

BRIEF COMMUNICATION

Double Blind Study of a Valerian Preparation

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Received 11 January 1988

LINDAHL, O. AND L. LINDWALL. *Double blind study of a valerian preparation*. PHARMACOL BIOCHEM BEHAV 32(4) 1065–1066, 1989.—Valerian root contains two substances of special pharmacological interest—valepotriates and sesquiterpenes. The former, which has been used for standardization of the drug, is cytotoxic. The latter has no such effect. Both have sedative effects. A double blind test has been carried out on a preparation (VALERINA NATT) containing primarily sesquiterpenes. When compared with placebo it showed a good and significant effect on poor sleep ($p < 0.001$). Forty-four percent reported perfect sleep and 89% reported improved sleep from the preparation. No side effects were observed.

Valerian	Sesquiterpenes	Valepotriates	Insomnia	Double blind
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OLD “herbal medicines” containing preparations of whole herbs or parts of herbs are rare today.

It is theoretically conceivable that a whole drug can sometimes be more effective and have fewer side effects than its individual components, which are common in modern drugs.

Interest in natural preparations can therefore be justified, although clinical studies of the effects are of course crucial in determining whether natural drugs are beneficial or perhaps even preferable to conventional medication. Valerian has been used as a medication for as long as historical information has been available. It was therefore of interest to test whether the reported effects could be verified in a controlled clinical study. For this purpose a double blind study with cross over technique was carried out on 27 persons with sleep difficulties.

PHARMACOLOGY

There are two substances in particular in the drug which have attracted medical interest, namely *valepotriates* and *sesquiterpenes*. Valepotriates have normally been designated as being responsible for the chief effect of valerian, which is sedative. Different commercial preparations have commonly been standardized according to the content of valepotriates, as have crude drugs. This content varies considerably between different species, from 0.5–8%, the highest percentage being present in *Valeriana edulis* (1). Consequently, price determinations have come to be governed by the content of valepotriates. These compounds are esters of unsaturated terpene alcohols and are strongly reactive. They

inhibit the synthesis of thymidin in DNA and cancer cell cultures and are in this sense cytostatic (2).

In an analysis of 60 commercially available preparations, the content of sesquiterpenes varied between 67 and 322 mg/100 g of the drug. In the most common drug obtained from *V. edulis*, sesquiterpenes were totally absent. Sesquiterpenes do not have any cytotoxic effects and have good sedative and tranquillizing properties (4).

Studies on isolated substances are relatively few. Specific central nervous system inhibition by sesquiterpenes has been demonstrated in the mouse (5), and a sedative effect of valepotriates has also been shown in the mouse (3). In a double blind study on people, the effect of a commercial preparation containing valerian and an extract of the drug was compared with placebo (7). Both preparations had a significant effect on sleep, which came quickly and was of a better subjective quality. No side effects were noted the following day. Both the preparations come from *V. officinalis L.*, which has a high content of sesquiterpenes and a low content of valepotriates. No analysis of the components was reported.

A double blind study on a commercial preparation of valerian standardized for valepotriates, was performed on geriatric patients with mental symptoms (6). The dose administered was 300 mg of valepotriates for one month, and the indications comprised various mental symptoms such as depression, loss of initiative, difficulty making contact with people, irritation and insomnia. There was a significant, positive effect on many of these symptoms, but they subsequently returned after termination of the medication.

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TABLE 1

The Effects of Valerina NATT and Placebo on Sleep Quality					
Sleep quality*	3	2	1	0	—
When Valerina NATT was given first	6	4	1	2	0
When placebo was given first	6	5	2	1	0
Total	12	9	3	3	0
	21 (78%)				
Effect of Placebo on Sleep Quality					
Sleep quality	3	2	1	0	—
When Valerina NATT was given first	2	0	2	8	1
When placebo was given first	0	3	5	6	0
Total	2	3	7	14	1
	5 (11%)				

*3 = perfect sleep, 2 = clearly better sleep, 1 = slight improvement, 0 = no effect, — = worse sleep.

Drug Under Investigation

VALERINA NATT contains a standardized *Radix valerianae* extract VS2 equivalent to 400 mg of the root, *Flores humuli* extract equivalent to 375 mg and *Herba melissae* extract (*Lemon melissa*) equivalent to 160 mg. The main effect can be assumed to come from valerian, in this case *Valerina officinalis L.*, which is cultivated in Europe. There is a large content of sesquiterpenes, which is standardized, and there is only a trace of valepotriates.

Test Methodology

VALERINA NATT in tablet form was compared with a preparation identical in appearance but containing an extract equivalent to only 4 mg of valerian root and a full dose of *Flores humuli* and *Lemon melissa*. Any differences in effect can therefore be attributed to the content of valerian. The study was carried out as a conventional double blind test with cross over on 27 consecutive subjects with sleep difficulties who were willing to take part in the investigation. The patients were being seen in a medical clinic for problems which they had had for from 1 to 22 years. The 20 women and 7 men ranged in age from 25–68 years, with an average age of 54 years. They all suffered from sleep difficulties and fatigue, and had a subjective length of sleep of 4–6 hours. Half of them periodically or regularly took conventional sedatives. The subjects were randomized with regard to which tablet should be taken the first night, after which the other type was taken the following night. They were informed that the purpose of the investigation was to study which of two valerian preparations had the better effect.

After having taken a tablet the two previous evenings the subjects evaluated the preparations the second morning by filling out a questionnaire in which they rated their sleep on a scale—perfect sleep, improved sleep, slight effect, no effect, poorer sleep—and also compared the effect of the two preparations—

better the first night, worse, the same. A sign test was used for evaluation of the comparison between the two preparations. The subjects were asked about side effects such as fatigue, drowsiness the next day and nightmares.

RESULTS

Twenty-one of 27 subjects rated the test preparation as better than the control. Two subjects rated the preparations as equally good and 4 preferred the control preparation. The difference between ratings of the two preparations was significant ($p < 0.001$). There was no significant difference between those who took the active preparation first and those who took the control preparation first (see Table 1). In the ratings of sleep quality, 24 of 27 subjects reported improved sleep from the test preparation, and 12 of these subjects, or 44%, reported "perfect sleep" after taking VALERINA NATT. No side effects were reported. Nightmares, which had previously occurred after customary sedatives, were nonexistent.

DISCUSSION

When significant effects are obtained from a medication as compared with a placebo, this does not always have to mean that the effects are good. In this case, however, the results are very satisfactory, since 44% of the subjects had perfect sleep and 89% reported better sleep from VALERINA NATT. The absence of side effects the next day can be regarded as favorable, as can the disappearance of nightmares and troubled sleep which had occurred with conventional medication.

These results cannot be extrapolated to long-term use, but clinical experience with the medication does not reveal any side effects over the long run, and the effects appear to be the same when the medication is used repeatedly. This natural medication can be regarded as a good alternative to conventional, strong medication which carries the risk of habituation and side effects.

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