

PLANT SOURCES OF HEPATOTOXIC PYRROLIZIDINE ALKALOIDS

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There is increasing recognition that the hepatotoxic pyrrolizidine alkaloids may be of greater importance as a cause of human disease than the presently known outbreaks of poisoning would indicate. The chronic and progressive character of their effects, including carcinogenicity, (1, 2) means that in the type of hazard they present, they resemble the mycotoxins rather than the main body of alkaloids. Disease is likely to be induced in man or animals by their ingestion over long periods of time in plants or foods in which they are present at low concentrations. In the interests of public health, present knowledge of plant species containing hepatotoxic pyrrolizidine alkaloids should be diffused as widely as possible and brought particularly to the people who are most at risk. The purpose of this compilation of plant sources is to make the information more readily available to the health-oriented investigators and educators who have this task.

Plants containing pyrrolizidine alkaloids are so numerous and widespread that they can be expected to be present in most environments. The main sources are the families Boraginaceae (all genera), Compositae (tribes Senecioneae and Eupatorieae) and Leguminosae (genus *Crotalaria*), the potential number of alkaloid-containing species being as high as 6000, or 3% of the world's flowering plants (3). There have now been several reported outbreaks and occurrences of human poisoning due to these alkaloids, the largest involving more than 2000 people in Afghanistan (4-12). In these instances, the causative plants were ingested as medicinal herbs or as weed contaminants of cereal grains. The plants found to be responsible by investigators were not suspected of toxicity by the populations or individuals affected.

The early warnings by Schoental (13, 14) about the hazard of pyrrolizidine alkaloids in medicinal herbs were probably overshadowed to a large extent by the discovery of the greater and more ubiquitous hazard of the mycotoxins. However, despite advances in medicine, herbs have remained in use without systematic testing for efficacy or safety even in technically advanced countries. Several such herbs have recently been reported to contain hepatotoxic pyrrolizidine alkaloids, e.g., comfrey (*Symphytum officinale* (15, 16), Russian comfrey (*S. x uplandicum*), (17), coltsfoot (*Tussilago farfara*) (18) and petasites (*Petasites japonicus* Maxim) (19, 20). The recognition of two fatalities in the USA due to consumption of *Senecio longilobus* as a medicinal herb has led to concern about the extent of use of this herb in Mexican American communities in the USA (21). Still greater human exposure is to be expected in developing countries where traditional herbal medicines remain in substantial use and may be officially recognized as necessary for a satisfactory level of health care (22).

The increasing concern about contamination of foodstuffs with pyrrolizidine alkaloids stems from the experimental findings that at the lowest levels so far administered to animals, approximately 1-4 ppm of whole diet, chronic liver damage and tumors have been observed (23, 24). The alkaloids of *Senecio jacobaea* have been found at the level of 1-4 ppm in milk (25) and honey (26) from cows and bees which had been foraging on this species. Some species of

TABLE 1. Plants containing hepatotoxic pyrrolizidine alkaloids.

Plant	Constituent Alkaloids	Plant Part	Ref.
APOCYNACEAE			
<i>Parsonsia eucalyptophylla</i> (F. Muell.)	lycopsamine	ae	28
<i>P. heterophylla</i> A. Cunn.	parsonsine	wh	417
	heterophylline	wh	418
<i>P. spiralis</i> Wall.	spiraline	lf	418
	spiranine		
	spiracine		
<i>P. straminea</i> ((R. Br.) F. Muell.)	lycopsamine	ae	28
<i>Urechites karwinskyi</i>	loroquin	rt	29
BORAGINACEAE			
<i>Amsinckia hispida</i> (Ruiz et Pav.) I. M. Johnston	intermedine	wh	30
	lycopsamine		
	echiumine		
<i>A. intermedia</i> Fisch et C. Mey.	intermedine	wh	30
	lycopsamine		
	echiumine		
<i>A. lycopsoides</i> Lehm.	sincamidine	wh	30
	intermedine		
	lycopsamine		
	echiumine		
<i>Anchusa arvensis</i> (L.) Bieb.	echinatine (or diastereoisomer)	wh	31
<i>A. officinalis</i> L.	lycopsamine	wh	32
	7-acetyllycopsamine (or diastereoisomer)		31
<i>Asperugo procumbens</i> L.	amabiline (or diastereoisomer)	wh	31
<i>Cynoglossum amabile</i> Stapf & Drummond	amabiline	wh	33, 34
	echinatine		
	7-acetylechinatine	wh	35
<i>C. australe</i> R. Br.	cynaustine	wh	33
	cynaustraline		
<i>C. creticum</i>	echinatine	ae	419
	heliosupine		
<i>C. glochidiatum</i> Wall. ex Lindl.	amabiline	wh	36
<i>C. lanceolatum</i> Forsk.	cynaustraline	wh	36
	cynaustine		
<i>C. latifolium</i> R. Br.	latifoline	ae	37
	7-angelylretronecine		
<i>C. officinale</i> L.	heliosupine	ae	38, 39, 40
	echinatine	rt, ae	41, 42
	acetylheliosupine	ae	43
	7-angelylheliotridine		
<i>C. pictum</i> Ait.	heliosupine	rt, ae	44, 45
	echinatine		
	pictumine	ae	46
<i>C. viridiflorum</i> Pallas ex Lehm.	viridiflorine	rt	47
	heliosupine		34
<i>Echium italicum</i> L.	echimidine	wh	35
<i>E. plantagineum</i> L. (<i>E. lycopsis</i> L.)	echiumine	ae	48
	echimidine		
<i>E. vulgare</i> L.	heliosupine	ae	49
	asperumine	ae	50
	lycopsamine (or diastereoisomer)	wh	31
<i>Heliotropium acutiflorum</i>	heliotrine	ae	51
<i>H. amplexicaule</i> Vahl	indicine	ae	35
<i>H. arbainense</i>	europine	ae	419
	lasiocarpine		
	heliotrine		
<i>H. arborescens</i> L. (<i>H. peruvianum</i> L.)	lasiocarpine	ae	52

TABLE 1. Continued.

