

TOXIC CONSTITUENTS OF SOME INDIAN PLANTS

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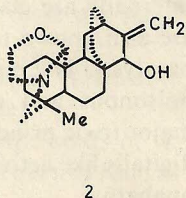
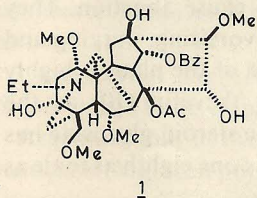
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A TOXIC substance can be classified in one of several ways, according to (i) its physiological manifestations *e.g.* as nerve and muscle poison, (ii) its chemical constitution *e.g.* alkaloid, glycoside or (iii) its botanical origin. It has been estimated that in India there are about 700 poisonous species belonging to over 90 families of flowering plants¹. In this article, which is not comprehensive, we have classified some important poisonous plants found in India, into four categories and surveyed the nature of their toxic principles.

I. PLANTS USED IN MEDICINE OR OF POTENTIAL USE IN MEDICINE

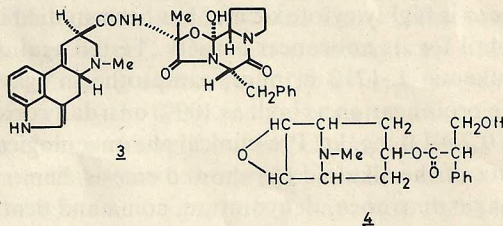
1. *Aconitum balfourii* Stapf. (Garhwal—Banwa), *A. heterophyllum* Wall. (Sanskrit—*Ativisha*) (Fam. Ranunculaceae).

The roots of these plants have been used in the Indian and Chinese systems of medicine as analgesic and anti-inflammatory agents. Plants belonging to the *Aconitum* species have been largely used as arrow poison in different parts of the world. There are 300 species belonging to this genus and more than 20 species are found in the Himalayan region². They owe their toxicity to complex C₁₉ and C₂₀ diterpenoid alkaloids like aconitine (1) and atisine (2), the latter type being less toxic than the former. Aconitine has LD₅₀ in mice at 0.166 mg/kg. The signs of toxicity include loss of muscular control, trembling and ultimately respiratory paralysis. At low doses, 0.01–0.05 mg/kg *i.v.* in cats and rats, aconitine causes bradycardia and hypotension. At higher doses there are positive inotropic and chronotropic effects.



2. *Claviceps purpurea* (Fr.) Tul. (Fam. Hypocreales)

The fungus (ergot) which affects rye and wheat finds use in medicine as vasoconstrictor, especially as an oxytocic and in migraine. The toxic symptoms of ergot are vomiting, diarrhoea, CNS disturbances, mental confusion and gangrene. The toxins are alkaloids containing lysergic acid, dimethylpyruvic acid, proline and phenylalanine joined in amide linkages *e.g.* ergotamine (3) is toxic at LD₅₀ *i.v.* in rat³ 62 mg/kg.

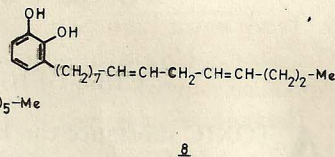
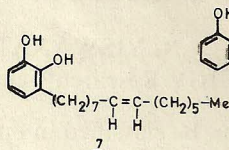
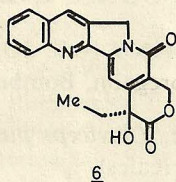
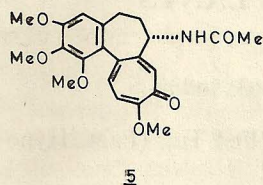


3. *Datura metel* Linn. (Hindi—*Sadah-dhatura*) (Fam. Solanaceae)

The leaves of *D. metel* var. *fastuosa* and *D. stramonium* have been used from ancient times as parasympatholytic agent for relaxation of G.I., biliary and G.U. tracts and the seeds are smoked as a treatment of asthma. Almost no other plant has such a history of crime as datura and the seeds are the favourite poisons used for this purpose. The clinical symptoms of poisoning due to datura are thirst, visual disturbance, flushed skin, convulsions, coma and death. The toxic ingredients are the tropane alkaloids—atropine, hyoscyamine and scopolamine (4).

