses of good vs irregular and poor sleepers showed that people who rated themselves as habitually good sleepers were largely unaffected by valerian (Fig. 2b) while 54% of habitually poor or irregular sleepers reported improved sleep quality after valerian (Fig. 2c). This observation allowed us to make a tentative identification of the people most sensitive to valerian. Table 4 shows the response patterns to valerian of younger and older men and women, good and poor sleepers.

The most marked increases in reports of better sleep

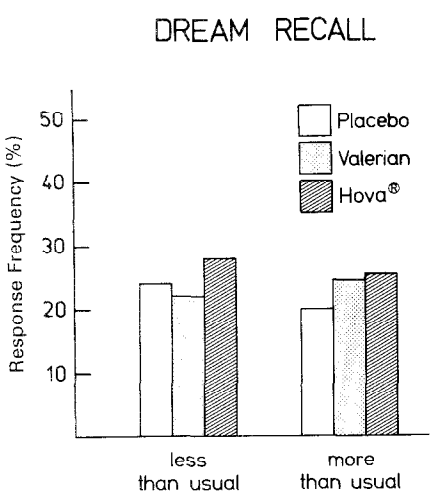

FIG. 3. Percentage of the whole population reporting less or more dream recall than usual after the different treatments. Dream recall patterns were unchanged.

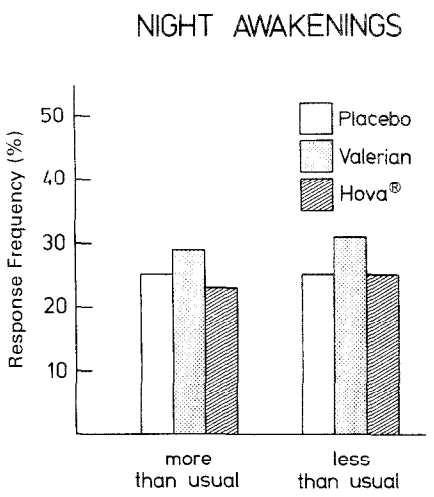

FIG. 4. Percentage of the whole population reporting more or less night awakenings than usual after the different treatments. Night awakening patterns were unchanged.

quality after valerian were from female poor sleepers and younger poor sleepers. Although 63% of the older poor sleepers reported better sleep quality than usual after valerian, 43% of them slept better than usual after placebo, suggesting either that many of them were susceptible to any pill taken in the evening, or that they were particulary pessimistic about their usual sleep quality.

Two other groups, smokers and people who habitually have long sleep latencies, showed significant changes in sleep quality. Among the smokers, 52% reported better sleep quality than usual after valerian while 22% reported better sleep with placebo and 27% better sleep with Hova®. In the other group, 50% reported better sleep after valerian (27% slept better after placebo and 41% slept better after Hova®).

Night awakenings and dream recall. For the whole population there were no significant changes either in night awakenings or in dream recall, and the response patterns for placebo, valerian and Hova® were similar (Figs. 3 and 4). Among the different subgroups the only marked change was in night awakening of poor or irregular sleepers with fewer awakenings than usual after valerian reported by 47% of these people but only by 28% after placebo or Hova®. The difference between placebo and valerian was statistically significant ($p<0.05$, Brownlee and Friedman test).

Sleepiness the next morning. Volunteers were asked to note whether they felt more (or less) sleepy than usual the next morning. This question was included because "hangover" effects are often reported with use of long-acting barbiturates or benzodiazepines [9,11] and we were interested to find out whether valerian produced a similar effect.

The frequency of "more sleepy than usual" responses was significantly greater with Hova® than with placebo ($p<0.01$) or valerian ($p<0.05$), see Fig. 5. Among the different subgroups, none distinguished valerian from placebo, but several groups reported significantly ($p<0.01$) more sleepiness in the morning after Hova® compared with placebo; these included non-smokers, non-coffee drinkers, the under-forties, those people who normally to to sleep quickly, and irregular sleepers.

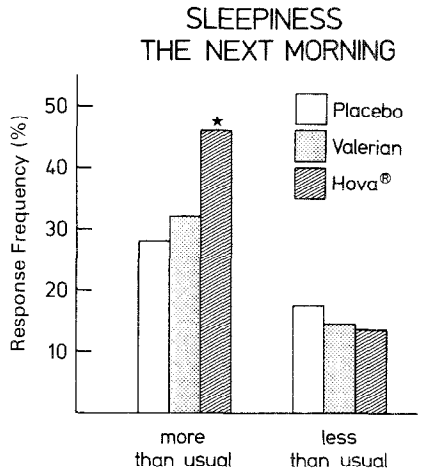

FIG. 5. Percentage of the whole population reporting more, or less, sleepiness the next morning after the different treatments (mean score for 3 nights). The frequency of reports or more sleepiness the next morning after Hova® was significantly higher than for placebo or valerian.

DISCUSSION

The results of this experiment show that, in a large human population, valerian improved subjectively recalled sleep quality. It was also possible to identify the groups of people most sensitive to valerian. Subjective and objective sleep measures are both important in the testing of any new hypnotic but subjective ratings are the final arbiters of utility [14]. Even when polygraphic measurements indicate that a new drug is an excellent hypnotic, if it does not produce a subjective sensation of improved sleep quality, or if it leaves an unpleasant "hangover" the next morning, it is of little use [20]. Alternatively, a mild hypnotic may not detectably change any of the classic EEG parameters, but if it improves subjective sleep quality, it is potentially useful.

