

 Open access • Journal Article • DOI:10.1002/PTR.2847

## Interactions of *Valeriana officinalis* L. and *Passiflora incarnata* L. in a patient treated with lorazepam — [Source link](#)

Maria Consuelo Carrasco, José Ramón Vallejo Villalobos, Manuel Pardo-de-Santayana, Diego Peral ...+2 more authors

**Institutions:** University of Extremadura, Autonomous University of Madrid

**Published on:** 01 Dec 2009 - Phytotherapy Research (Phytother Res)

**Topics:** Valeriana officinalis

Related papers:

- [Fatal seizures due to potential herb-drug interactions with Ginkgo biloba.](#)
- [Imatinib and Panax Ginseng: A Potential Interaction Resulting in Liver Toxicity](#)
- [Herb–Drug Interactions with St John’s Wort \(Hypericum perforatum\): an Update on Clinical Observations](#)
- [Clinical assessment of effects of botanical supplementation on cytochrome P450 phenotypes in the elderly: St John's wort, garlic oil, Panax ginseng and Ginkgo biloba.](#)
- [Interaction between a commercially available St. John’s wort product \(Movina\) and atorvastatin in patients with hypercholesterolemia](#)

Share this paper:    

View more about this paper here: <https://typeset.io/papers/interactions-of-valeriana-officinalis-l-and-passiflora-wqjs0qpvy8>

**Interactions of Valeriana officinalis L. and Passiflora incarnata L. in a patient treated with lorazepam**

Journal:	<i>Phytotherapy Research</i>
Manuscript ID:	PTR-09-0195.R1
Wiley - Manuscript type:	Letter to the Editor
Date Submitted by the Author:	04-Mar-2009
Complete List of Authors:	Carrasco, María Consuelo; Servicio Extremeño de Salud, Centro de Salud Pueblonuevo del Guadiana Vallejo, José Ramón; Universidad de Extremadura, Facultad de Medicina (Historia de la Medicina) Pardo-de-Santayana, Manuel; Universidad Autónoma de Madrid, Biología (Botánica) Peral, Diego; Universidad de Extremadura, Facultad de Medicina (Historia de la Medicina) Martín, Miguel Ángel; Universidad de Extremadura, Facultad de Medicina (Historia de la Medicina) Altimiras, Jacinto; Universidad de Extremadura, Facultad de Medicina (Historia de la Medicina)
Keyword:	benzodiazepines, herbal remedies, interactions, valerian, passionflower



## LETTER TO THE EDITOR

**Interactions of *Valeriana officinalis* L. and *Passiflora incarnata* L. in a patient  
treated with lorazepam**

María Consuelo Carrasco<sup>1</sup>, José Ramón Vallejo<sup>2</sup>, Manuel Pardo-de-Santayana<sup>3</sup>,  
Diego Peral<sup>2</sup>, Miguel Ángel Martín<sup>2</sup>, Jacinto Altimiras<sup>2</sup>

<sup>1</sup>Consultorio Local Nuestra Sra. de la Soledad de Gadiana del Caudillo. Centro de Salud Pueblonuevo del Gadiana (Badajoz). Travesía de la Constitución s/n. 06184 Pueblonuevo del Gadiana. (Badajoz). Spain

<sup>2</sup>Grupo de Investigación en Humanidades Médicas. Facultad de Medicina. Universidad de Extremadura. Avda. de Elvas s/n. 06071 Badajoz. Spain.

<sup>3</sup>Departamento de Biología (Botánica). Universidad Autónoma de Madrid. c/ Darwin 2. Campus de Cantoblanco, 28049 Madrid. Spain.