4. *Gloriosa superba* Linn. (Hindi—*Kalihari*; Sanskrit—*Shakrapushpi*) (Fam. Liliaceae)

The roots have been used to bring about abortion. Colchicine (5), the major alkaloid of the plant, is used for the treatment of gout, for the treatment of mammary tumours and is a research tool used in plant genetics. The signs of poisoning are numbness, nausea, convulsions and inflammation of gastric mucous membrane.



5. *Mapeea foetida* Miers (Fam. Olacaceae)

This is a small tree abundant in the Western Ghats and has no reputation of being a poisonous plant. During a widespread phytochemical screening of plants for biological activity, the stem of *M. foetida* was found to contain a high yield (0.1%) of the rare alkaloid camptothecin⁴ (6). The alkaloid found earlier in trace amounts (0.005%) in the Chinese tree *Camptotheca acuminata* is highly cytotoxic and has been studied in detail for its anticancer activity. Tested against leukemia L-1210 in mice, camptothecin⁵ gave life prolongation as high as 100% on a daily dose of 0.25–1.0 mg/kg. Pre-clinical pharmacological data of the alkaloid (6) showed emesis, hemorrhagic diarrhoea, dehydration, coma and death in the monkey and dog. In mice and rats oral administration was more toxic⁶ than *i.v.* injection. It is surprising that the toxicity data have not affected the extensive clinical use of (6) in the People's Republic of China⁷.

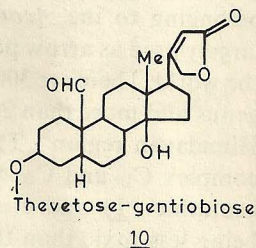
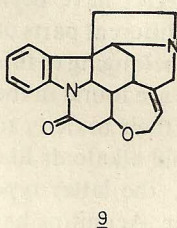
Although several syntheses of camptothecin have been published, none appears to be suitable for its preparation in large amounts and if interest in it is revived, *M. foetida* should be an excellent source for its isolation.

6. *Semecarpus anacardium* Linn. (Hindi—*Bhilawa*; Marathi—*Bibba*) (Fam. Anacardiaceae)

The oil from the nuts is widely used in Ayurvedic medicine both internally and externally as an anti-inflammatory agent and in the treatment of leprosy nodules. There have been recent reports of its use as an anticancer drug. The crude oil shows hypotensive activity at 5 mg/kg *i.v.* and anti-inflammatory activity at 100 mg/kg *p.o.* in rats. The oil obtained from the seed pericarp is highly vesicant and contains the catechols (7) and (8) which are also constituents of poison ivy⁸.

7. *Strychnos nux vomica* Linn. (Hindi—*Kuchla*; Sanskrit—*Visha-mushti*) (Fam. Loganiaceae)

This evergreen tree native to India, grows to a height of about 12 metres, has glossy leaves, small yellowish flowers and orange coloured fruit. Its seeds contain a highly toxic, bitter alkaloid strychnine (9), whose structure had baffled organic chemists for decades. On ingestion, strychnine causes violent death. Severe symptoms begin to appear within 10 to 30 minutes, the muscles begin to twitch, muscular spasms occur and the person falls in a violent convulsion. Strychnine is lethal in rats at 5 mg/kg orally. The alkaloid has been used as a stimulant in very small doses, and as an antidote for depressant drug poisoning and as an ingredient in tonic preparations.

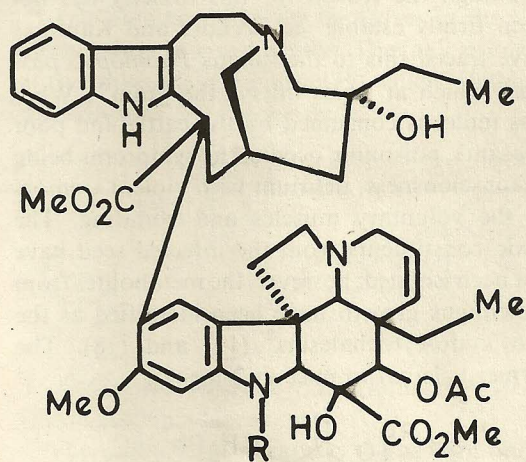


8. *Thevetia nerifolia* Juss. Syn. *T. peruviana* (Pers.) Schum (Hindi—*Pila-kaner*) (Fam. Apocynaceae)

A native of South America and West Indies, this plant is now naturalised in India. The seeds have been used in arrow-poisons and when taken internally are claimed to cause abortion. They are also known to cause vomiting, purging and paralysis. The milky juice of the plant is highly poisonous and contains thevetin (10) as the major toxic principle. The steroid glycoside has digitalis like activity and is one eighth as toxic as ouabain.

