Pergamon

PII: S0031-9422(97)00425-1

Phytochemistry, Vol. 47, No. 2, pp. 155–162, 1998

Printed in Great Britain
0031-9422/98 $19.00+0.00

REVIEW ARTICLE NUMBER 124

WHY ARE SO MANY FOOD PLANTS CYANOGENIC?

DAVID A. JONES

Department of Botany, University of Florida, Gainesville, Florida 32611, U.S.A.

(*Received in revised form* 30 *April* 1997)

Key Word Index—Cereals; pulses; food plants; cyanogenesis, cyanoglycosides; plant defence; detoxification; herbivory.

Abstract—A disproportionately large number of the most important human food plants is cyanogenic. The accumulated research of numerous people working in several different disciplines now allows a tenable explanation for this observation. Cyanogenesis by plants is not only a surprisingly effective chemical defence against casual herbivores, but it is also easily overcome by careful pre-ingestion food processing, this latter skill being almost exclusive to humans. Moreover, humans have the physiological ability to detoxify cyanide satisfactorily, given an adequate protein diet. It appears that early in the domestication of crop plants the cyanogenic species would have been relatively free of pests and competitive herbivores, as well as having good nutritional qualities, and thus ideal candidates for cultivation by the first farmers. © 1997 Elsevier Science Ltd

INTRODUCTION

In his account of cyanogenesis in plants, Gibbs [1] recorded 262 (11%) cyanogenic species among the 2378 he had tested. If cyanogenesis were distributed at random among the 24 leading food plants in the world then only 2.64 would be expected to be cyanogenic. Current evidence shows that at least 16 of these plants are cyanogenic ($\chi^2_{[1]} = 77.0$, $P \ll 0.001$). Why?

Similarly, of the 318 food plants listed in [2] at least 68 (21.4%) are cyanogenic. Comparing this with the number expected from the list in [1], $\chi^2_{[1]} = 34.96$, $P \ll 0.001$. Again, a statistically significant excess of all human food plants is cyanogenic.

Table 1. Cyanogenesis and world production (10^6 metric tonnes) of major food crops in 1994

Crop	Tonnage	Crop	Tonnage
Maize	570.9	**Wheat**	535.8
Paddy Rice	530.0	Potatoes ?	275.7
Barley	158.7	**Cassava**	157.7
Soya Beans ?	136.2	**Sugar Cane**	109.6
Tomatoes	77.0	**Sorghum**	60.6
Taro	unknown	Oranges ?	58.7
'Pulses'	58.0	Bananas ?	52.2
Apples	48.2	**Oats**	34.1
Onions, dry ?	32.1	**Rapeseed**	29.9
'Millets'	27.1	**Peanuts**	25.9
Rye	24.3	*Sunflower*	22.6
Mangoes	18.0	*Pineapples*	12.0

Source: Food and Agriculture Organization, Quarterly Bulletin of Statistics 8, 1/2—1995.

Bold—cyanogenic; ? not known to be cyanogenic, but there are cyanogenic species in the same genus; *italics*—cyanogenesis not known in genus.

CYANOGENESIS IN FOOD PLANTS

Table 1 lists the 23 food crops produced in the largest tonnage world wide in 1994, as estimated by the UN Food and Agriculture Organization. The scientific names have not been used because in some cases the food name includes a number of species within a genus (e.g. for wheats: *Triticum aestivum* L. and *T. durum* Desf.) or even of different genera (e.g. for pulses: *Phaseolus vulgaris* L., *Pisum sativum* L., *Vigna unguiculata* (L.) Walp. and *Dolichos lablab* L.; and for millets: *Panicum miliaceum* L., *Eleusine coracana* (L.) Gaertner and *Echinochloa* Pal. spp.). Furthermore, production is not listed by species in FAO publications. Taro (*Colocasia esculenta* (L.) Schott) appears in the table as a floating entry because although grown in vast quantities in the Pacific basin, it is produced by so many small-scale farmers that the FAO cannot estimate the production. Note that the total tonnage of entries 9–24 (tomatoes to pineapples), less taro, almost exactly equals the annual production of maize, thus emphasizing the dominance of three cereal crops. Of these plants the cyanogenic glycosides

