

## 参考文献等一覧

- 1 ) FDA advices dietary supplement manufacturers to remove comfrey products from the market.  
U.S. Food and Drug Administration Center for Food Safety and Applied Nutrition, July 6, 2001
- 2 ) PYRROLIZIDINE ALKALOIDS IN FOOD, A toxicological review and risk assessment,  
Australia New Zealand Food Authority, November 2001
- 3 ) Health Canada advices consumers not to use the herb comfrey or health products that contain  
comfrey.  
Health Canada, December 12, 2003
- 4 ) Botanical Safety Handbook, American Herbal Products Association
- 5 ) Natural Medicine comprehensive database fifth edition,  
Therapeutic Research Faculty
- 6 ) 再びコンフリーの毒性について  
Comfrey toxicity revisited.  
Rode D.  
Trends Pharmacol Sci. 2002 Nov;23(11):497-9.
- 7 ) コンフリーの有効性と安全性 (総説)  
The efficacy and safety of comfrey.  
Stickel F, Seitz HK.  
Public Health Nutr. 2000 Dec;3(4A):501-8.
- 8 ) ピロリジジン含有ダイエタリーサプリメントの摂取による肝静脈閉塞性疾患  
Hepatic veno-occlusive disease associated with the consumption of  
pyrrolizidine-containing dietary supplements.  
Ridker PM, Ohkuma S, McDermott WV, Trey C, Huxtable RJ.  
Gastroenterology. 1985 Apr;88(4):1050-4.
- 9 ) コンフリー摂取による肝臓静脈閉塞性疾患  
Hepatic veno-occlusive disease associated with comfrey ingestion.  
Yeong ML, Swinburn B, Kennedy M, Nicholson G.  
J Gastroenterol Hepatol. 1990 Mar-Apr;5(2):211-4.
- 10 ) コンフリー茶と肝臓の静脈閉塞性疾患 (VOD)  
Comfrey herb tea and hepatic veno-occlusive disease.  
Ridker PM, McDermott WV.  
Lancet. 1989 Mar 25;1(8639):657-8.
- 11 ) Toxicity of comfrey.  
Winship KA.

Adverse Drug React Toxicol Rev. 1991 Spring;10(1):47-59.

1 2 ) 市販のコンフリー製品中のピロリジジンアルカロイドの定量  
Determination of pyrrolizidine alkaloids in commercial comfrey products  
(Symphytum sp.).

Betz JM, Eppley RM, Taylor WC, Andrzejewski D.

J Pharm Sci. 1994 May;83(5):649-53.

1 3 ) Comfrey and liver damage.

Roitman, J.N., Lancet. 1981 Apr 25;1(8226):944.

1 4 ) Comfrey toxicity in perspective.

Anderson, C., Lancet. 1981 Jun 27;1(8235):1424.

1 5 ) Toxic pyrrolizidine alkaloids in comfrey.

Mattocks, A.R., Lancet. 1980 Nov 22;2(8204):1136-7.

Environmental Health Criteria 80, "PYRROLIZIDINE ALKALOIDS",  
World Health Organization 1988

1 6 ) ハーブ治療薬の使用による異常な実験結果と毒性影響

Review of abnormal laboratory test results and toxic effects due to use of herbal medicines.

Dasgupta A.

Am J Clin Pathol. 2003 Jul;120(1):127-37.

1 7 ) 食品中のピロリジジンアルカロイド

Pyrrolizidine alkaloids in foods.

Coulombe RA Jr.

Adv Food Nutr Res. 2003;45:61-99.

1 8 ) 発がん性ピロリジジンアルカロイドリデリイン及びその代謝物のラット及びマウスでのトキシコ  
キネティクス

Toxicokinetics of riddelliine, a carcinogenic pyrrolizidine alkaloid, and metabolites in rats and mice.

Williams L, Chou MW, Yan J, Young JF, Chan PC, Doerge DR.