Plant	Constituent Alkaloids	Plant Part	Ref.
<i>H. arguzioides</i> Kar. et Kir.....	heliotrine	ae	53
<i>H. curassavicum</i> Linn.....	trichodesmine	ae, rt	54, 55
	heliotrine	wp	56
<i>H. dasycarpum</i> Ledeb.....	lasiocarpine		
	angelylheliotridine		
	curassavine	ae	57
	coromandaline		
	heliovicine		
	trachelanthamidine	ae	58
<i>H. eichwaldi</i> Steud. ex DC.....	heliotrine	ae, rt	54
	sd		59
	wh		60, 61
	ae		62
<i>H. europaeum</i> L.....	7-angelylheliotrine	ae	63
	heliotrine	wh	64, 65
	lasiocarpine		
	europine		66, 67
	supinine		
	heleurine		
<i>H. indicum</i> L.....	N-(dihydropyrrolizino- methyl)-heliotrine	wh	68
	chloride		
	acetylasiocarpine	wh	69
	indicine	ae	70
	acetylindicine	ae	71
	indicine		
	echinatine	ae	72
	supinine		
	heleurine		
	lasiocarpine		
<i>H. lasiocarpum</i> Fisch. et Mey.....	heliotrine	ae	73
	lasiocarpine		
<i>H. maris mortui</i>	europine	ae	74
	lasiocarpine	ae	419
<i>H. olgae</i>	heliotrine	ae, rt	75
	incanine		76
<i>H. popovii</i> H. Riedl. subsp. <i>gillianum</i> H. Riedl.....	heliotrine	sd	77
<i>H. ramosissimum</i> (syn. <i>H. persicum</i> L., <i>H. undulatum</i> , <i>H. bacciferum</i>).....	heliotrine	ae	78, 79
<i>H. rotundifolium</i>	europine	ae	74
<i>H. steudneri</i> Vatke.....	lycopsamine	lf	80
<i>H. supinum</i> L.....	supinine	rt	81
	heliosupine	rt	82
	echinatine	wh	83
	7-angelylheliotridine		
	trachelanthic and viridifloric esters of 7-angelylheliotridine		
<i>H. transoxanum</i>	heliotrine	ae	51
<i>Lappula glochidiata</i>	echinatine	ae	84
<i>L. intermedia</i>	lasiocarpine	ae	85
<i>Lindelofia angustifolia</i> (Schrenk) Brand.....	echinatine	ae	62, 36
	amabiline		
<i>L. spectabilis</i> Lehm.....	echinatine	ae	62, 63
	7-acetylechinatine		
<i>L. stylosa</i> (Kar. et Kir.) Brand.....	monocrotaline		
	viridiflorine	ae	86
	echinatine	sd	75
	lindelofine		

TABLE 1. Continued.

Plant	Constituent Alkaloids	Plant Part	Ref.
<i>L. tschimganica</i>	carategine echinatine viridiflorine	ae	87
<i>Myosotis sylvatica</i> Hoffm.....	viridiflorine 9-angelylretronecine heliosupine acetylheliosupine	wh	35
<i>Paracynoglossum imeritinum</i> Kusn. M. Pop.....	heliosupine echinatine	ae, rt	88 89, 90
<i>Rindera austroechinata</i> M. Pop.....	echinatine	lf, st, sd, rt	87
<i>R. baldschuanica</i> Kusnezov.....	rinderine echinatine trachelanthamine turkestanine	ae ae ae	91 87
<i>R. cyclodonta</i> Bge.....	echinatine	ae	59
<i>R. echinata</i> Regel.....	echinatine trachelanthamine	ae ae	92 59
<i>R. oblongifolia</i> M. Pop.....	carategine echinatine turkestanine	ae	87
<i>Solenanhus circinnatus</i> Ledeb.....	echinatine	sd, ae, rt	93
<i>S. coronatus</i>	echinatine	ae	75
<i>S. karategenius</i> Lipsky.....	carategine echinatine	ae	93
<i>S. turkestanicus</i> Regel et Smirnov.....	rinderine turkestanine	ae	94
<i>Symphytum asperum</i> Lepech.....	asperumine echinatine heliosupine	ae, rt ae, rt	95, 96 97
	7-acetyllycopsamine (or diastereoisomer) acetylechimidine (or diastereoisomer)	wh	31
<i>S. caucasicum</i>	lasiocarpine asperumine echinatine echimidine	ae, rt ae, rt	95 98, 99
<i>S. officinale</i>	symphytine echimidine lasiocarpine heliosupine viridiflorine echinatine	rt ae, rt ae, rt rt rt	15, 16 100 95 101
	7-acetyllycopsamine (or diastereoisomer) 7-angelylretronecine viridiflorate (or diastereoisomer) acetylechimidine (or diastereoisomer)	wh	31
<i>S. orientale</i>	anadoline symphytine echimidine	wh	102, 103, 104
<i>S. tuberosum</i>	echimidine anadoline	wh	105
<i>S. x uplandicum</i> Nyman.....	symphytine symlandine echimidine 7-acetyllycopsamine 7-acetylintermediate uplandicine lycopsamine intermediate	ae	31, 17, 106

TABLE 1. Continued.

