Comfrey

Species (Family)

Symphytum officinale L. (Boraginaceae)

Synonym(s)

Consolidae Radix, *Symphytum peregrinum* Ledeb., Symphytum Radix

Related species include Prickly Comfrey (*Symphytum asperum*), Quaker and Russian Comfrey (*Symphytum uplandicum*, hybrid of *S. officinale* × *S. asperum*)

Part(s) Used

Leaf, rhizome, root

Pharmacopoeial and Other Monographs

BHC 1992[G6]
BHP 1996[G9]
Complete German Commission E[G3]
Martindale 32nd edition[G43]
PDR® for Herbal Medicines 2nd edition[G36]

Legal Category (Licensed Products)

GSL (external use only)[G37]

Constituents[G2,G6,G22,G41,G48,G64]

Alkaloids Pyrrolizidine-type. 0.3%. Symphytine, symlandine, echimidine, intermidine, lycopsamine, myoscorpine, acetyllycopsamine, acetylintermidine, lasiocarpine, heliosupine, viridiflorine and echiumine.[1–5]

Carbohydrates Gum (arabinose, glucuronic acid, mannose, rhamnose, xylose); mucilage (glucose, fructose).

Tannins Pyrocatechol-type. 2.4%.

Triterpenes Sitosterol and stigmasterol (phytosterols), steroidal saponins and isobauerenol.

Other constituents Allantoin 0.75–2.55%, caffeic acid, carotene 0.63%, chlorogenic acid, choline, lithospermic acid, rosmarinic acid and silicic acid.

Food Use

Comfrey is occasionally used as an ingredient o soups and salads. It is listed by the Council of Europe as natural source of food flavouring (category N4) This category indicates that although comfrey is permitted for use as a food flavouring, insufficient data are available to assess toxicity.[G16]

Herbal Use

Comfrey is stated to possess vulnerary, cell-proliferant, astringent, antihaemorrhagic and demulcent properties. It has been used for colitis, gastric and duodenal ulcers, haematemesis, and has been applied topically for ulcers, wounds and fractures.[G2,G6,G7,G8,G49,G64]

Dosage

Dried root/rhizome 2–4 g in a decoction three times daily.[G7]

Root, liquid extract 2–4 mL (1:1 in 25% alcohol) three times daily.[G7]

Ointment symphytum root 10–15% root extractive in usual type ointment basis three times daily.[G7]

Dried leaf 2–8 g or by infusion three times daily.[G7]

Leaf, liquid extract 2–8 mL (1:1 in 25% alcohol) three times daily.[G7]

Pharmacological Actions

The classical pharmacology of pyrrolizidine alkaloids is overshadowed by the well-recognised toxicity of this class of compounds. Consequently, the majority of data documented for comfrey involve toxicity. Many useful reviews have been published on the toxicity of pyrrolizidine alkaloids in humans (*see below*).[5–11]

In vitro and animal studies

Wound-healing and analgesic activities have been documented in rats administered comfrey extract orally.[12] Percutaneous absorption of pyrrolizidine alkaloids obtained from comfrey is reported to be low in rats, with minimal conversion of the pyrrol-

izidine alkaloid *N*-oxides to the free pyrrolizidine alkaloids in the urine (reduction of the *N*-oxides is required before they can be metabolised into the reactive pyrrolic esters).[13,14]

Rosmarinic acid has been isolated from comfrey (*S. officinale*) as the main constituent with *in vitro* anti-inflammatory activity.[15] Biological activity was determined by inhibition of malonic dialdehyde formation in human platelets. Minor components, chlorogenic and caffeic acids, were not found to exhibit any significant activity. The pyrrolic esters have been reported to possess mild antimuscarinic activity, which is more pronounced in the non-hepatotoxic esters of saturated amino alcohols.[16] Conversely, the free amino alcohols are reported to exert indirect cholinomimetic action involving the release of acetylcholine from postganglionic sites in the guinea-pig ileum.[16]

Comfrey has been reported to stimulate the activity of the hepatic drug-metabolising enzyme aminopyrine *N*-demethylase in rats.[17]

A comfrey extract has been reported to enhance uterine tone *in vitro*.[18] The action of comfrey was reported to be weaker than that exhibited by German chamomile, calendula and plantain, but stronger than that shown by shepherd's purse, St. John's wort and uva-ursi.

