

Tuberous Comfrey (*Symphytum tuberosum*)

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Volume 1: Botany and History of Comfrey; Garden Uses of Comfrey

Pages 258-259. By Nancy Shirley.

S. tuberosum and Alkaloids

(Low in Alkaloids, High in Allantoin)

"The alcoholic extract of *Symphytum tuberosum* also yielded six alkaloids, two of them identified as anadoline and echimidine. In the aqueous (water) extract of the plant the following amino acids were detected:

aspartic acid glycine, leucine, serine, valine, alanine, glutamic acid, proline, methionine, isoleucine, phenylalanine, histidine and lysine."

- 'Alkaloids and Other Compounds of *Symphytum Tuberosum*' by A. Ulubelen and F. Ocal, Faculty of Pharmacy, University of Istanbul, Turkey, *Phytochemistry*, Volume 16, Issue 4, pages 499-500, **1977**.



"In a previous communication (*Gray et al 1983) we reported the isolation of two pyrrolizidine alkaloids, symlandine and echimidine together with a large quantity of allantoin from the roots and rhizomes of *Symphytum tuberosum* L. (Tuberous Comfrey, family Boraginaceae).

*Allantoin is used in the treatment of psoriasis and other skin diseases and is a component of many cosmetics (Nakao et al 1982). The occurrence of pyrrolizidine alkaloids in *Symphytum* spp. (species) is of considerable importance owing to their hepatotoxicity and carcinogenicity (**Schoental 1982).*

*The dried leaves (2.5 kg = 5.5 pounds) of *S. tuberosum* (collected May 1984 at the National Botanic Garden, Glasnevin, Dublin, Ireland) were percolated with CHCl_3 and then MeOH. Work up (cf. Gray et al 1983) led to the isolation of two pyrrolizidine N-oxides, symlandine-N-oxide (1, 0.0032% w/w {weight by weight}) and echimidine-N-oxide (2, 0.004% w/w).*

The structures were determined on the basis of physico-chemical studies using high resolution $^1\text{H-NMR}$ with spin decoupling, $^{13}\text{C-NMR}$ and MS, by comparison of spectral data with those of the free bases (3 & 4, respectively), which were also found in the CHCl_3 extract, and by conversion into the free bases.

Once again (cf. Gray et al 1983) the yield of allantoin was high (0.98% w/w from the MeOH extract) and that of the pyrrolizidine alkaloids low in comparison with *S. officinale* L. (**Tittel et al 1979), the species used in herbal medicine.

This confirms that *S. tuberosum* is a useful alternative source of allantoin."

- 'Pyrrolizidine Alkaloid N-Oxides from *Symphytum Tuberosum*' by P. Bhandari and A.I. Gray, Department of Pharmacognosy, School of Pharmacy, Trinity College, Ireland, *Journal of Pharmacy and Pharmacology*, Volume 37, Issue S12, December **1985**.

(* - 'Hepatotoxic Alkaloids and Allantoin in *Symphytum Tuberosum*' by Gray, A.I. et al, *Journal of Pharmacy and Pharmacology*, Volume 35, 13P, 1983. I was unable to get a copy of this report. If you have one, could you send it to me.)

(** - 'Health Hazards of Pyrrolizidine Alkaloids: A Short Review' by R. Schoental; *Toxicology Letters*, Amsterdam, Netherlands, Volume 10, Issue 4, pages 323-326, 1982.)

(*** - 'Quantitative Estimation of the Pyrrolizidinealkaloids of Radix *Symphyti*' by HPLC' by G. Tittel, H. Hinz and H. Wagner; *Planta Medica: Journal of Medicinal Plant Research*, Volume 37, Issue 9, pages 1-8, 1979. In German except abstract is in English.)

(cf. = compare to other literature)

"In S. tuberosum subsp., tuberosum and nodosum, S. grandiflorum and S. ibericum the presence of the pyrrolizidine alkaloids lycopsamine, echimidine and symphytine could be demonstrated.