Plant	Constituent Alkaloids	Plant Part	Ref.
<i>Tournefortia sarmentosa</i> Lam.....	supinine	lf, st	107
<i>Trichodesma africana</i>	europine	wh	419
<i>T. incanum</i> Alph. DC.....	intermediate		
	trichodesmine	ae	108, 109
	incanine	sd, ae, rt	110, 111, 112
<i>T. zeylanicum</i> (Burm. f.) R. Br.....	supinine	sd	113
<i>Ulegbekia tschimganica</i> (B. Fedtsch.) Zak.....	uluganine		114
COMPOSITAE			
<i>Adenostyles alliariae</i>	platyphylline seneciophylline	rt	115
^a <i>Adenostyles rhombifolia</i> (Willd.) M. Pimen. ssp. <i>platyphyloides</i>	platyphylline seneciophylline	ae	116
<i>Brachyglottis repanda</i> Forst. et Forst.....	senecionine senkirkine	ae	117
<i>Cacalia floridana</i>	brachyglottine		118
	otosenine	ae	119
	floresenine		
	floridanine		
	floricaline		
<i>C. hastata</i> L. subsp. <i>orientalis</i> Kitamura.....	integerrimine	rt	120
<i>C. yatabei</i> Maxim.....	yamataimine	rt	121
<i>Doronicum macrophyllum</i>	otosenine	rt	122
	floridanine		
	doronine		
<i>Emilia flammea</i> Cass.....	otosenine	ae, rt	123, 124, 125
	emiline		
<i>E. sonchifolia</i> DC.....	senecionine	ae	35
<i>Erechtites hieracifolia</i> (L.) Raf. ex DC.....	senecionine seneciophylline	ae	126, 127
<i>E. quadridentata</i> (see <i>Senecio</i> <i>quadridentatus</i> Labill.)			
<i>Eupatorium cannabinum</i> L.....	echinatine	ae	128
	supinine		
<i>E. maculatum</i> L.....	echinatine	rt	129
	trachelanthamide		
<i>E. purpureum</i>	probably echinatine	ae	130
<i>E. serotinum</i> Michx.....	supinine	ae	131
	rinderine		
<i>E. stoechadosmum</i> Hance.....	lindelofine	rt	132
	supinine		
<i>Farfugium japonicum</i>	senkirkine	rt, lf	133
<i>Ligularia brachyphylla</i> Hand-Mazz.....	clivorine	ae	134
	ligularine		
	ligudentine		
<i>L. clivorum</i>	clivorine	ae	135, 136, 137, 138
<i>L. dentata</i> (A. Gray) Hara.....	clivorine	ae	134
	ligularine		
	ligudentine		
	ligularidine	rt, ae	436

^aPimenov *et al.* (116) have given the name *Adenostyles rhombifolius* to the species which have previously been known as *Senecio platyphyllus*, *S. platyphyloides*, and *S. rhombifolius* (251, 208). They have divided the species into two subspecies, one of which is further divided into two chemovariants, each with different alkaloidal content. Since plant material examined in earlier publications cannot be related to the classification of Pimenov *et al.*, each alkaloidal isolation is listed under the species name by which it was originally published.

TABLE 1. Continued.

Plant	Constituent Alkaloids	Plant Part	Ref.
<i>L. elegans</i> (Cass.) (syn <i>L. macrophylla</i> (Ledeb. DC.)).....	clivorine ligularine ligudentine	ae	134
<i>Nardosmia laevigata</i> (Willd.) DC. (see <i>Petasites laevigatus</i> (Willd.) Reichenb.)			
<i>Petasites hybridus</i> (L.) P. Gaertn. <i>et al.</i>	senecionine	lf	35
<i>P. japonicus</i> Maxim.....	fukinotoxin (petasitenine) neopetasitenine	ae	20, 19, 139
	senkirkine	st	140
	petasinine	ae	141
	petasinoside		
<i>P. laevigatus</i> (Willd.) Reichenb.....	platyphylline	ae	142
	senkirkine (renardine)	ae	143, 144
<i>Senecio aegypticus</i> L.....	senecionine	wh	145, 146
	senecionine		
	otosenine		
	riddelliine		
<i>S. alpinus</i> (L.) Scop.....	seneciphylline	ae	147
	jacozine		
<i>S. ambrosioides</i>	seneciphylline	wh	148
	senecionine		
	retrorsine		
	riddelliine		420
<i>S. ampullaceus</i> Hook.....	senecionine	wh	149, 150, 151
	seneciphylline		
	retrorsine		
<i>S. antiuephorbium</i> (L.) Sch. Bip.....	integerrimine	ae	152
	senkirkine		
	senaetnin	ae	421
	isosenaetnin		
<i>S. aquaticus</i> Hill.....	seneciphylline	ae	153, 154
<i>S. aureus</i> L.....	senecionine	ae	155, 156
<i>S. auricola</i> Bourg.....	neosenkirkine	ae	157
<i>S. bipinnatisectus</i> Belcher.....	retrorsine	ae, rt	158
<i>S. borysthenticus</i>	seneciphylline	ae, rt	159, 160
<i>S. brasiliensis</i> DC.....	senecionine	lf	161, 162
	seniciphylline		148, 163
	jacobine		
	integerrimine	ae	
	retrorsine		
<i>S. bupleuroides</i> DC.....	retrorsine	ae	164
<i>S. cannabifolius</i> Less.....	seneciphylline	ae	165
<i>S. carthamoides</i> Greene.....	senecionine	wh	149, 151
	seneciphylline		
<i>S. chrysanthemoides</i>	seneciphylline		166
<i>S. cineraria</i> DC.....	jacobine	ae	153, 167
	senecionine	sd	168
	seneciphylline	ae	169
	otosenine	ae	170
	retrorsine	ae	171
<i>S. cruentus</i> DC.....	cruentine A		172
	cruentine B		
<i>S. cymbalarioides</i>	senecionine		420
<i>S. desfontainei</i> Druce.....	senecionine	ae	173, 145
	otosenine		
	riddelliine		
	seneciphylline	ae	146
<i>S. discolor</i> DC.....	retrorsine	lf	174
	senecionine	ae	175
<i>S. doronicum</i> L.....	doronine	wh	176
	bulgarsenine		

TABLE 1. Continued.