9. *Vinca rosea* Linn. Syn. *Catharanthus roseus* G. Don. (Marathi—*Sada-Phuli*) (Fam. Apocynaceae).

The reputation of the leaves of this plant (Periwinkle) as an oral hypoglycaemic agent led to extensive studies resulting in the isolation of some 75 alkaloids⁹. Of these, the dimeric alkaloids vinblastine (11) and vincristine (12) are currently prescribed in cancer chemotherapy. The major toxic effects of these drugs are leukopenia, nausea and anorexia. Vinblastine has LD₅₀ *i.v.* in mice 17 mg/kg whereas vincristine has 2 mg/kg. These compounds are especially useful in the treatment of Hodgkin's disease and leukemia.



11 R = Me

12 R = CHO

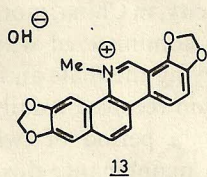
II. EDIBLE PLANTS AND THOSE USED AS ADULTERANTS IN FOODS

There are many plants which are used for edible purposes that contain some toxic constituents. In addition, very often, plants are used to adulterate foods and some of these are listed below.

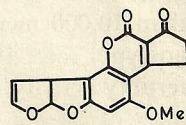
1. *Argemone mexicana* Linn. (Hindi—*Shialkanta*) (Fam. Papaveraceae)

Argemone oil, derived from the seeds of *A. mexicana* (Mexican poppy) is frequently found as an adulterant of ground nut, sesame or mustard

oil. The toxic principle has been identified to be the alkaloid sanguinarine (13) which interferes with the carbohydrate metabolism and causes circulatory failure¹⁰. Chronic consumption of such adulterated oil leads to epidemic dropsy, liver enlargement and pulmonary congestion.



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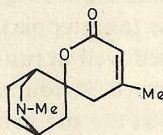
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2. *Aspergillus flavus* Link ex. Fries

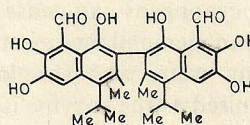
Aflatoxins are a group of toxic metabolites of the fungus *Aspergillus flavus* Link ex. Fries and *A. parasiticus*¹¹. These furocoumarins are often found in ground nuts (*Arachis hypogaea*) infected by the fungi and the toxic substance can be eliminated only by autoclaving or alkaline treatment. Aflatoxins are hepatotoxic and their toxicity and carcinogenicity may result due to its ability to bind DNA. Aflatoxin B₁ (14), a typical member of this class, has LD₅₀ 18.2 μg per 50 g of body weight orally in day old ducklings.

3. *Dioscorea hispida* Dennst. Syn. *D. hirsuta* Dennst. *D. triphylla* Linn. (Hindi—*Karukandu*) (Fam. Dioscoreaceae)

The tubers of *Dioscorea* sp. are frequently eaten by the tribal people in times of food scarcity. The country brew 'Khopadi' prepared from the tubers of *D. hispida* has been of the source of much tragedy¹². It causes burning of mouth, nausea, vomiting, drowsiness, tachycardia, coma, respiratory depression and even death. Victims complain of intense thirst and burning. The tuber sometimes placed inside the carcasses of mauled animals to poison tigers and hence the tuber is known in vernacular as 'Wagh kand'. The toxic substance is the spiro alkaloid dioscorine (15) whose LD₅₀ *i.p.* in mice is 120 mg/kg¹³.



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4. *Gossypium* sp. (Hindi—*Kapas*) (Fam. Malvaceae)

Unrefined cotton seed oil contains a yellow pigment named gossypol (16). It is toxic and irritates the G.I. tract and in experimental animals causes pulmonary edema, shortness of breath and paralysis. Its reported LD₅₀ in rat is 2.57 g/kg p.o. In spite of this toxicity, in China, more than 10,000 men have been administered with gossypol since 1972 for studying the male anti-fertility activity¹⁴. Each person received a daily dose of 20 mg gossypol for a period of two months, and subsequently a maintenance dose of 75–100 mg taken twice monthly. Gossypol has been shown to inhibit lactate dehydrogenase found in sperm and testicular cells¹⁵.