Some aspects of the night's sleep such as sleep latency, sleep time or the number of night awakenings, can be measured using both objective (EEG) and subjective (questionnaire) techniques. The reasonably good correlations between the two measures suggest that the subjective recall rating are quite reliable [18,21]. Estimating the reliability of sleep quality is more complex. People do have definite impressions about whether they are "good" or "poor" sleepers [13], they can easily rate the quality of a night's sleep as good or bad [17], and EEG sleep records of good sleepers differ significantly from those of poor sleepers [13].

Unfortunately, the several studies which have compared subjective sleep quality ratings with EEG sleep stage measures have observed poor correlations and contradictory results [4, 13, 18, 21]. Monroe [13], for example, found that good sleepers tended to have less stage 2 sleep while Saletu [18] found that "restful and uninterrupted" sleep ratings correlated with increased amounts of stage 2. In spite of more than 30 years of detailed electrophysical analysis of sleep, there is still no easy formula for defining a good night's sleep in terms of sleep stages and one must still rely on subjective reports as to whether or not a particular treatment really improves sleep. In common with most sleep researchers, we find no consistent strong correlation between any of these EEG measures and sleep quality [4].

Subjective sleep state questionnaires have been used in many previous investigations [2,17], and vary considerably in style and complexity. The questionnaire used in this study was chosen on the basis of a pilot test which showed that a short questionnaire with 3-point scale ratings relative to "usual" sleep was the most acceptable. The preliminary questionnaire (Table 1) was included to allow division of the population into different subgroups based on sex, age, smoking patterns, usual sleep characteristics, etc.

The sensitivity of this approach is amply demonstrated in that it was possible to identify the people most influenced by valerian. For the whole population, sleep latencies ($p<0.05$) and sleep quality was improved ($p<0.05$). Analyses based on the different subgroups defined in Table 2 showed that poor and irregular sleepers were especially sensitive to valerian while people who considered themselves to be good sleepers detected no significant change in sleep quality. Further subdivision on the basis of age or sex suggested that women and younger people who rated themselves as habitually poor or irregular sleepers were most sensitive to valerian. The small numbers involved and changing patterns of response to placebo, reduced the utility of any finer subdivisions. Dream recall, night awakenings and sleepiness the next morning showed no significant changes.

In a study of the effects of a barbiturate and two benzodiazepines on subjective sleep parameters, Hindmarch [11] found that amylobarbital (100 mg) and Temazepam (15 mg) produced no significant changes in subjective ratings for sleep latency, sleep quality or morning somnolence. Larger doses (20 and 30 mg) of Temazepam shortened subjectively recalled sleep latency ($p<0.05$) but did not change sleep quality. At 30 mg, Temazepam produced a marked increase in morning sleepiness ($p<0.001$). Another benzodiazepine, Nitrazepam (5 mg), shortened sleep latency ($p<0.05$), improved sleep quality ($p<0.05$) and increased morning sleepiness ($p<0.01$). While it is difficult to draw comparisons between different studies because the results are likely to be affected by the sleep characteristics and the size of the test population, the changes we observed with 400 mg valerian (a significant decrease in recalled sleep latency, an improvement in sleep quality and no change in sleepiness the next morning) suggest that it is at least as effective as small doses of barbiturates and benzodiazepines.

Hova®, the commercially available sedative based on valerian and hops, did not influence ratings for sleep latency, night awakenings, sleep quality or dream recall. The only change was a marked increase in reports of feeling more sleepy than usual the next morning. Unfortunately we have no details of the method of preparation of Hova®, so we are unable to suggest an explanation for the discrepancy in the results for the two extracts.

Although we have demonstrated that an aqueous extract of valerian can improve sleep quality, we have not identified the active component. Extracts of valerian are to be found in a variety of pharmaceutical preparations [5], and several possible active components have been suggested. The valepotriate esters isolated by von Eickstedt and Rahman [23] appear to be useful as daytime calmants (anti-stress agents) rather than as sedatives. Furthermore, they are insoluble in water and are not found in aqueous extracts [24]. Other possible active components are found in valerian root [7], but until these have been tested in man we cannot be sure that they improve sleep.

In parallel with this study of subjective sleep measures we carried out a small-scale EEG experiment comparing placebo and valerian [4]. There were no significant changes either in EEG parameters or in subjective measures (subjects filled in a sleep questionnaire the morning after each EEG night). There are several possible explanations for the discrepancy between results of the two experiments. The sample size in the EEG study was very small with recordings from 10 subjects for 4 nights each while in the subjective sleep evaluation we analysed questionnaires from 128 subjects for 9 nights each. There were also important differences in the structure of the samples: the population in the questionnaire study included young and old, men and women, good and poor sleepers, while the EEG subjects were all men and were predominantly young and good sleepers. The questionnaire study showed that young good sleepers were unaffected by valerian (see Table 4). Finally, the variability of the EEG measures was high, so even if valerian had small but real effects on sleep physiology, prohibitively large sample sizes would be required to detect them. In this context, it is interesting to note that Holm *et al.* [12], in a study on 11 cats, found no consistent changes in cortical EEG at 250 mg/kg of valerian extract.

This difference between the questionnaire and EEG studies raises an important question in the analysis of mild sedatives. If EEG evaluation on small samples fails to detect objective effects of substances thought to be mildly sedating, it may be premature to conclude that the treatment (or the dose level used) was ineffective. Our EEG study, taken alone, would suggest no effect of valerian, while subjective evaluation on a much larger population showed that a significant proportion of the people could detect an improvement of sleep.

In summary, subjective evaluation of sleep quality using a simple questionnaire provides a sensitive means of detecting mild sedative effects and is useful for identifying the sensitive subgroups within a population. In the present study we showed that an aqueous extract of valerian root improved sleep quality of poor or irregular sleepers without producing a detectable "hangover" effect the next morning.

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