The taxon S. tuberosum contains an unknown compound that seems to be specific for this taxon. This compound is not the pyrrolizidine alkaloid anadoline which has previously been reported for this species. It is possibly represented by a peak on GC/MS (Gas Chromatography/Mass Spectrometry) with a molecular ion peak at m/z 623 (as TMS derivative) and can be used as a chemotaxonomic marker for the species S. tuberosum.

The pyrrolizidine alkaloid pattern of the two subspecies of S. tuberosum reinforces the close relationship. Fresh material of S. tuberosum contained the triterpene isobauerenol, but in herbarium material isobauerenol was lacking."

-‘Chemo- and Karyotaxonomic Studies on Some Rhizomatous Species of the Genus Symphytum (Boraginaceae)’ by T.A. Jaarsma, E. Lohmanns, H. Hendriks, T.W.J. Gadella and T.M. Malingre, Plant Systematics and Evolution, Volume 169, pages 31-39, **1990**.

"Symphytum tuberosum L., Tuberous Comfrey (German: Knoten-Beinwell, French: Consoud tubereuse), grows in south-east Europe. Its allantoin content is very high; besides, it contains symlandine, echimidine and anadoline respectively the N-oxides of these alkaloids in a total concentration of only 0.02%*.

Tuberous Comfrey is recommended for medicinal purposes as an alternative to the other Comfrey species**."

-‘Medicinal Plants in Europe Containing Pyrrolizidine Alkaloids’ by Erhard Thomas Roeder, Pharmazeutisches Institut (Pharmaceutical Institute) der Rheinischen Friedrichs-Wilhelms, University of Bonn, Germany, Pharmazie (Pharmacy) 50, pages 83-98, March **1995**.

(* -‘Alkaloids and Other Compounds of Symphytum Tuberosum’ by A. Ulubelen and F. Ocal, Faculty of Pharmacy, University of Istanbul, Turkey, Phytochemistry, Volume 16, Issue 4, pages 499-500, 1977.)

(** -‘Pyrrolizidine Alkaloid N-Oxides from Symphytum Tuberosum’ by P. Bhandari and A.I. Gray, Department of Pharmacognosy, School of Pharmacy, Trinity College, Ireland, Journal of Pharmacy and Pharmacology, Volume 37, Issue S12, December 1985.)

"S. tuberosum L. has been shown to contain 72 mg/kg PA (Pyrrolizidine Alkaloid) N-oxides in the leaf, and 180 mg/kg in the root. S. tuberosum contains PA levels significantly lower than other Symphytum spp. (species) and relatively high levels of allantoin, 0.96% in the root and 0.98% in the leaf.

These findings are only on single samples, but it may become the preferred species for medicinal use."

-‘Using Herbs that Contain Pyrrolizidine Alkaloids’ by Alison Denham, B.A., MNIMH (National Institute of Medical Herbalists), University of Central Lancashire, England; The European Journal of Herbal Medicine, Volume 2, No. 3, pages 27-38, **1996**.

"To the extent that some members of the Comfrey plant family do not contain PAs, then the concerns FDA (Food and Drug Administration of the United States) has about a Comfrey-containing dietary supplement product or ingredient depends upon the exact species identified.

The FDA ruling banned the internal use of Symphytum officinale (Common Comfrey), S. asperum (Prickly Comfrey), and S. x uplandicum (Russian Comfrey), as well as any other plant/substance containing pyrrolizidine alkaloids.

While FDA did not examine the safety of other Comfrey species such as Symphytum tuberosum L. (Tuberous Comfrey), which is suggested to contain negligible amounts of pyrrolizidine alkaloids, FDA would rely on the presence of the pyrrolizidine alkaloid to determine whether this species was permitted to be used as a dietary ingredient."

-Bioactive Compounds in Food: Edited by John Gilbert (United Kingdom) and Hamide Z. Senyuva (Turkey), United Kingdom, Oxford: Blackwell Publishing Ltd, **2008**, page 619.