5. *Lathyrus sativus* Linn. (Hindi—*Khesari*) (Fam. Leguminosae)

Lathyrism or paralysis of the lower limbs caused by the lentils of *L. sativus* continues to be a public health problem in India. The crippling disease affects the poorer section of the people who consume 'Khesari dal' and also feed their live stock in days of food scarcity. Neurolathyrism is characterised by muscular rigidity and paralysis of leg muscles. Osteolathyrism affects the spine and causes curvature of the long bones. The toxins^{16,17} are β -aminopropionitrile, β -cyanoalanine, 2,4-diaminobutyric acid and 3-N-oxalyl-2,3-diaminopropionic acid. The toxins are almost completely removed by steeping the dehusked seeds in hot water, but in the process, the B-vitamins are also lost.

6. *Manihot esculenta* Crantz (Hindi—*Sakarkanda*, Malayalam—*Marakoli*, *Kappa*) (Fam. Euphorbiaceae)

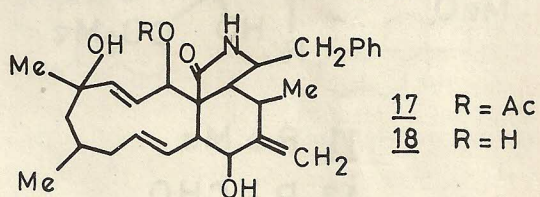
The tubers of this plant (tapioca) form a part of the daily diet of many Indians. However, the tubers cannot be stored for long periods as these turn to a bluish colour and contain cyanogenic glycosides¹⁸. Repeated intakes of sublethal doses of cyanogens can cause blindness (amblyopia). Cyanogenic plants must be washed well in running water and should be rejected if found bruised as the enzyme is released at the site and hydrogen cyanide gets accumulated.

7. *Myristica fragrans* Houtt (Hindi—*Jaiphal*) (Fam. Myristicaceae)

Nutmeg is used as a flavouring agent but ingestion of 5–15 g can cause intoxication with giddiness, vertigo, nausea and a feeling of congestion in chest and abdomen. Delirium and stupor persist for 6–12 hr, followed by heavy sleep. Sometimes a person becomes terrified of impending doom or death¹⁹. Myristicin present in nutmeg may be aminated in the body to give an amphetamine-like psychotropic compound.

8. *Paspalum scrobiculatum* Linn. (Hindi—*Kodo*, *Harik*) (Fam. Graminae)

The millet of *P. scrobiculatum* sometimes develops toxicity due to an odd rainfall. Although the reason for this toxicity has not been firmly established, Pendse and Kanitkar have traced this to the fungus *Phomopsis paspalli* which at times infects the grain²⁰. When this millet is consumed by the cattle and poor peasants, poisoning occurs, the symptoms being unconsciousness, delirium with violent tremors of the voluntary muscles and vomiting. The toxic constituents from the infected seed have not been isolated; however, the metabolites from the fungus growth have been identified as the two kodo-cytochalesins² (17) and (18). The former is lethal to mice at 2 mg/kg.



III. TOXIC PLANTS

There are many plants which have no medicinal value and are not used for edible purpose but which are at times ingested through oversight, particularly by children. Many of these are responsible for poisoning of cattle. Some of the plants under this heading have been used for poisoning purposes and for committing suicide.

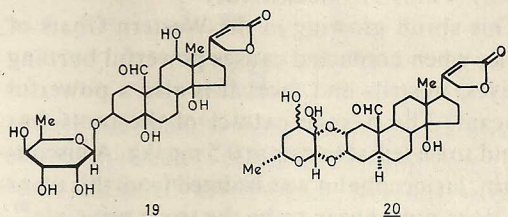
1. *Abrus precatorius* Linn. (Hindi—*Ghungchi*) (Fam. Leguminosae)