Table 2. Major food plants in which cyanogenic glycosides have been identified

Crop	Cyanoglycosides	Reference
Wheat		
Triticum aestivum	Dhurrin	
T. spelta		3
T. monococcum	Linamarin Lotaustralin Epilotaustralin	4
Barley		
Hordeum vulgare	Epiheterodendrin	5
	4 additional cyanoglycosides	6
Oats		
Avena sativa	Linamarin	7
Rye		
Secale cereale	Dhurrin	3
Sorghum		
Sorghum bicolor	Dhurrin	3, 8
Cassava		
Manihot esculenta	Linamarin Lotaustralin	9
Pulses		
Lima/Butter bean		
Phaseolus lunatus	Linamarin	10
	Lotaustralin	11
French/Kidney/Haricot beans		
P. vulgaris	Linamarin Lotaustralin	11
Millets		
Eleusine coracana	Triglochinin	12
Apple		
Malus pumila hybrids	Amygdalin Prunasin	13
Taro		
Colocasia esculenta	Triglochinin	14

have been identified and characterized in at least 10 (Table 2).

Cyanogenesis is not known to occur in the genera *Lycopersicon* Miller (tomatoes), *Helianthus* L. (sunflowers) and *Ananas* Miller (pineapple). Although *Solanum tuberosum* L. (potatoes), *Citrus sinensis* (L.) Osbeck (oranges) and the edible species in the genera *Musa* L. (bananas) and *Allium* L. (onions) are not known to be cyanogenic, other species in these four genera are [1]. There is some confusion with rice. *Oryza perenis* (as spelled in [15]) is recorded as being cyanogenic. Gibbs [1] attributes to others the finding of cyanogenesis in one species of *Oryza* without recording which one. The data for *Glycine max* (L.) Merr. (soya beans) are also equivocal; he [1] reports positively, whereas others failed to find any cyanogenic glycosides in this plant [16]. In general, Gibbs own work is reliable, but he was rather uncritical of the work of others. Fortunately, he gives details of the work of others independently of his own. Thus, by using only Gibbs' own data for my comparisons, I have been able to ignore the data that certainly include species listed incorrectly as being positive for cyanogenesis. As it happens, if Gibbs did have false positives in his own data, the true proportion of cyanogenic species in his table would be lower, so increasing the statistical significance of cyanogenesis in human food plants.

Table 3 lists the sources of information on cyanogenesis of those species in Table 1 for which the cyanogenic compounds are not known. In Table 4 there are other food plants whose cyanogenic glycosides have been identified.

THE EFFECTS OF CYANOGENESIS ON MAMMALS

Among the cyanogenic food plants, the HCN potential often varies in different parts of a plant and between the same parts of different individuals of the same species. The content in cassava ranges from 240–890 mg kg^{-1} in the tuberous roots to 1040 mg kg^{-1} in leaves; lima beans contain 100–4000 mg kg^{-1}, sorghum grain as little as 6 mg kg^{-1} and bamboo shoots as high as 8000 mg kg^{-1} (e.g., [39]). We can compare these concentrations with the acute lethal dose of HCN, in mg kg^{-1} body weight, for humans 0.5–3.5 [40], sheep 2.4 [41], cattle 2.0 [42], mice 3.7, cats 2.0,

Table 3. Plants reported to be cyanogenic and in which the cyanogenic compounds have yet to be identified

Crop	Reference
Sugar cane	
Saccharum spontaneum	17
Maize/corn	
Zea mays	3, 18
Rice	
Oryza sp.	1
O. perenis	15
Peanuts	
Arachis hypogea	1
Garden pea	
Pisum sativum	19–20
Mango	
Mangifera indica	1
Rape	
Brassica napus	1

Table 4. Other cyanogenic food plants for which the cyanogenic glycoside has been identified

Crop	Cyanoglycoside	Reference
Loquot		
Eriobotrya japonica	Amygdalin	21
Almond		
Prunus dulcis	Amygdalin	22
Peach		
P. persica	Amygdalin	23
	Prunasin	24
Sweet cherry	Amygdalin	
P. avium	Prunasin	25
Sour cherry		
P. cerasus	Amygdalin	
	Prunasin	26
Macadamia nut		
Macadamia ternifolia	Dhurrin	
	Prunasin	27–29
	(doubtful *)	
Elder		
Sambucus nigra	Holocalin	
	Prunasin	
	Sambunigrin	
	Zierin	30
Giant taro		
Alocasia macrorrhiza	Isotriglochinin	
	Triglochinin	31
Quince		
Cydonia oblonga	Prunasin	32
Papaya		
Carica papaya	Prunasin	
	Tetraphyllin B	33
Bamboo shoots		
Dendrocalamus latiflorus	Taxiphyllin	34
D. giganteus		
D. hamiltonii	Taxiphyllin	35
Bambusa vulgaris		
B. guadua	Taxiphyllin	36
Passion fruit		
Passiflora edulis	Prunasin	37
Sapote		
Pouteria sapota	Lucumin	38