Corresponding author:

Manuel Pardo de Santayana. Departamento de Biología (Botánica). Universidad Autónoma de Madrid. c/ Darwin 2. Campus de Cantoblanco, E-28049 Madrid; e-mail: [manuel.pardo@uam.es](mailto:manuel.pardo@uam.es); phone: 0034+914978110; fax: 0034+914978344

1  
2  
3 **Interactions of *Valeriana officinalis* L. and *Passiflora incarnata* L. in a patient**  
4  
5 **treated with lorazepam**  
6

7 MC Carrasco, JR Vallejo, M Pardo-de-Santayana, D Peral, MA Martín, J

8  
9 Altimiras  
10

11  
12  
13  
14 **ABSTRACT**  
15

16 There is an increasing interest in the health risks related to the use of herbal  
17 remedies. Although most consumers think that phytomedicines are safe and without  
18 side-effects, interactions between complementary alternative-and-conventional  
19 medicines are being described.  
20  
21  
22  
23

24  
25 The aim of this clinical-case-report is to highlight the importance of the safe use  
26 of herbal remedies by providing a clinical interaction study between pharmaceutical  
27 medicines and herbal medicinal products.  
28  
29  
30

31 The case of a patient self-medicated with *Valeriana officinalis* L. and *Passiflora*  
32 *incarnata* L. while he was on lorazepam treatment is described. Handshaking, dizziness,  
33 throbbing and muscular fatigue were reported within the 32 hours before clinical  
34 diagnosis. The analysis of family medical history ruled out essential tremor, Parkinson's  
35 disease, Wilson's disease and other symptom-related pathologies. His medical history  
36 revealed a Generalized Anxiety Disorder and medicinal plant consumption but no  
37 neurological disorder. Appropriate physical examination was carried out.  
38  
39  
40  
41  
42  
43  
44

Deleted: along a 32-hour-progress

45  
46 An additive or synergistic effect is suspected to have produced these symptoms.  
47 Valerian and passionflower active principles might increase the inhibitory activity of  
48 benzodiazepines binding to the GABA receptors, causing severe secondary effects.  
49  
50  
51

Deleted: ra

Due to the herbal–product–self–medication increase, [the use of herbal remedies](#) [should be registered while taking](#) personal clinical history. Multidisciplinary teams should be created to raise studies on medicinal plants with impact on medical praxis.

**Deleted:** Primary Health Attention team considers the benefits of registering these remedies' use in

**Keywords:** herbal remedies, interactions, benzodiazepines, valerian, [passionflower](#).

**Deleted:** flora

## Introduction

The simultaneous consumption of medicaments and herbal remedies (including dry or fresh medicinal plants and phytopharmaceuticals or vegetable drugs), [might](#) cause interactions, much of which are not described nowadays (Farah *et al.*, 2000).

**Deleted:** ay

**Deleted:** There are two different types of interactions: a) Pharmacokinetic interactions which are based in the decrease of medicine absorption, its metabolizing or its elimination process, b) Pharmacodynamic interactions that provoke additive, synergistic or antagonistic effects (Castillo and Martínez, 2007).

Nowadays, there is an increasing interest on health risks related to the use of herbal remedies. There is uncertainty with regard to their quality, safety and efficacy. Besides, the increasing trend of self-medication and consumers' perception that phytopharmaceuticals are always safe and have no side-effects, can lead to an increase of the incidence of adverse effects associated to the consumption of herbal medicines (Elvin-Lewis, 2005; Williamson, 2005).

During the visit to the general practitioner in Guadiana del Caudillo (Badajoz, Spain), we reported a clinical case (not previously described in available scientific literature) of a 40 years old male patient self-medicated with [valerian](#) (*Valeriana officinalis* L.) and [passionflower](#) (*Passiflora incarnata* L.) while on lorazepam treatment.

**Deleted:** flora

### Results: Clinical Case

Handshaking, dizziness, throbbing and muscular fatigue were reported within the 32 hours before clinical diagnosis. No other neurological symptoms such as cephalgia, paresthesia, loss of any extremity strength neither language nor walking gait alterations were reported.

Family medical history ruled out essential tremor, including Parkinson's and Wilson's disease. Clinical history revealed a generalized anxiety disorder (GAD) and dream disorders. No endocrine-metabolic pathologies, hepatopathies, nephropathies, breathing problems neither personal history of neurological pathologies, consumption of toxic substances, high blood pressure or drug allergies were reported. The patient only mentioned that he had recently consumed medicinal plants.