In small doses, the seeds of *A. precatorius*

(*Gunj*) which are bright red with black tip are purgative and emetic. In large doses they are used for poisoning cattle and for producing abortion. The toxic symptoms include nausea, diarrhoea, drowsiness, disorientation, stupor and circulatory collapse. Abrin, the toxic principle, is a glycoprotein of molecular weight about 65,000, having LD_{50} i.p. in mice 0.02 mg/kg. The lethal dose for humans is about 0.5 mg. It has strong haemagglutinating property. Abrin is more toxic to malignant than to normal cells and inhibits protein synthesis²²

2. *Antiaris toxicaria* (Pers.) Lesch. (Sanskrit—*Valkala*) (Fam. Moraceae)

The latex derived from the leaves or the bark of the tree is an arrow poison. The toxic principle is the glycoside α -antiarin (19) which is lethal to animals at 0.116 mg/kg i.v.²³



3. *Calotropis gigantea* Linn (Sanskrit—*Arka*) (Fam. Asclepiadaceae)

The milky juice is caustic to the skin and is dangerous to the eyes, causing keratoconjunctivitis. Many mendicants blind themselves with the latex. The steroidal glycoside, calotropin (20) isolated from this plant²⁴ is lethal at 0.12 mg/kg.

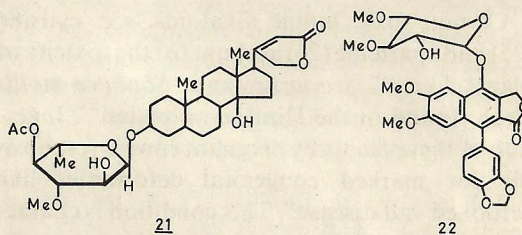
4. *Cerbera odollum* Gaertn. Syn. *C. manghas* Linn. (Marathi—*Sukanu*; Tamil—*Kattarali*) (Fam. Apocynaceae)

The kernel of the fruit is used to commit suicide²⁵. The seeds contain the steroidal glycosides cerberin (21) and cerberoside, the latter being present in *Thevetia neriiifolia* also. The latex causes blindness if it gets into the eyes.

5. *Cleistanthus collinus* Benth. & Hook. f. (Hindi—*Garari*; Tamil—*odaichi*) (Fam. Euphorbiaceae)

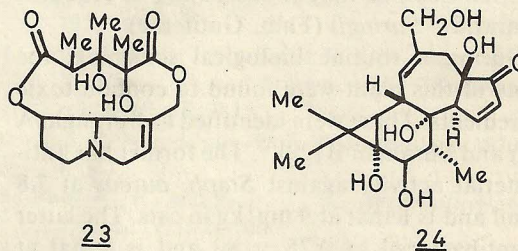
The leaves of this plant have been known to be

used for homicidal and suicidal purposes. The toxic constituent has been identified as a lignan lactone cleistanthin²⁶ (22). It is lethal to cats and dogs at 0.5 mg/kg i.v. and causes cardiac slowing. It has a pronounced effect on the bone marrow, increasing the neutrophilic granulocytic count in experimental animals^{27,28}



6. *Crotalaria* sp. (Fam. Leguminosae)

There are a large number of species belonging to this genus found in India. Almost all of these and the *Senecio* sp. contain pyrrolizidine alkaloids which are found to be hepatotoxic. *C. juncea* Linn. (Hindi—*Sunn*) the Indian hemp, is cultivated for its stem fibre. *C. spectabilis*, (Hindi—*Jhunjhunia*) common throughout India, contains 3.2% of the toxic alkaloid monocrotaline^{29,30} (23). It is lethal to chicken at 65 mg/kg. These plants are toxic to cattle and cause teratogenic defects, particularly malformations of the ribs and palate. Poisoning from these plants is not a serious problem in India, but in Northern Australia, they are responsible for the "walk-about syndrome" observed in horses; the horses begin to stagger and roar before ultimate death.



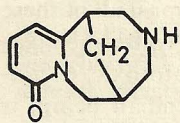
7. *Croton tiglium* Linn. (Hindi—*Jamalgota*) (Euphorbiaceae)

The croton seed oil is an irritant and a violent

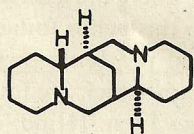
purgative³¹. It contains several cocarcinogens, being esters of the diterpene phorbol (24). Saha³² has reported that the roots of *C. tiglium* are used as abortifacient.