Plant	Constituent Alkaloids	Plant Part	Ref.
<i>S. douglasii</i> DC.....	retrorsine riddelliine seneciphylline senecionine	wh	149, 150, 151
<i>S. durieui</i> Gay.....	integerrimine	wh	157
<i>S. eremophilus</i> Richards.....	senecionine seneciphylline retrorsine riddelliine	wh	149, 150, 151
<i>S. erraticus</i> Berthol.....	senecionine otosenine floridanine	ae	177
<i>S. erraticus</i> Berthol. subsp. <i>barbaraeifolius</i> Krock.....	senecionine otosenine erucifoline seneciphylline	ae	178, 179, 180
<i>S. erucifolius</i> L.....	integerrimine senecionine seneciphylline erucifoline (base S-C)	lf ae ae ae	181 182 153 183, 180
<i>S. fluviatilis</i> Wallr.....	retrorsine seneciphylline otosenine	ae ae	184 185
<i>S. formosus</i>	florosenine integerrimine	ae	186
<i>S. fremonti</i> Torr. et A. Gray.....	retrorsine senecionine seneciphylline	wh	148
<i>S. fuchsii</i> K. C. Gmel. (see <i>S.</i> <i>nemorensis</i> L. ssp. <i>fuchsii</i> Gmelin)			
<i>S. glabellus</i> (Turez.) DC.....	senecionine	wh	187
<i>S. glaberrimus</i> DC.....	retrorsine	ae	153
<i>S. graminifolius</i> N. J. Jacq.....	retrorsine graminifoline platyphylline seneciphylline	ae ae	188
<i>S. grandifolia</i>	retrorsine	rt, lf, st	189
<i>S. griesebachii</i>	senecionine	ae	190
<i>S. ilicifolius</i> Thunb.....	senecionine seneciphylline retrorsine	ae	191, 192, 188, 127
<i>S. incanus</i> L. subsp. <i>carniolicus</i> (Willd.) Br.....	seneciphylline	ae	147
<i>S. integerrimus</i> Nutt.....	integerrimine senecionine platyphylline neoplatyphylline	ae	156 420
<i>S. isatideus</i> DC.....	retrorsine	ae	153, 193
<i>S. jacobaea</i> L.....	seneciphylline senecionine jacobine jacanine jacoline jacozine	ae	194, 195 196, 167 153, 197, 198, 199, 200, 201, 202
	otosenine senkirkine	ae	51
<i>S. kirkii</i> Hook. f. ex Kirk.....	retrorsine senkirkine	ae bk, lf	184 203
<i>S. kleinia</i> Sch. Bip.....	O-acetylsenkirkine	lf	204
	integerrimine	st	205
	senkirkine	st	206
<i>S. krylovii</i>	seneciphylline	ae	207

TABLE 1. Continued.

Plant	Constituent Alkaloids	Plant Part	Ref.
<i>S. kubensis</i> Grossh.....	seneciphylline	ae	208
<i>S. lampsanoides</i>	seneciphylline	ae, rt	209, 210
<i>S. latifolius</i> DC.....	retrorsine	ae	211, 212
	seneciphylline	ae	213
	platyphylline		
<i>S. lautus</i> Forst. f.....	senecionine	wh	35
<i>S. longilobus</i> Benth.....	seneciphylline	wh	156, 214, 150
	retrorsine		151
	riddelliine		149
<i>S. magnificus</i> F. Muell.....	senecionine	ae	215
	integerrimine		216
<i>S. minimus</i> Poir.....	seneciphylline	ae	158
<i>S. morrisonensis</i> Hayata.....	integerrimine	wh	217
<i>S. nebrodensis</i> L. var. <i>sicula</i>	integerrimine	wh	218
	senecionine		
<i>S. nemorensis</i> L. var. <i>bulgaricus</i> (Vel) Stoj. et Stef.....	bulgarsenine	lf	219
	retroisosenine		
	nemorensine		
<i>S. nemorensis</i> L. var. <i>subdecurrens</i> Griseb.....	nemorensine	ae	371
	retroisosenine	rt	422
	bulgarsenine		
<i>S. nemorensis</i> L. ssp. <i>fuchsii</i> Gmelin.....	fuchsisenecionine	ae	362, 363, 364, 365, 423
	senecionine		
<i>S. othonnae</i> Bieb.....	otosenine	ae	220
	onetine	rt	221
	seneciphylline		
	floridanine	ae, rt	222
	doronine	ae	223
<i>S. othonniformis</i> Fourcade.....	bisline	ae	224, 225
	isoline		
<i>S. palmatus</i> Pall.....	seneciphylline	rt	226
<i>S. paludosus</i> L.....	seneciphylline	rt, ae	153, 227, 228
	jacobine		
<i>S. pampeanus</i>	senecionine	ae	229
<i>S. paucicalyculatus</i> (Platt.).....	paucicaline	wh	230
	retrorsine		
<i>S. paucifolius</i> S. G. Gmel.....	seneciphylline		231
<i>S. petasitis</i> DC.....	senecionine	lf	146
	probably bisline	ae	232
^a <i>S. platyphylloides</i> Somm. et Lev.....	platyphylline	rt	233, 234, 235
	seneciphylline		
^a <i>S. platyphyllus</i> (Bieb.) DC.....	platyphylline	rt, ae	236, 237, 238
	seneciphylline	lf	239
	neoplatyphylline	rt	240, 241
	sarracine	rt	242
<i>S. pojarkovae</i>	sarracine	rt	243
	seneciphylline		
<i>S. procerus</i> L. var. <i>procerus</i> Stoj. Stef. et Kit.....	senkirkine	ae, rt	244
	procerine		
<i>S. propinquus</i> Ait.....	seneciphylline	ae, rt	209, 245
<i>S. pseudo-arnica</i> Less.....	senecionine	ae	156
<i>S. pterophorus</i> DC.....	senecionine	ae	192, 188, 127
	seneciphylline		
	retrorsine		
	rosmarinine	ae	246
	acetyl-seneciphylline		
	pterophorin	ae	424

^aSee footnote on page 133.

TABLE 1. Continued.