Since two months ago and without side effects, the patient was following a 2mg/24 h lorazepam treatment. Approximately two hours before bedtime and during two days in a row, the patient took the infusion of [valerian](#), subterranean parts. Just before going to bed the patient took the same infusion mixed with unlimited-quantity of [passionflower](#), dry herb without side effects. The estimated dose for an infusion is 300 mg. Instead of taking an infusion, the third day before going to bed, the patient took a similar dose of the plants but in tablets of dry extract from valerian rhizomes and roots and aerial parts of [passionflower](#). Each tablet contained 300 mg of valerian and 380 mg of [passionflower](#) extract according to the product label. The patient took three tablets at one-hour intervals before going to sleep. Nerves and light-and-rhythmical shaking disappeared shortly after going to bed, followed by a strong drowsiness. As the fourth day the phytopharmaceutical treatment was repeated, strong handshaking, dizziness and palpitations appeared before going to bed, followed by a heavy drowsiness which made

Deleted: *Valeriana officinalis* L.

Deleted: ra

Deleted: *Passiflora incarnata* L.

Deleted: flora

Deleted: ra

1  
2  
3 him fall asleep.  
4

5  
6 Along the physic exploration, nervousness while speaking and anxiety gestures  
7 without shaking were observed. The cardio respiratory auscultation was normal and  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

rhythmical, with a frequency of 60 beats per minute. Goiter on palpation of the neck region was not detected. Blood pressure was 128/74 mmHg. During the neurologic exploration, no communication or understanding problems were observed, cranial pairs were normal, neither meningeal signs nor alterations in tone or muscular strength were detected. Reflexes were normal, Romberg sign was negative and cerebellar function normal. No sensitivity or movement alterations appeared when the patient was invited to walk through the doctor's office.

Deleted: (bpm)

First of all the patient was calmed down, then he was explained that the episodic movement disorder he suffered, could be due to an interaction between the herbal and conventional medicines taken. He was also advised that control and monitoring was needed. He continued taking lorazepam and stopped consuming valerian and passionflower and symptoms disappeared.

Deleted: a

### Discussion and Conclusions

Lorazepam and other benzodiazepines are described as causing-and-aggravating drug-induced tremor (Sweetman, 2006). Moreover, although valerian drug have low toxicity, when their intake exceeds 20 times the 2-3 g therapeutic doses, intoxication takes place. Its symptoms that include handshaking or fatigue, abdominal cramps, chest tightness, dizziness and mydriasis, disappear within 24 hours (Villar del Fresno and Carretero, 2001; Willey *et al.*, 1995).

1  
2  
3 The examined patient suffered from excessive drowsiness and dizziness, which  
4 can be related to the increase in the sedative effect of valerian observed in animal's  
5 clinical trials that had been previously treated with benzodiazepines and other  
6 barbiturics. No valerian-benzodiazepine human-related interactions had been previously  
7 reported (Castillo and Martínez, 2007).  
8  
9  
10  
11  
12

13 However interactions between benzodiazepines (alprozolam) and sedative plants  
14 such as kava (*Piper methysticum* G. Forst.) have been already described (Almeida and  
15 Grimsley, 1996).  
16  
17

18  
19  
20 ~~Passionflower drug, normally prescribed for the treatment of anxiety and~~  
21 insomnia, has a sedative effect that may also increase when combined with other  
22 sedative drugs. It provokes nausea and dizziness when doses are high (Castillo and  
23 Martínez, 2007). This was one of the patient's symptoms.  
24  
25  
26  
27

Deleted: ra

28  
29 It can be suspected that the symptoms of the case were caused by an interaction  
30 between the herbal remedies and lorazepam. The symptoms disappeared when the  
31 patient stopped the herbal treatment. An additive or synergistic effect on the central  
32 nervous system (CNS) is suspected to have produced these symptoms. Benzodiazepines  
33 facilitate the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) by binding  
34 to the alpha subunit of the GABA receptor (Bowery and Smart, 2006). Valerian and  
35 ~~passionflower~~ might increase the inhibitory activity of benzodiazepines binding to the  
36 GABA receptors, causing severe secondary effects as well.  
37  
38  
39  
40  
41  
42  
43  
44

Deleted: ra

45 Due to the increase in the use of herbal remedies, it seems advisable for  
46 the general practitioners to ask on the habit of consuming these remedies while taking  
47 personal history and anamnesis. This could be a difficult task, since many patients hide  
48  
49  
50



these uses in order to avoid being misunderstood by the doctor. Most Spanish practitioners lack an adequate training on phytotherapy and although many reject it, there is an increasing acceptability of herbal medicine.