Toxicol Appl Pharmacol. 2002 Jul 15;182(2):98-104.

Hepatic veno-occlusive disease as a result of a traditional remedy: confirmation of toxic  
pyrrolizidine alkaloids as the cause, using an in vitro technique.

Zuckerman M, Steenkamp V, Stewart MJ.

J Clin Pathol. 2002 Sep;55(9):676-9.

1 9 ) ピロリジジン中毒：ヒト毒物学上軽視されてきた分野

Pyrrolizidine poisoning: a neglected area in human toxicology.

Stewart MJ, Steenkamp V.

Ther Drug Monit. 2001 Dec;23(6):698-708

Toxicity of dietary *Heliotropium dolosum* seed to mice.  
Eroksuz Y, Eroksuz H, Ozer H, Sener B, Tosun F, Akyuz C.  
Vet Hum Toxicol. 2001 Jun;43(3):152-5. (echimidine の記述有り)

20) 卵中へのピロリジジンアルカロイドの移行：食品の安全性との関連  
Transfer of Pyrrolizidine Alkaloids into Eggs: Food Safety Implications.  
EDGAR J A, SMITH L W,  
ACS Symp Ser (Am Chem Soc), 745, 118-128; (2000)

21) 南アフリカの伝統的治療によって起こったピロリジジン中毒の臨床および分析法  
Clinical and Analytical Aspects of Pyrrolizidine Poisoning Caused by South African Traditional Medicines.  
STEENKAMP V, et al.  
Ther Drug Monit 22(3), 302-306 (2000)

22) Medicinal plants in China containing pyrrolizidine alkaloids.  
Roeder E.  
Pharmazie. 2000 Oct;55(10):711-26.

Unsafe and potentially safe herbal therapies.  
Klepser TB, Klepser ME.  
Am J Health Syst Pharm. 1999 Jan 15;56(2):125-38; quiz 139-41.

[Hepatic veno-occlusive disease: report of a case] [Article in Portuguese]  
Magnabosco EM, Rivera ML, Prolla IR, Verney YM, Mello ES.  
J Pediatr (Rio J). 1997 Mar-Apr;73(2):115-8

23) ピロリジジンアルカロイドを含有するヨーロッパの薬用植物  
Medicinal plants in Europe containing pyrrolizidine alkaloids.  
ROEDER, E.  
Pharmazie, 50(2), 83-98 (1995)

24) 市販のコンフリー製品中のピロリジジンアルカロイドの定量  
Determination of pyrrolizidine alkaloids in commercial comfrey products (*Symphytum* sp.).  
Betz JM, Eppley RM, Taylor WC, Andrzejewski D.  
J Pharm Sci. 1994 May;83(5):649-53.

Hepatocyte membrane injury and bleb formation following low dose comfrey toxicity in rats.  
Yeong ML, Wakefield SJ, Ford HC.  
Int J Exp Pathol. 1993 Apr;74(2):211-7.

25) 食品中の有毒植物成分  
Toxic plant constituents in foods.  
CULVENOR, C. C. J.

Food Aust., 44(2), 73-75 (1992)

26) Toxicity of comfrey.

Winship KA.

Adverse Drug React Toxicol Rev. 1991 Spring;10(1):47-59.

The Budd-Chiari syndrome and hepatic veno-occlusive disease. Recognition and treatment.

McDermott WV, Ridker PM.

Arch Surg. 1990 Apr;125(4):525-7.

(Toxline で検索)

[Studies on the effect of an alkaloid extract of *Symphytum officinale* on human lymphocyte cultures]

[Article in German]

Behninger C, Abel G, Roder E, Neuberger V, Goggelmann W.

Planta Med. 1989 Dec;55(6):518-22.

Comfrey: assessing the low-dose health risk.

Abbott PJ.

Med J Aust. 1988 Dec 5-19;149(11-12):678-82.

Veno-occlusive disease of the liver secondary to ingestion of comfrey.