See [1] for: Yam, *Dioscorea* spp.; Sweet potato, *Ipomoea batatas*; Guava, *Psidium guajava*; Aubergine (egg plant), *Solanum melongena*; Common millet, *Panicum milliaceum*; Sugar beet/Beet/Chard/Sea Kale, *Beta vulgaris*; Watercress, *Nasturtium officinale*; Apricot, *Prunus armeniaca*; Black current, *Ribes negra*; Lemon, *Citrus limon*; Lime, *Citrus aurantifolia*; Borage, *Borago officinalis*.

* Nahrstedt, A. Personal communication, 1997.

rats 0.5–10.0 and dogs 1.5 [43]. Not surprisingly, accidental acute cyanide poisoning from food is not uncommon [39, 44].

Most of the HCN obtained from food is generated from endogenous cyanogenic glycosides that are degraded by more or less specific β-glycosidases either endogenous to the food (e.g. [45, 46]) or produced by micro-organisms in the mammalian digestive tract [47, 48]. Sheep, for example, will ingest linamarin and lotaustralin in cyanogenic white clover (*Trifolium repens* L.) [41]. Cyanogenesis here results both by the action of linamarase in the masticated plant tissue and the rumen flora. The role of these micro-organisms is well demonstrated by an experiment with rats. Control rats fed orally 600 mg kg^{-1} amygdalin died in 3–5 hr. When free of micro-organisms, rats fed the same mass of amygdalin showed no visible signs of toxicity [49].

DETOXIFICATION

When cyanogenic plants are eaten slowly or over a period of time there may be no symptoms of cyanide poisoning. Sheep can consume 15–20 mg kg^{-1} per day when ingestion is distributed over the whole day [41]. Humans can consume 30–35 mg HCN per day from cassava in the form of gari [50]. This is approximately 50% of the acute lethal dose for a 70 kg human. Thus when doses are relatively small, mammals are capable of detoxifying HCN. There are five main ways by which this can occur (Table 5, [51]). The most effective appears to be by using sulphurtransferases, but an adequate supply of sulphur-containing amino acids (methionine and cysteine) is essential. When the diet is low in protein, chronic cyanide poisoning often results. This is very noticeable in societies where cassava is the staple food, especially when food preparation is carelessly done or is almost nonexistent.

Ironically, the one part of the tuberous root of cassava in which there is a reasonable amount of protein is the corky periderm, but this is usually peeled off and discarded at the beginning of processing. Cassava meal has only 22 mg methionine in 0.26 g protein per

Table 5. Sulphurtransferases

E.C.	
2.8.1.1	Rhodanese. 33 kDa—mammalian liver and kidney mitochondria (thiosulphate: cyanide transferase. S-S cleaved).
2.8.1.2	3-Mercaptopyruvate sulphurtransferase. ≈33 kDa—mammalian kidney (C-S bonds cleaved).
—	Serum albumin. (Colloidal elemental sulphur).
2.8.1.3	Thiosulphate: thiol transferase—yeast.
—	Sulphane sulphurtransferase—*Acinetobacter*.

(From [51])

100 g food. For comparison, polished rice has 150 mg methionine in 1.13 g protein while cowpeas have 273 mg methionine in 3.74 g protein per 100 g food [52]. Additionally, people suffering from sickle cell disease [50], Leber's disease [53], or tobacco smokers with a vitamin B_{12} deficiency [54] are all less efficient at detoxifying cyanide than people not so afflicted.

CYANIDE POISONING AND DISEASE

Table 6 shows some of the conditions caused by chronic cyanide poisoning in humans. Clearly cyanide poisoning from food is a major problem in some regions of the world. On the other had, even when foods are not processed properly, humans can still detoxify the cyanide so long as they do not eat too much of the plant too quickly. In animals other than humans chronic cyanide poisoning leads to different behaviours. In sheep, for example, the animal stops eating until the concentration of cyanide in the blood falls below a certain threshold level [41]. The golden bamboo lemur (*Hapalemur aureus*), however, apparently eats approximately 50 mg kg^{-1} body weight of cyanide a day from *Cephalostachyum* cf *viguieri* without showing any adverse effects at all [61].