### Acknowledgements

We are grateful to the Health Centre of Plueblonuevo del Guadiana and the School of Medicine of the University of Extremadura for their support in studying and promoting a safe use of herbal medicine. We thank V. Mazimpaka for revising and improving the manuscript.

### References

- Almeida JC, Grimsley EW. 1996. Coma from the Health Food Store: Interaction between Kava and Alprazolam. *Ann Intern Med* **125**: 940-941
- Bowery NG, Smart TG. 2006. GABA and glycine as neurotransmitters: a brief history. *Br J Pharmacol* **147(S1)**: S109–S119
- Castillo E, Martínez I. 2001. *Manual de Fitoterapia*. Elsevier, Masson: Madrid.
- Elvin-Lewis, M. 2005. Safety Issues Associated with Herbal Ingredients. *Adv Food Nutr Res* **50**: 219-313.
- Farah MD, Edwards R, Linquist M, Leon C, Shaw D. 2000. International Monitoring of Adverse Health Effects Associated with Herbal Medicines. *Pharmacoepidemiol Drug Saf* **9**: 105-112.

**Deleted:** Furthermore Health Education programs should be developed in order to change the generalized idea that herbal products are natural and always innocuous. Moreover, the quality-, security- and efficiency-control mechanisms of phytopharmaceuticals will be useless if people do not use them consistently. In order to reinforce the Primary Health Care system, multidisciplinary teams of several professional fields including ethnopharmacologists should be created in order to have a complete overview of the use of herbal remedies and thus help in the prevention of adverse effects of herbal remedies.¶  
In this sense we are conducting a Health Program in Guadiana, in which we inform the local population on the need of making an adequate use of traditional and modern herbal remedies. In addition, we are promoting preventive measures to avoid intoxications (Vallejo et al. 2008a) and interactions of herbal remedies with medicaments. We give short and concise information to the patients of the primary health care centre on the risks on consuming herbs and herbal products inadequately. Meanwhile, we have put posters in the health centre that induce reflexion when using herbal remedies and that promote asking the general practitioner before consuming them. We have also conducted an ethnopharmacological survey compiling all the traditional remedies of the area in order to contribute to health planification (Vallejo et al., 2008b). ¶

1  
2  
3 Sweetman SC (ed). 2006. *Martindale: Guía Completa de Consulta*  
4 *Farmacoterapéutica*. 2nd Spanish ed. Pharma: Barcelona. Translation of the 33rd ed  
5  
6 of "Martindale: the complete drug reference".  
7  
8

9  
10 Villar del Fresno AM, Carretero E. 2001. *Valeriana officinalis*. Fitoquímica,  
11 farmacología y terapéutica. *Farm Prof* **10**: 98-106.  
12

13  
14 Willey LB, Mady SP, Cobaugh DJ, Wax PM. 1995. Valerian Overdose: A Case Report.  
15 *Vet Hum Toxicol* **37(4)**: 364-365.  
16  
17

18  
19 Williamson EM. 2005. Interactions between Herbal and Conventional Medicines.  
20 *Expert Opin Drug Saf* **26(15)**:1075-1092.  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

**Deleted:** Valledo JR, Pardo-de-Santayana M, Peral D, Carrasco MC, López D. 2008a. Uso medicinal de *Atractylis gummifera* L. en Guadiana del Caudillo (Badajoz, España). Toxicidad y especies afines. *Rev Fitoterapia* **8(2)**: 161-169. ¶  
Valledo JR, Peral D, Carrasco MC. 2008b. *Catálogo de remedios de la medicina popular de Guadiana del Caudillo*. Ayuntamiento de Guadiana del Caudillo: Badajoz. Spain. ¶