Weston CF, Cooper BT, Davies JD, Levine DF.

Br Med J (Clin Res Ed). 1987 Jul 18;295(6591):183.

27) Toxicity of comfrey-pepsin preparations.

Huxtable RJ, Luthy J, Zweifel U.

N Engl J Med. 1986 Oct 23;315(17):1095.

28) Hepatic venoocclusive disease associated with the consumption of pyrrolizidine-containing dietary supplements.

Ridker PM, Ohkuma S, McDermott WV, Trey C, Huxtable RJ.

Gastroenterology. 1985 Apr;88(4):1050-4.

29) ピロリジジナルカロイドの摂取 大量の健康被害

Ingestion of pyrrolizidine alkaloids: A health hazard of global proportions.

ROITMAN, J. N.

ACS Symp Ser (Am Chem Soc), 234, 345-378 (1983)

30) Mutagenic effects of aqueous extracts of *Symphytum officinale* L. and of its alkaloidal fractions.

Furmanowa M, Guzewska J, Beldowska B.

J Appl Toxicol. 1983 Jun;3(3):127-30.

Consumption of poisonous plants (*Senecio jacobaea*, *Symphytum officinale*, *Pteridium aquilinum*,

Hypericum perforatum) by rats: chronic toxicity, mineral metabolism, and hepatic drug-metabolizing enzymes.

Garrett BJ, Cheeke PR, Miranda CL, Goeger DE, Buhler DR.  
Toxicol Lett. 1982 Feb;10(2-3):183-8.

Symphytum officinale L (コンフリー) 由来ピロリジジンアルカロイド及びそのラットでの経皮吸収  
Pyrrolizidine alkaloids from Symphytum officinale L. and their percutaneous absorption in rats.

Brauchli J, Luthy J, Zweifel U, Schlatter C.  
Experientia. 1982 Sep 15;38(9):1085-7.

3 1 ) ロシアンコンフリーのアルカロイド

The alkaloids of Symphytum × uplandicum (russian comfrey).  
CULVENOR C C J, EDGAR J A, FRAHN J L, SMITH L W,  
Aust J Chem, 33(5), 1105-1113 (1980)

3 2 ) Symphytum officinale の発がん性

Carcinogenic activity of Symphytum officinale.  
Hirono I, Mori H, Haga M.  
J Natl Cancer Inst. 1978 Sep;61(3):865-9.

3 3 ) IPCS INCHEM HOME

International programme on chemical safety  
Environmental health criteria 80  
Pyrrolizidine alkaloids

3 4 ) Workshop Overview: Hepatotoxicity Assessment for Botanical Dietary  
Supplements

ToxSci Advance Access published February 19, 20

3 5 ) Pyrrolizidine alkaloids in foods.

Coulombe RA Jr.  
Adv Food Nutr Res. 2003;45:61-99

3 6 ) Honey from plants containing pyrrolizidine alkaloids: a potential threat to health.

Edgar JA, Roeder E, Molyneux RJ.  
J Agric Food Chem. 2002 May 8;50(10):2719-30.

3 7 ) Pyrrolizidine alkaloids in human diet

Prakash AS, Pereira TN, Reilly PE, Seawright AA.  
Mutat Res. 1999 Jul 15;443(1-2):53-67.

3 8 ) Natural plant toxicants in milk: a review.

Panter KE, James LF.  
J Anim Sci. 1990 Mar;68(3):892-904.