8. *Cytisus scoparius* Link (Yellow broom) (Fam. Leguminosae)

Certain toxic lupine alkaloids, e.g. cytisine (25) and sparteine (26) account for the toxicity of plants like *C. scoparius* and *Sophora mollis* Grah. found in the Himalayan region³³. Ingestion of these plants by pregnant cows is responsible for marked congenital deformities like "crooked calf disease". This condition is characterised by fornicollis and scoliosis (lateral curvature of the spine).



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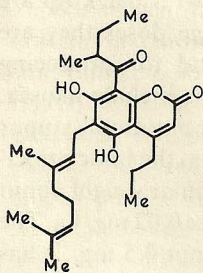
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9. *Dieffenbachia* sp. (Fam. Araceae)

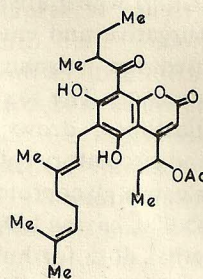
These are ornamental plants, used in arrow poison in the Amazon. Ingestion of the stem causes irritation of the throat, choking and even death³⁴. The toxic constituents have not been identified but are likely to be proteolytic enzymes or cyanogenic glycosides.

10. *Ochrocarpus longifolius* Benth. & Hook. f. (Marathi—*Suringi*) (Fam. Gutiferae)

During a routine biological screening, the roots of this plant were found to contain toxic ingredients. These were identified as Surangin A (27) and Surangin B (28)³⁵. The former has antibacterial activity against *Staph. aureus* at 7.8 γ /ml and is lethal at 9 mg/kg in cats. The latter is antibacterial at 0.25 γ /ml and is lethal at 1 mg/kg. Surangin B has insecticidal activity, especially mosquito larvae and houseflies. The activity is ascribed to its being an uncoupler of oxidative phosphorylation³⁶.



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IV. ALLERGENS

A very large number of plants are known to cause allergic contact dermatitis or allergic skin reaction³⁷. Three of such plants are discussed below.

1. *Lasiosiphon eriocephalus* Dcne (Marathi—*Rami*) (Fam. Thymelacaceae)

This shrub growing in the Western Ghats of India, when contacted causes powerful burning of eyes, nostrils and face. It is also a powerful vesicant. The hexane extract of the roots was found to be lethal to cats at 0.5 mg/kg. A biscoumarin, lasiocephalin was isolated from this plant but does not appear to be the toxic principle³⁸. The toxic constituents are probably diterpenoids of the daphnetoxin group.

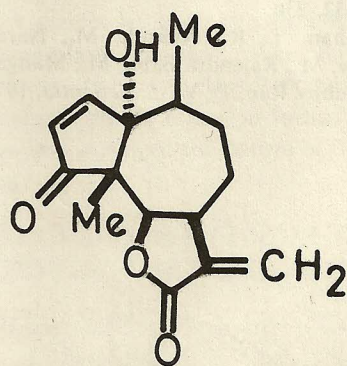
2. *Mucuna prurita* Hook. (Hindi—*Kawanch*; Sanskrit—*Atmagupta*) (Fam. Leguminosae)

The hair on the outer cover of the pods are extremely irritant to the skin and to the intestinal tract. The active pruritogenic principle is a proteolytic enzyme, mucunin³⁷.

3. *Parthenium hysterophorus* Linn. (Fam. Compositae)

American wheat imported in India in the 1950s brought along with it the seeds of the rag-weed *P. hysterophorus* and has been the cause of serious outbreaks of eczema in many parts of the country³⁹. The allergen is the sesquiterpene lactone parthenin (29). Scanning electron microscopy of the leaf surface showed the presence of 4 types of glandular and non-glandular trichomes⁴⁰. Chemical analysis established the

presence of sesquiterpene lactones in the trichomes that cause eczematous dermatitis. Calves fed on this weed develop itching and diarrhoea and die within 8–30 days. Severe ulcerations were noticed in the liver, G.I. tract and kidney⁴¹. *P. hysterophorus* poses a danger to livestock, particularly under drought conditions.



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There are literally hundreds of plants which could be included in such a list as being toxic; the plants discussed above relate to some recent work as well as the already well established toxic plants. A large amount of chemical and toxicological information has become available in recent years on poisonous plants and this has greatly increased our knowledge of the active principles involved.

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