No. 7 March 2000

Herbs for the Treatment of Insomnia, Restlessness and Anxiety

Valerian

Valeriana officinalis contains a variety of constituents including valepotriates, valerenic acid and bornyl acetate which may contribute to the sedative activity of the whole root. Although other species of Valerian contain higher levels of valepotriates (such as *V. edulis*), valerenic acid and acetoxyvalerenic acid are unique to *V. officinalis.* ^{1,2} Traditionally Valerian has been used primarily for the treatment of nervous system disorders especially nervous unrest, stress, sleeplessness and anxiety. ² Reference has been made to the extensive use of Valerian to treat shell shock after World War I and as a sedative for the civilian population in Britain during World War II. ^{3,4}

The essential oil, valepotriates and valerenic acid and derivatives all contribute to the sedative activity. The mechanism of action of Valerian is not clearly known but it may be related to inhibition of GABA breakdown in the brain or interaction with GABA receptors. A short placebo-controlled study conducted over 3 nights in elderly poor sleepers found that Valerian extract (containing valerenic acid) had selective effects on non-REM sleep (particularly an increase in slow-wave sleep) while REM sleep was unaltered.

In two double-blind, placebo-controlled trials conducted over 4 weeks in patients with insomnia, Valerian extract improved the symptoms of sleep disturbance, sleep quality and feelings of being rested after sleep. 8-10 Aqueous dried Valerian extract containing valerenic acid was used in one of the trials. In the other trial a relatively high dose of aqueous ethanolic extract (equivalent to about 2.4 g of dried root/rhizome per day) did not produce the paradoxical stimulation which Valerian can induce in some patients.

In double-blind trials on volunteers, Valerian did not have a negative impact on reaction time, alertness and concentration the morning after intake compared to placebo¹¹ and impairment of vigilance was less marked than that of a benzodiazepine drug.¹²

Passionflower

The main active constituents of dried aerial parts of *Passiflora incarnata* are flavonoids (up to 1.2%), specifically flavone-C-glycosides including isovitexin.¹ The presence of even trace amounts of the harmane alkaloids appears to be dependent upon the stage of development of the plant.² The German Commission E recommends that Passionflower not contain more than 0.01% of harmane alkaloids.¹³

Passionflower has been used traditionally as a sedative and antispasmodic for the treatment of insomnia, neuralgia, generalised seizures, hysteria, nervous tachycardia and spasmodic asthma. In addition to these uses the Eclectic physicians recommended its use for spasmodic dysmenorrhoea, headache and the treatment of pain. In recent decades Passionflower has been utilised in Germany in preparations for the treatment of insomnia. The German Commission E lists its use as nervous restlessness with animal studies indicating a motility-inhibiting activity. ¹³ Passionflower extract did not interact with benzodiazepine, dopaminergic or histaminergic receptors *in vitro*¹⁴ and has demonstrated sedative and anxiolytic activity *in vivo*. ^{15,16}

A Passionflower and Valerian combination demonstrated improvement in symptoms of insomnia in uncontrolled clinical trials. After three weeks of herbal treatment, 82% of patients described improvement in symptoms.¹⁷ Patients treated for an average of 10.8 days found that the combination caused them to fall asleep more easily and wake up less frequently during the night. Side effects characteristic of benzodiazepine tranquillisers (e.g. impaired vigilance) were not observed.¹⁸

Zizyphus

Some species of Ziziphus (also spelt Zizyphus) are used for their timber and edible fruit (called jujube) which is dried like dates. In Traditional Chinese Medicine Ziziphus jujuba var. spinosa seed is listed amongst herbs that nourish the Heart and calm the Spirit which are primarily used for palpitations with anxiety and insomnia from Deficient Heart Blood and Deficient Liver Yin. Ziziphus jujuba var. spinosa (botanical synonym: Ziziphus spinosa) which is

known as sour date seed in English and Suanzaoren in Mandarin, is listed in the current Chinese Pharmacopoeia with the following indications: insomnia, dream-disturbed sleep; excessive sweating due to debility and thirst due to consumption of body fluid. 19,20 Note: *Z. jujube* (*Z. jujube* var. *inermis*) is a different species and its fruit is used for different indications in TCM.

