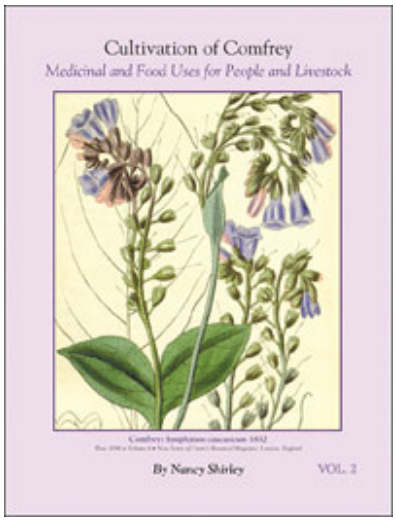

Volume 2, Comfrey Book: Cultivation of Comfrey Medicinal and Food Uses for People and Livestock

Chapter 30 (first 2 of 43 pages)

Alkaloids in Comfrey: Scientific Studies and Various Perspectives

Scientific Studies Showing Dangers of Alkaloids in Comfrey

With Some Rebuttals: Rebuttal is a statement that a claim or criticism is not true.
It is an argument or proof to contradict or disprove something previously stated.

"The citing of earlier papers proceeds on the assumption of certainty, which, as we have seen, is not always as sure as it is portrayed. According to authors Bone and Pembery: Mohabbat, Culvenor and Hirono research reports are flawed to some extent, yet their conclusions are interpreted as sure.

In particular, as mentioned above, Hirono's paper is regularly quoted as proof of the carcinogenicity (cancer causing) of Comfrey.

In 1978, Lawrence Hills of the 'Henry Doubleday Research' Institute published an article, reported in the British Medical Journal 1979, which concluded that until further research clarified the long-term health hazards of Comfrey ingestion, 'no human being or animal should eat, drink, or take Comfrey in any form.'*

The report by Pembery was subsequently published in 1982 (1983) in which the foreword by Hills revoked the 1978 report, and Comfrey was declared safe. Many post 1982 papers on Comfrey quote the 1978 warning and fail to acknowledge the 1982 revocation."

-'In Defence of Comfrey' by Margaret Whitelegg, MNIMH. Paper presented to 'Department of Health' and 'Ministry of Agriculture, Fisheries and Food', 'National Institute of Medical Herbalists', United Kingdom, January 1993. Published in European Journal of Herbal Medicine, Exeter, England, Volume 1, No. 1, pages 11-17, **1994**.
(* -'Letter from Chicago: Henry Doubleday Research Association', The British Medical Journal, London, England, page 598, March 3 1979.)
(** -The Safety of Comfrey: Report from the Henry Doubleday Research Association by J.A. Pembery B.Sc., Special Advisor, Research Chemist, Aldgate Press: London, England, 20 pages, 1983.)

The following scientific reports are discussed: (in chronological order from older to recent)
1. 'Toxicity of Pyrrolizidine Alkaloids' by Mattocks, **1968**.
2. 'Studies on Constituents of Crude Drugs. I. Alkaloids of Symphytum Officinale Linn.' by Furuya, **1968**.

3. 'An Outbreak of Hepatic Veno-Occlusive Disease in North-Western Afghanistan' by Mohabbat, **1976**.
4. 'Carcinogenic Activity of Symphytum Officinale' by Hirono, **1978**.

5. 'The Alkaloids of Symphytum x uplandicum (Russian Comfrey)' by Culvenor, **1980**.
6. 'Structure and Toxicity of the Alkaloids of Russian Comfrey (Symphytum x uplandicum, Nyman), a Medicinal Herb and Item of Human Diet' by Culvenor, **1980**.
7. 'Toxic Pyrrolizidine Alkaloids in Comfrey' by Mattocks, **1980**.
8. 'Comfrey and Liver Damage' by Roitman, **1981**.
9. 'Mutagenic Effects of Aqueous Extracts of Symphytum Officinale L. and of Its Alkaloidal Fractions' by Furmanowa, **1983**.
10. 'Hepatic Venocclusive Disease Associated with Consumption of Pyrrolizidine Containing Dietary Supplements' by Ridker, **1985**.
11. 'Toxicity of Comfrey-Pepsin Preparations' by Huxtable, **1986**.
12. 'Veno-Occlusive Disease of the Liver Secondary to Ingestion of Comfrey' by Weston, **1987**.
13. 'Comfrey: Assessing the Low-Dose Health Risk' by Abbott, **1988**.
14. 'Hepatic Veno-Occlusive Disease in Newborn Infant of a Woman Drinking Herbal Tea' by Roulet, **1988**.

15. 'Comfrey Herb Tea-Induced Hepatic Veno-Occlusive Disease' by Bach, **1989**.
16. 'Studies on the Effect of an Alkaloid Extract of Symphytum Officinale on Human Lymphocyte Cultures' by Behninger, **1989**.

17. 'Comfrey Herb Tea and Hepatic Veno-Occulusive Disease' by Ridker, **1989**.