Plant	Constituent Alkaloids	Plant Part	Ref.
<i>S. quadridentatus</i> Labill.	senecionine seneciphylline retrorsine	ae	247
<i>S. racemosus</i>	seneciphylline	rt	248
<i>S. renardii</i> Winkl.	seneciphylline senkirkine (renardine) otosenine	ae	249, 250
<i>S. retrorsus</i> DC.	retrorsine	ae	194, 193
^a <i>S. rhombifolius</i> (Willd.) Sch. Bip.	sarracine platyphylline neoplatyphylline seneciphylline	rt ae, rt	251, 233 208
<i>S. riddellii</i> Torr. et A. Gray	riddelliine	ae wh	156 252, 253
<i>S. riddellii</i> Torr. et A. Gray var. <i>parksi</i> (Cory)	retrorsine riddelliine	ae	149
<i>S. rivularis</i> DC.	7-angelyliheliotridine (rivularine)	ae	182, 135
<i>S. ruderalis</i> Harvey	retrorsine	ae	254
<i>S. ruwenzoriensis</i> S. Moore	ruwenine ruzorine	wh	255
<i>S. scandens</i>	senecionine seneciphylline	wh	256
<i>S. sceleratus</i> Schweikerdt	retrorsine sceleratine chlorodeoxyscleratine	ae	257, 258, 259 260 261
<i>S. spartioides</i> Torr. et A. Gray	seneciphylline spartioidine senecionine retrorsine riddelliine	ae ae	156, 262 420
<i>S. spathulatus</i> A. Rich.	senecionine integerrimine seneciphylline	ae, rt	158 263
<i>S. squalidus</i> L.	senecionine integerrimine seneciphylline	ae	153, 264, 265 205 266
<i>S. stenocephalus</i> Maxim.	senecionine	ae	267
<i>S. subalpinus</i> C. Koch	senecionine seneciphylline	lf ae	147
<i>S. swaziensis</i> Compton	retrorsine swazine	ae	268, 269, 270
<i>S. tomentosus</i>	senecionine otosenine (tomentosine)	ae	271, 179
<i>S. triangularis</i> Hook.	senecionine	ae	272
<i>S. uintahensis</i>	senecionine senkirkine		420
<i>S. venosus</i> Harvey	retrorsine	ae	153
<i>S. vernalis</i> Waldst. et Kit.	senecionine senkirkine retrorsine		273, 274
<i>S. viscosus</i> L.	senecivernine senecionine integerrimine	ae ae	264, 153 182
<i>S. vulgaris</i> L.	senecionine seneciphylline retrorsine riddelliine	ae ae ae	275, 264, 153 155, 276, 277 420
<i>S. werneriaefolius</i>	senecionine retrorsine		420

^aSee footnote on page 133.

TABLE 1. Continued.

Plant	Constituent Alkaloids	Plant Part	Ref.
<i>Syneilesis palmata</i> Maxim.....	syneilesine acetylsyneilesine senecionine	ae, rt	278, 279
<i>Tussilago farfara</i> L.....	senkirkine	fl, lf	18, 425
LEGUMINOSAE			
<i>Crotalaria aegyptica</i> Benth.....	monocrotaline / crosemperine	ae	419
<i>C. agatiflora</i> Schweinf.....	7 β -hydroxy-1-methylene- 8 β -pyrrolizidine	ae	426
	madurensine	ae	280
	anacrotine		281
	7-acetylmadurensine		
	6-acetylanacrotine		
	7-acetyl- <i>cis</i> -madurensine		
<i>C. anagyroides</i> Humb. et al.....	6-acetyl- <i>trans</i> -anacrotine		
	crotaflorine		
	6-angelyl- <i>trans</i> -anacrotine		
	1-methylenepyrrolizidine	sd	282, 283
<i>C. assamica</i> Benth.....	senecionine	sd	284
	anacrotine	sd	280
<i>C. axillaris</i> Ait.....	monocrotaline /		285, 286
	axillarine	sd	287, 288
<i>C. barbata</i> R. Graham ex Wight et Walk.-Arn.....	axillaridine		
	crobarbatine	sd	289
<i>C. brevifolia</i>	integerrimine	sd	290
	usaramine	sd	291
<i>C. burhia</i> Buch.-Ham.....	crotalarine (croburhine)	ae	292, 293
	monocrotaline /		
<i>C. crassipes</i> Hook. (see <i>C. novae- hollandiae</i> DC. subsp. <i>novae- hollandiae</i>)			
<i>C. crispata</i> F. Muell. ex Benth.....	monocrotaline / fulvine	wh	294
<i>C. dura</i> J. M. Wood et Evans.....	crispatine		
	dicrotaline	ae	295, 296
<i>C. fulva</i> Roxb.....	fulvine	ae	297
<i>C. globifera</i> E. Mey.....	dicrotaline	ae	295, 296
<i>C. grahamiana</i> R. Wight et Walk.- Arn.....			
	monocrotaline /	sd	298
	grahamine	sd	299
	monocrotalinine	wh	300
<i>C. grantiana</i> Harvey.....	grantianine	sd	301, 259
	grantaline	sd	35
	1-hydroxymethyl-1 β ,2 β - epoxy pyrrolizidine		
<i>C. incana</i> L.....	integerrimine	sd	187
	anacrotine	ae	302
	usaramine	sd	303
<i>C. intermedia</i> Kotschy.....	integerrimine	sd	304
	usaramine		
<i>C. juncea</i> L.....	senecionine	sd	305, 306, 307
	seneciphylline		
	riddelline		
	trichodesmine		
	junceine		
	anacrotine	sd	308, 309, 310,
<i>C. laburnifolia</i> L.....	(crotalaburnine)		291, 311
	1-methylenepyrrolizidine	sd	35
<i>C. laburnifolia</i> L. subsp. <i>eldomae</i>	madurensine	ae	312
	anacrotine		
	senkirkine		
	hydroxysenkirkine		
	crotafoline		

TABLE 1. Continued.