The active constituents of *Zizyphus spinosa* include dammarane-type saponins called jujubosides A and B, and a flavone C-glycoside called spinosin.²¹ Oral administration of Zizyphus seed has demonstrated sedative activity *in vivo*.²²⁻²⁴

Suanzaorentang is a formula containing mainly Zizyphus. It has been studied in double-blind trials. One study of patients with anxiety found that it significantly improved mood, decreased sympathetic nervous system symptoms and improved performance.²⁵ Another study of insomnia showed a significant improvement in sleep quality and well-being without side effects.²⁶

Synergistic Formulation

The three herbs would complement each other in a very potent formulation with the following actions:

- mild sedative,
- anxiolytic,
- spasmolytic.

Indications

- Insomnia, restlessness, irritability.
- Mild anxiety.
- Nervous tension, stress.

Contraindications & Cautions

None known. A few individuals may however find Valerian stimulating.

REFERENCES

¹ Wagner H, Bladt S. *Plant Drug Analysis: A Thin Layer Chromatography* Atlas, 2nd Edn. Berlin: Springer-Verlag, 1996. ² British Herbal Medicine Association. British Herbal Compendium. Bournemouth: BHMA, 1992. Chopra RN et al. Chopra's Indigenous Drugs of India, 2nd Edn, 1958, reprinted Academic Publishers, Calcutta, 1982. ⁴ Grieve M. A Modern Herbal. Dover Publications, New York, 1971. 5 Houghton Pl. / Pharm Pharmacol 1999; **51**: 505 ⁶ Ortiz JG et al. Neurochem Res 1999; **24**: 1373 ⁷ Schulz H et al. *Pharmacopsychiatry* 1994; 27: 147 8 Jansen W. Therapiewoche 1977; **27**: 2779 ⁹ Vorbach EU, Arnold KH. *6th Phytotherapy Conference*, Berlin, October 5-7, 1995. ¹⁰ Vorbach EU et al. Psychopharmakother 1996; 3: 109 11 Kuhlmann J et al. Pharmacopsychiatry 1999; 32: 235 12 Gerhard U et al. Schweiz Rundsch Med Prax 1996; 85: 473 13 Blumenthal M et al (eds). The Complete German Commission E Monographs: Therapeutic Guide to Herbal Medicines. American Botanical Council, Austin, 1998. 14 Burkard W et al. Pharm Pharmacol Lett 1997; 7: 25 15 Capasso A, Pinto A. Acta Therapeutica 1995; **21**: 127 ¹⁶ Speroni E et al. *Phytother Res* 1996; **10**(Suppl 1): S92 ¹⁷ Kammerer E, Wegener T. *Natura Med* 1995; **10**: 1 ¹⁸ Mollenhauer C. Z Phytother Abstractband 1995; p 22 19 Pharmacopoeia

Commission of the People's Republic of China. *Pharmacopoeia of the People's Republic of China*, English Edn. Chemical Industry Press, Beijing, 1997. ²⁰ Bensky D, Gamble A. *Chinese Herbal Medicine Materia Medica*. Eastland Press, Seattle, 1986. ²¹ Tang W, Eisenbrand G. *Chinese Drugs of Plant Origin*. Springer Verlag, Berlin, 1992. ²² Chang HM, But PP. *Pharmacology and Applications of Chinese Materia Medica*. World Scientific Publishing, Singapore, 1987. ²³ Lou SN et al. *Abst Chin Med* 1988; **2**: 39; Abstract No. 880171 ²⁴ Morishita S et al. *Gen Pharmacol* 1987; **18**: 637 ²⁵ Chen HC et al. *Int J Clin Pharmacol Ther Toxicol* 1986; **24**: 646 ²⁶ Chen HC, Hsieh MT. *Clin Ther* 1985; **7**: 334

Author: Michelle Morgan
© Copyright 2000 MediHerb Pty Ltd.