18. 'Hepatic Veno-Occlusive Disease Associated with Comfrey Ingestion' by Yeong, **1990**.
19. 'The Effects of Comfrey Derived Pyrrolizidine Alkaloids on Rat Liver' by Yeong, **1991**.
20. 'CPMP Listing of Herbs and Herbal Derivatives Withdrawn for Safety Reasons: Herbal Drugs with Serious Risks' by Committee for Proprietary Medicinal Products, **1992**.
21. 'Hepatic and Pulmonary Complications of Herbal Medicines' by Miskelly, **1992**.
22. 'Hepatocyte Membrane Injury and Bleb Formation Following Low Dose Comfrey Toxicity in Rats' by Yeong, **1993**.
23. 'Determination of Pyrrolizidine Alkaloids in Commercial Comfrey Products (Symphytum sp.)' by Betz, **1994**.
24. 'Medicinal Plants in Europe Containing Pyrrolizidine Alkaloids' by Roeder, **1995**.
25. 'Pyrrolizidine Alkaloids in Human Diet' by Prakash, **1999**.
26. 'Acute Hepatitis After Ingestion of Herbs' by Shad, **1999**.

27. 'Pyrrolizidine Poisoning: A Neglected Area in Human Toxicology' by Stewart, **2001**.
28. 'Systematic Review: Hepatotoxic Events Associated with Herbal Medicinal Products' by Pittler, **2003**.

29. 'Analysis of Herbal Teas Made from the Leaves of Comfrey (Symphytum officinale): Reduction of N-oxides Results in Order of Magnitude Increases in the Measureable Concentration of Pyrrolizidine Alkaloids' by Oberlies, **2004**.
30. 'Mutagenicity of Comfrey (Symphytum Officinale) in Rat Liver' by Mei, **2005**.
31. 'Comparison of Gene Expression Profiles Altered by Comfrey and Riddelliine in Rat Liver' by Guo, Mei, et al., **2007**.
32. 'Bioactive Compounds in Food' by Gilbert, **2008**.
33. 'Severe Pulmonary Hypertension Possibly Due to Pyrrolizidine Alkaloids in Polyphytotherapy' by Gyorika, **2009**.

34. 'Metabolism, Genotoxicity, and Carcinogenicity of Comfrey' by Mei, **2010**.
35. 'Toxicity of Pyrrolizidine Alkaloids to Humans and Ruminants' by Wiedenfeld, **2011**.
36. 'Herbal Hepatotoxicity: A Tabular Compilation of Reported Cases' by Teschke, **2012**.
37. 'Pyrrolizidine Alkaloids in Medicinal Plants from North America' by Roeder, **2015**.
38. 'The Effect of Aqueous Leaf Extract of Symphytum Officinale (Common Comfrey) on the Liver of Adult Wistar Rats' by Ezejindu, **2015**.
39. 'The Comparative Toxicity of a Reduced, Crude Comfrey (Symphytum Officinale) Alkaloid Extract and the Pure, Comfrey-Derived Pyrrolizidine Alkaloids, Lycopsamine and Intermedine in Chicks' by Browna, **2016**.

1. 'Toxicity of Pyrrolizidine Alkaloids' by A.R. Mattocks, Toxicology Research Unit, MRC Laboratories, Carshalton, Surrey, England; Nature: International Journal of Science, Volume 217, pages 723-728, February 24 **1968**.
*"**A new class of metabolite, with a pyrrole-like structure, has been demonstrated in the tissues of animals poisoned by Pyrrolizidine Alkaloids. There is some correlation between the degree of hepato-toxicity and the amount of 'pyrrole' found in the liver.** Evidence has been found of the types of reactions such metabolites might undergo with tissue constituents. Certain Pyrrolizidine Alkaloids, such as heliotrine, lasiocarpine, and retrorsine. have long been known to cause chronic liver poisoning in animals, and the pathology has been well described.*, **
The 'metabolic pyrroles' are partly excreted in urine, but some are also bound strongly to the tissues of the liver and to a decreasing extent, the lungs and other organs for 48 hours or more after being formed.
With the exception of rosmarinine, there is a rough correlation between the hepatotoxicity of the alkaloids and the amounts of pyrroles to which they give rise in vivo.
The following hypothesis is consistent with these results: **The alkaloids themselves are not hepatotoxic. A proportion of the alkaloid (depending on its structure) is metabolized in the liver (by a process amounting to dehydrogenation) to a pyrrole-like derivative."***
(* -'The Action of Retrorsine on Rat's Liver' by James Davidson, Department of Pathology, University of Edinburgh, Scotland; The Journal of Pathology, Volume 40, Issue 2, pages 285-295, March 1935.)
(** -'The Acute Toxic Effects of Heliotrine and Lasiocarpine, and their N-oxides, on the Rat' by L.B. Bull, A.T. Dick and J.S. McKenzie, Division of Animal Health and Production, CSIRO, Animal Health Research Laboratory, Victoria, Australia, The Journal of Pathology, Volume 75, Issue 1, pages 17-25, January 1958.)
(Correlation is a mutual connection between two or more things.)
('In Vitro' means done in laboratory equipment as opposed to in/on a living animal that is called 'in vivo'.)
(This report is one of the first about Pyrrolizidine Alkaloids. Comfrey is not mentioned.)

2. 'Studies on Constituents of Crude Drugs. I. Alkaloids of Symphytum Officinale Linn.' by T. Furuya and K. Araki; Kitasato University, Japan; Chemical and Pharmaceutical Bulletin, Volume 16, No. 12, pages 2512-2516, **1968**.
"Preliminary investigation disclosed that the alkaloids were present mainly in the form of N-oxides. After reduction of the aqueous (water) acid solution of total base, the reduced bases were investigated.
***Two pyrrolizidine alkaloids, symphytine (I), a new compound, and echimidine (II) have been isolated from the dried roots of Symphytum officinale.** Both have a retronecine nucleus esterified on the 7-hydroxyl group with angelic acid.*