- 3 9 ) Simultaneous determination of N-oxides and free bases of pyrrolizidine alkaloids by cation-exchange solid-phase extraction and ion-pair high-performance liquid chromatography. Mroczek T, Glowniak K, Wlaszczk A. J Chromatogr A. 2002 Mar 8;949(1-2):249-62.
- 4 0 ) Isolation of Symplandine from the Roots of Common Comfrey (*Symphytum officinale*) Using Countercurrent Chromatography. Kim, N-C, et al. (Res. Triangle Inst., North Carolina) J Nat Prod, 2001, 64(2), 251-253
- 4 1 ) Pyrrolizidine Alkaloids from *Echium setosum* and *Echium vulgare*. El-Shazly, A, et al. J Nat Prod, 1996, 59(3), 310-313.
- 4 2 ) Determination of pyrrolizidine alkaloids in commercial comfrey products (*Symphytum* sp.). Betz JM, Eppley RM, Taylor WC, Andrzejewski D. J Pharm Sci. 1994 May;83(5):649-53.
- 4 3 ) Venous Occlusive Disease in a Fetus Caused by Pyrrolizidine Alkaloids of Food Origin R. Rasenack, C. Muller, M. Kleinschmidt, J. Rasenack, H. Wiedenfeld Fetal Diagn Ther 2003;18:223-225
- 4 4 ) Pyrrolizidine alkaloids James R. Liddell Covering: July 1999 to June 2000. Previous review: Nat. Prod. Rep., 2000, 17, 455.
- 4 5 ) Directly Toxic Effects of Plant Chemicals Which May Occur in Human and Animal Foods Alan A. Seawright National Research Centre for Environmental Toxicology, Coopers plains, Queensland, Australia NATURAL TOXINS 3:227-232(1995)
- 4 6 ) Hepatotoxicity of botanicals Felix Stickel, Gerlinde Egerer and Helmut Karl Seitz Submitted 23 September 1999; Accepted 12 January 2000 Public Health Nutrition: 3(2), 113-124
- 4 7 ) Risks associated with consumption of herbal teas. Manteiga R, Park DL, Ali SS. Rev Environ Contam Toxicol. 1997;150:1-30.
- 4 8 ) Determination of pyrrolizidine alkaloids in honey from selected sites by solid phase extraction and HPLC-MS. Crews C, Startin JR, Clarke PA. Food Addit Contam. 1997 Jul;14(5):419-28.

4 9 ) Comfrey herb tea and hepatic veno-occlusive disease.

Ridker PM, McDermott WV.

Lancet. 1989 Mar 25;1(8639):657-8.

5 0 ) Pyrrolizidine alkaloids in honey from *Echium plantagineum* L.

Culvenor CC, Edgar JA, Smith LW.

J Agric Food Chem. 1981 Sep-Oct;29(5):958-60.

5 1 ) WHO (2002): IARC Monographs on the Evaluation of Carcinogenic Risks to

Humans." Vol. 82 Some Traditional Herbal Medicines, Some Mycotoxins,

Naphthalene and Styrene" D. Senecio species and riddelliine. P.153-168

5 2 ) Naturally Occurring Carcinogens of Plant Origin, Toxicology, Pathology and Biochemistry 2

Pyrrolizidine Alkaloids:p25-51 (Edited by I.Hirono, ELSEVIER)

5 3 ) Peter P.Fu et al., 2004. Pyrrolizidine Alkaloids-Genotoxicity, Metabolism Enzymes, Metabolic

Activation, and Mechanisms. *Drug Metabolism Reviews* Vol.36(1):pp1-55.

5 4 ) Toxicity and carcinogenicity of riddelliine in rat and mice.

Po C.Chan et al.,2003.

*Toxicology Letters* 144:pp295-311.

5 5 ) Variation in pyrrolizidine alkaloid patterns of *Senecio jacobaea*.

Mirka Macel et al.,2004.

*Phytochemistry* 65:pp865-873.

5 6 ) Human Liver Microsomal Metabolism and DNA Adduct Formation of the Tumorigenic  
Pyrrolizidine Alkaloid, Riddelliine.

Qingsu Xia et al.,2003

*Chem.Res. Toxicol.* 16 :66-73.

5 7 ) 厚生労働省提供資料

・「Nコンフリー 50 中のアルカロイドについて」

・仁科淳由、中野裕之「コンフリーの抗アレルギー作用」FRAGRANCE JOURNAL 12 月号 1996