Plant	Constituent Alkaloids	Plant Part	Ref.
<i>C. lechnaultii</i>	monocrotaline crispatine	sd	313
<i>C. leiloba</i> Barth. (syn. <i>C. ferruginea</i> Wall.).....	monocrotaline	sd	314
<i>C. madurensis</i> R. Wight.....	madurensine crispatine fulvine cromadurine isocromadurine	sd sd ae	280 315
<i>C. mitchellii</i> Benth.....	monocrotaline retusamine	sd wh	62, 316 317 318
<i>C. mucronata</i> Desv. (see <i>C. pallida</i> Ait.).....			
<i>C. mysorensis</i> Roth.....	monocrotaline	sd	319
<i>C. nana</i> Burm.....	croatananine cronaburmine	sd	320 427
<i>C. novae-hollandiae</i> DC. subsp. <i>lasiophylla</i> (Benth) A. Lee.....	monocrotaline retusamine	wh	318
<i>C. novae-hollandiae</i> DC. subsp. <i>novae-hollandiae</i>	retusamine	sd	318
<i>C. pallida</i> Ait. (syn. <i>C. mucronata</i> Desv., <i>C. striata</i> DC.).....	usaramine integerrimine mucronatine (usaramine?) nilgirine	sd	291, 35 321 322
<i>C. paniculata</i> Willd.....	crotastratine fulvine	sd sd	323, 324 325
<i>C. quinquefolia</i> L.....	monocrotaline	sd	35
<i>C. recta</i> Steud. ex A. Rich.....	monocrotaline trichodesmine	ae	326
<i>C. retusa</i> L.....	monocrotaline retusine retusamine retronecine	sd sd, ae	327 328
<i>C. rubiginosa</i> Willd. (<i>C. wightiana</i> R. Graham ex R. Wight et Walk.- Arn.).....	junceine trichodesmine	sd	329
<i>C. sagittalis</i> L.....	monocrotaline	sd	330
<i>C. semperflorens</i> Vent.....	crosemperine	sd	331
<i>C. sericea</i> Retz.....	monocrotaline spectabiline	sd	332, 333
<i>C. spartioides</i> DC.....	retrosine	ae	334
<i>C. spectabilis</i> Roth.....	monocrotaline spectabiline retusine	sd sd, wh sd	335, 327 336 35
<i>C. stipularia</i> Desv.....	monocrotaline	sd	314
<i>C. tetragona</i> Roxb.....	integerrimine trichodesmine	sd	314
<i>C. usaramoensis</i> E. G. Baker.....	integerrimine usaramine senecionine retrosine	sd sd	187 337
<i>C. verrucosa</i> L.....	1-methylenepyrrolizidine anacrotine crotaverrine acetylcrotaverrine	sd sd	35 338 339
<i>C. walkeri</i> Arnott.....	crotaverrine acetylcrotaverrine	sd	340
<i>C. sp. aff. mitchellii</i>	retusamine	wh	318

TABLE 1. Continued.

Plant	Constituent Alkaloids	Plant Part	Ref.
RANUNCULACEAE			
<i>Caltha biflora</i>	senecionine	ae	341
<i>C. leptosepala</i>	senecionine	ae, rt	341
SCROPHULARIACEAE			
<i>Castilleja rhexifolia</i> Rydb.....	senecionine		342

Abbreviations: wh = whole plant
 ae = above ground parts of plant
 rt = root
 st = stem
 bk = bark
 lf = leaf
 fl = flower
 sd = seed

TABLE 2. Plants with known alkaloids which are non-hepatotoxic aminoalcohols and esters.

(a) In families in which hepatotoxic alkaloids occur.

Plant	Constituent Alkaloids	Plant Part	Ref.
APOCYNACEAE			
<i>Alafia multiflora</i>	alafine	sd	343
<i>Anodendron affine</i> Druce.....	allanodendrin anodendrin	ae	344, 345
BORAGINACEAE			
<i>Caccinea glauca</i> Savi.....	7,9-dibenzoylretronecine	fl	346
<i>Heliotropium strigosum</i> Willd.....	strigosine trachelanthamidine	ae	347
<i>Lindelofia macrostyla</i> (Bunge) M. Pop. (syn. <i>Lindelofia anchlussoides</i> , <i>Paracaryum heliocarpum</i> Kern.).....	lindelofine lindelofamine quaternary chloride, C ₁₇ H ₃₂ NO ₃ Cl	ae	348
<i>L. olgae</i> (Regel et Smirnov) Brand....	viridiflorine	ae	94
<i>L. pierocarpa</i> (Rupr.) M. Pop.....	viridiflorine	ae	93
<i>Macrotomia echioides</i> Boiss.....	macrotomine	ae	350
<i>Paracaryum himalayense</i> (Klotsch) C. B. Clark.....	viridiflorine	ae	93
<i>Tournefortia sibirica</i> L.....	turneformine	ae	351
<i>Trachelanthus hisoricus</i> Lipsky.....	viridiflorine trachelanthamine	lf	352
<i>T. korolkovii</i> (Lipsky) B. Fedtsch....	trachelanthamine	ae	353, 354, 355, 94
CELASTRACEAE			
<i>Bhesa archboldiana</i> (Merr. & Perry) Hou (syn. <i>Kurrimia archboldiana</i> (Merr. & Perry)).....	9-angelylretronecine	bk	356
COMPOSITAE			
^a <i>Adenostyles rhombifolia</i> (Willd.) M. Pimen. ssp. <i>rhombifolia</i> chemovar <i>sarracinifera</i>	sarracine	ae	116
^a <i>Adenostyles rhombifolia</i> (Willd.) M. Pimen ssp. <i>rhombifolia</i> chemovar. <i>platyphyllinifera</i>	platyphylline	ae	116

^aSee footnote on page 133.

TABLE 2. Continued.