Clinical studies

The antimuscarinic properties of certain pyrrolic esters have been utilised. Two non-hepatotoxic pyrrolizidine alkaloids, sarracine and platyphylline, have been used for the treatment of gastrointestinal hypermotility and peptic ulceration.[16]

Side-effects, Toxicity

Two reports of human hepatotoxicity associated with the ingestion of comfrey have been documented.[19,20] One case involved a 13-year-old boy who had been given a comfrey root preparation in conjunction with acupuncture to treat Crohn's disease.[19] The boy was diagnosed with veno-occlusive disease of the liver and the authors concluded comfrey to be the only possible causal factor of the liver disease. The second case involved a 49-year-old woman diagnosed with veno-occlusive disease.[20] She had been taking various food supplements including a herbal tea and comfrey-pepsin pills. Pyrrolizidine alkaloids were identified in both the tea (stated to contain ginseng) and the comfrey-pepsin pills. The authors estimated that over a period of six months the woman had ingested 85 mg of pyrrolizidine alkaloids, equivalent to 15 µg/kg body weight per day. This report highlighted the potential toxicity associated with chronic ingestion of relatively small amounts of pyrrolizidine alkaloids.

The toxicity of pyrrolizidine alkaloids is well recognised. Pyrrolizidine alkaloids with an unsaturated pyrrolizidine nucleus are metabolised in the liver to toxic pyrrole metabolites.[8] Acute toxicity results in hepatic necrosis, whereas chronic toxicity typically results in veno-occlusive disease characterised by the presence of greatly enlarged liver cells.[8,10]

Reports of human hepatotoxicity associated with pyrrolizidine alkaloid ingestion have been documented.[5,8–10,21–30] Many of these reports have resulted from crop (and subsequently flour and bread) contamination with *Crotalaria*, *Heliotropium* and *Senecio* species and from the use of pyrrolizidine-containing plants in medicinal 'bush' teas. In addition, pyrrolizidine alkaloid poisoning has been associated with the use of herbal teas in Europe and the United States.[20,25–27] The diagnosis of veno-occlusive disease in a newborn infant who subsequently died highlights the susceptibility of the fetus to pyrrolizidine alkaloid toxicity.[30] In this case, the mother had consumed a herbal tea as an expectorant during pregnancy. The tea, which was purchased from a pharmacy in Switzerland, was analysed and found to contain pyrrolizidine alkaloids. The mother did not exhibit any signs of hepatotoxicity.

Interestingly, liver function tests in 29 chronic comfrey users have been reported to show no abnormalities.[31]

The hepatotoxicity of pyrrolizidine alkaloids is well documented in animals.[5] In addition, carcinogenicity has been described in rats fed a diet supplemented with comfrey.[32] The mutagenicity of comfrey has been attributed to lasiocarpine,[23] which is known to be mutagenic and carcinogenic. However, other workers have reported a lack of mutagenic activity for comfrey following assessment using direct bacterial test systems (Ames), host mediated assay (Legator), liver microsomal assay and the micronucleus technique.[33,34]

Contra-indications, Warnings

In view of the hepatotoxic properties documented for the pyrrolizidine alkaloid constituents, comfrey should not be taken internally. The topical application of comfrey-containing preparations to broken skin should be avoided.

Pregnancy and lactation The safety of comfrey has not been established. In view of the toxicity asso-

ciated with the alkaloid constituents, comfrey should not be taken during pregnancy or lactation.

Pharmaceutical Comment

Comfrey is characterised by its pyrrolizidine alkaloid constituents. The hepatotoxicity of these compounds is well known, and cases of human poisoning involving comfrey have been documented. Human hepatotoxicity with pyrrolizidine-containing plants is well documented, particularly following the ingestion of *Crotalaria*, *Heliotropium* and *Senecio* species. Comfrey has traditionally been used topically for treating wounds. Percutaneous absorption of pyrrolizidine alkaloids present in comfrey is reported to be low, although application of comfrey preparations to the broken skin should be avoided.

Licensed herbal products intended for internal use are not permitted to contain comfrey.

The inclusion of comfrey in products intended for topical application is permitted, provided the preparation is only applied to the unbroken skin and that its use is restricted to ten days or less at any one time.

As a result of a report by the Committee on Toxicity of Chemicals in Food to the Food Advisory Committee and the Ministry of Agriculture, Fisheries and Food, the health food trade voluntarily withdrew all products, such as tablets and capsules, and advice was issued that the root and leaves should be labelled with warnings against ingestion. It was considered that comfrey teas contained relatively low levels of pyrrolizidine alkaloids and did not need any warning labels.[35]

References

See also General References G2, G3, G6, G9, G10, G16, G18, G19, G22, G29, G31, G32, G36, G37, G41, G43, G48, G49, G56 and G64.

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