Plant	Constituent Alkaloids	Plant Part	Ref.
<i>Cacalia hastata</i> L.	hastacine	rt	357, 241
<i>C. robusta</i>	hastacine		358
<i>Kleinia kleinoides</i> (Sch. Bip.) M. R. F. Taylor	isosenaetnin 12,18-dehydroiso- senaetnin	ae	428
<i>Notonia petraea</i> R. E.	senaetnin	ae	429
<i>Senecio adnatus</i> DC. (see <i>S.</i> <i>hygrophyllus</i>)			
<i>S. aetnensis</i> Jan.	senaetnin	ae, rt	430
<i>S. amphibolus</i>	macrophylline	ae	359
<i>S. angulatus</i> L.	angularine rosmarinine	wh	360
<i>S. aronicoides</i>	hygrophylline		420
<i>S. aucheri</i> DC.	senaetnin transsenaetnin pterophorin	ae	431
<i>S. brachypodus</i> DC.	rosmarinine	ae, rt	361
<i>S. cissampelinus</i> (DC.) Sch. Bip.	senampelin A senampelin B senampelin C senampelin D	ae, rt	424
<i>S. francheti</i> Winkl.	sarracine franchetine	ae	352
<i>S. hygrophyllus</i> R. A. Dyer et C. A. Smith	platyphylline rosmarinine hygrophylline	ae	366, 361 367
<i>S. inaequidens</i> DC.	inaequidenin pterophorin	rt	430
<i>S. longiflorus</i>	senaetnin	rt	431
<i>S. macrophyllus</i> Bieb.	macrophylline	ae	368
<i>S. mikanioides</i> Otto. ex Walp.	sarracine senampelin C senampelin D senampelin E senampelin F senampelin G	ae ae	155, 369, 370 431
<i>S. nemorensis</i> L. ssp. <i>Jaquinianus</i> (Rehb.) Durand	nemorensine	ae	371
<i>S. nemorensis</i> L. ssp. <i>fuchsii</i> var <i>nova</i> (Zlatnik)	nemorensine	ae	371
<i>S. pauciligulatus</i> Dyer et Sm.	rosmarinine	ae	361
<i>S. pubigerus</i> L.	senaetnin	ae	432
<i>S. pulviniformis</i> Hieron.	pterophorin isopterophorin	ae	433
<i>S. rosmarinifolius</i> L.	rosmarinine	ae	191, 192, 188
<i>S. sagittus</i> (see <i>Cacalia hastata</i>)			
<i>S. sarracenus</i> L.	sarracine	ae	153, 372, 373
<i>S. schvetzovii</i> Korsh.	macrophylline	ae	231
<i>S. sylvaticus</i> L.	silvasenecine sarracine	ae	362, 153 374
<i>S. taiwanensis</i> Hayata	rosmarinine	ae	217
<i>S. tournefortii</i> Lap.	platyphylline	ae	375
LEGUMINOSAE			
<i>Crotalaria albida</i> Heyne ex Roth. (syn. <i>C. montana</i> Roxb.)	croalbidine	ae	376, 377
<i>C. aridicola</i> Domin.	1-methoxymethyl-1,2-de- hydropyrrolizidine, 7 β -hydroxy-1-methoxy- methyl-1,2-dehydro- pyrrolizidine 7 β -acetoxy-1-methoxy- methyl-1,2-dehydro- pyrrolizidine	ae wh	378 379

TABLE 2. Continued.

Plant	Constituent Alkaloids	Plant Part	Ref.
<i>C. candicans</i> W. and A.	crocandine isocrocandine	sd	380
<i>C. damarensis</i> Engl.	1-methylenepyrrolizidine	wh, sd	381, 283
<i>C. goreensis</i> Guillem et Perrott.	7 β -hydroxy-1-methylene-8 β -pyrrolizidine, 7 β -hydroxy-1-methylene-8 α -pyrrolizidine, base C ₁₅ H ₁₃ ON	ae, sd	382
<i>C. grandistipulata</i> Harms.	1-methylenepyrrolizidine	sd	434
<i>C. lachnophora</i> A. Rich.	1-methylenepyrrolizidine	sd	434
<i>C. maypurensis</i> Humb. et al.	7 β -hydroxy-1-methylene-8 β -pyrrolizidine 7 β -hydroxy-1-methylene-8 α -pyrrolizidine	ae, sd	383
<i>C. medicaginea</i> Lamk.	1-methoxymethyl-1,2-dehydro-8 α -pyrrolizidine 7 β -hydroxy-1-methoxymethyl-1,2-dehydro-8 α -pyrrolizidine 1 α -methoxymethyl-1 β ,2 β -epoxy-8 α -pyrrolizidine	wh, sd	378
	7 α -hydroxy-1-methoxymethyl-1,2-dehydro-8 α -pyrrolizidine	wh, sd	384
	1-hydroxymethyl-1 β ,2 β -epoxy-8 α -pyrrolizidine	sd	385, 386
	1-hydroxymethyl-1 β ,2 β -epoxy-8 α -pyrrolizidine		379
<i>C. natalitia</i> Meissn.	1-methylenepyrrolizidine	sd	434
<i>C. podocarpa</i> DC.	7 β -hydroxy-1-methylene-8 β -pyrrolizidine	sd	435
<i>C. rhodesiae</i>	1-methylenepyrrolizidine	sd	35
<i>C. stolzii</i> (Baf. F.) Milne Redh.	1-methylenepyrrolizidine	sd	434
<i>C. trifoliatum</i> Willd. (see <i>C. medicaginea</i> Lamk.)			
<i>Cytisus laburnum</i> L.	laburnine 1-hydroxymethyl-7-hydroxypyrrolizidine laburnamine	sd	387, 388, 389 390

(b) In families in which hepatotoxic alkaloids are unknown.

ORCHIDACEAE			
<i>Chysis bractescens</i> Lindl.	1 α -methoxycarbonyl-8 β -pyrrolizidine 1 α -ethoxycarbonyl-8 β -pyrrolizidine	wh	391, 392
<i>Doritis pulcherrima</i> (syn. <i>Phalaenopsis esmeralda</i>)	phalaenopsine La or T	wh	393
<i>Hammarbya paludosa</i> L.	paludosine hammarbine	wh wh	394 395
<i>Kingiella taenialis</i> (Lindl.) Rolfe	phalaenopsine La	wh	396
<i>Liparis auriculata</i> (Blume)	auriculine	wh	397
<i>L. bicallata</i> Sehltr.	laburnine malaxine	wh wh	397 398, 399
<i>L. hachijoensis</i> Nakai	laburnine malaxine	wh	397 398
<i>L. keitaoensis</i> Hay	keitaoine keatine	wh	395
<i>L. kumokiri</i> F. Maekawa	kumokirine	wh	400, 398
<i>L. krameri</i> French. et Sav.	kuramerine	wh	400, 398, 399

TABLE 2. Continued.

Plant	Constituent Alkaloids	Plant Part	Ref.
<i>L. toeselii</i> (L.) L. E. Rich.	auriculine	wh	394
<i>L. nervosa</i> Lindl.	nervosine	wh	398, 401
<i>Malaxis congesta</i> comb. nov. (Rehb. f.)	malaxin	wh	402
<i>M. grandifolia</i> Sehltr.	grandifoline	wh	403
<i>Phalaenopsis amabilis</i> Bl.	phalaenopsine T	wh	404, 405, 393
<i>P. amboinensis</i>	phalaenopsine La	wh	393
<i>P. aphrodite</i>	phalaenopsine T	wh	393
<i>P. cornu-cervi</i> Rehb. f.	cornucervine	wh	406, 393
<i>P. equestris</i> Rehb. f.	phalaenopsine Is	wh	393
<i>P. fimbriata</i>	phalaenopsine T	wh	393
<i>P. hieroglyphica</i>	phalaenopsine La or T	wh	393
<i>P. lueddemanniana</i>	phalaenopsine La or T	wh	393
<i>P. mannii</i> Rehb. f.	phalaenopsine La	wh	393
<i>P. sanderiana</i> Rehb. f.	phalaenopsine La	wh	393
	phalaenopsine T		
<i>P. schilleriana</i>	phalaenopsine La	wh	393
<i>P. stuartiana</i> Rehb. f.	phalaenopsine La	wh	393
	phalaenopsine T		
<i>P. sumatrana</i>	phalaenopsine La	wh	393
<i>P. violacea</i>	phalaenopsine La or T	wh	393
<i>Vanda cristata</i> Lindl.	laburnine acetate	wh	407
<i>V. helvola</i> Bl.	laburnine	wh	408
	laburnine acetate		
<i>V. hindsii</i> Lindl.	laburnine acetate	wh	408
<i>V. luzonica</i> Loher.	laburnine acetate (or lindelofidine acetate)	wh	408
<i>Vandopsis gigantea</i> Pfitz.	laburnine	wh	408
	lindelofidine		
	laburnine acetate		
	lindelofidine acetate		
<i>V. lissochiloides</i> Pfitz.	laburnine	wh	408
	lindelofidine		
	laburnine acetate		
	lindelofidine acetate		
RHIZOPHORACEAE			
<i>Cassipourea gummiflua</i> Tulasne var. <i>verticellata</i> Lewis.	cassipourine	st, lf bk	409 410
SANTALACEAE			
<i>Thesium minkwitzianum</i> B. Fedtsch.	thesine	ae	411
	thesinine		412, 413
	thesinicine		
	isoretronecanol	rt	
SAPOTACEAE			
<i>Mimusops elengi</i> L.	1-hydroxymethyl-pyrrolizidine tiglata		414
<i>Planchonella anteridifera</i> (C. T. White et W. D. Francis) H. J. Lamb.	planchonelline	lf	415
	laburnine angelate		
<i>P. thyrosoidea</i> C. T. White ex F. S. Walker.	planchonelline	lf	415
	laburnine tiglata		
	laburnine benzoate		
<i>Planchonella</i> sp. (NGF 24744)	(-)-isoretronecyl <i>trans</i> - β -methyl thioacrylate	lf	416
	(-)-isoretronecyl tiglata		

Abbreviations:

wh = whole plant
 ae = above ground parts of plant
 rt = root
 st = stem

bk = bark
 lf = leaf
 fl = flower
 sd = seed

Boraginaceae are well known as honey sources and honey derived from *Echium plantagineum*, for example, has recently been shown to contain up to 1 ppm alkaloid (Culvenor *et al.*, unpublished data). There are probably many regions in the world where the degree of surveillance is inadequate to ensure that cereal grains are not occasionally contaminated with alkaloid at this and higher levels.

The main table, table 1, lists the species known to contain alkaloids of demonstrated hepatotoxicity or of a structural type which makes them very probably hepatotoxic (27). The ingestion of these plant species, in any form, should be avoided or minimized as far as possible. The supplementary list, table 2, is of species whose known alkaloids do not have all the features needed for hepatotoxicity but are pyrrolizidine aminoalcohols or esters needing only minor modification to be in the hepatotoxic category. The species in table 2a are also in the same genera or taxonomic groups as hepatotoxic species and there is a possibility that hepatotoxic alkaloids will be found on further examination, as minor constituents, in strains or plant parts not yet investigated, or under specific conditions of growth. Table 2a includes several species for which the only pyrrolizidine derivatives yet isolated are acylpyrroles, which are 5-oxo- derivatives of the toxic metabolites of hepatotoxic alkaloids. Tables 1 and 2a also include 3 species (*Senecio antieuphorbium*, *S. pierophorus* and *S. mikanioides*) in which acylpyrroles and pyrrolizidine alkaloids are known to co-occur. Thus the species in table 2a are not entirely free of suspicion.

The species in table 2b are in families, notably the Orchidaceae, to which no suspicion of hepatotoxicity has attached and which, we believe, may still be regarded as free of suspicion of chronic pyrrolizidine alkaloid toxicity.

The species for which there is information available at present are few in relation to the total number of species in the genera concerned. It would be prudent to regard all species in the family Boraginaceae and the genera *Crotalaria*, *Eupatorium*, *Senecio* and other related genera of the tribe Senecioneae as potentially hepatotoxic if they have not yet been investigated.

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