We know more about cyanogenesis in cassava than in almost any other food plant because the part of the plant that is eaten is cyanogenic. This is not true of many of the other cyanogenic species. It is the leaves of the cereals that are cyanogenic, not the grains. The seeds of apples are cyanogenic, not the 'flesh'. The leaves of papaya and mango are cyanogenic, not the parts we eat. We do, however, eat bitter almonds, lima beans, bamboo shoots, passion fruits, beansprouts, macadamia nuts and pepperwort seedlings, all of which are cyanogenic.

The type of processing used can have an effect on the remaining cyanide content of the processed food. There are numerous papers describing the problems encountered with processing cassava (e.g., [59, 52]). Another example is with lima beans, *Phaseolus vulgarus*, [63]. With apples, we normally discard the core and thus the seeds of an apple, but when cider is manufactured the whole fruit is used. People with the potential for Leber's disease can go blind because of the effects of cyanide in cider [53].

Bitterness in almonds and cassava is based on the presence of cyanoglycosides. After almonds are ground in a mortar and left for a few hours, they lose the bitter flavour and become sweet. The reason is that not only does cyanogenesis release volatile HCN and aglycones (e.g. acetone and benzaldehyde), but the glucose remains behind in the plant tissue so sweetening it to our taste. A direct relationship between the cyanoglycoside content of cassava and bitterness has been claimed [64], although this has been disputed for a variety from Venezuela (Seigler, pers. comm. 1996).

The major food plants are all plants of open spaces and five of the first eight (Table 1) are grasses. The archeological records indicate that maize, wheat and rice were domesticated independently in different parts of the world, maize in the Americas, wheat in the Near East and rice in China. As these three cyanogenic species became the staple sources of carbohydrate, they replaced earlier staples, which were more often than not also cyanogenic species. These latter plants were by no means dropped from the diet; indeed many of them remain important food crops in these same areas. Thus maize superseded sweet potato, cassava and other tubers, various pulses and pseudo cereals [65]. Rice superseded millets of various kinds and, in the Far East, wheat replaced barley, though not rice [66]. In the Near East, it appears that wheat was domesticated very early because the 'native grasses were highly productive' [67].

Table 6. Conditions caused by chronic cyanide poisoning in humans

Country	Disorder
Jamaica	Peripheral neuritis (at the end of the last century, cassava and *Phaseolus lunatus*) [55].
Senegal	Bilateral pyramidal tract disorder (sorghum) [56].
Nigeria	Tropical ataxic neuropathy (cassava, partly offset by the oil boom and a rise in the level of protein in the diet, but now being reversed) [57–58].
Mozambique	Severe paralysing illness (following an enormous increase in cassava consumption during drought (including leaves) [59].
Zaire and Nigeria	Goitre (cassava, probably an effect of thiocyanate) [58].
Singapore	Amblyopia (prisoners of war camps. Diet contained a high proportion of cassava, yam and sweet potatoes) [60].
World-wide	A number of recognized diseases related to abnormal metabolism of cyanide mostly derived from tobacco smoke [53].

CYANOGENESIS AND PLANT DEFENCE AGAINST HERBIVORES

Cyanogenesis is one of the few situations where it has been possible to prove chemical defence against herbivores beyond reasonable doubt [68–75, and other references in Table 7]. Cyanogenesis is no defence against specialist herbivores that use β-cyanoalanine synthetase (74, 75) or a sulphur transferase (e.g. *Zygaena filipendulae*, *Polyommatus icarus* and numerous other species [76]) to detoxify the cyanide. A further complication is that some herbivores of cyanogenic plants are themselves cyanogenic [77, 78]. The experiments with *Lotus corniculatus* and *Trifolium repens* show that molluscs and insects will eat cyanogenic plants when there were no alternatives, but when given a choice they prefer to eat the acyanogenic form of a polymorphic species [68, 71–74]. Rabbits show the

Table 7. Plants for which chemical defence by cyanogenesis is known

Plant species	Defended against
Acacia spp.	Insects, in those species not defended by ants [82].
Amelanchier alnifolia	*Odocoileus hemicorus hemicorus* (Mule deer) [83].
Cynodon plectostachys	Complex interaction between insects, mammal grazers and trampling [84].
Lotus corniculatus	Slugs, snails and insects [68–72, 74].
Manihot esculenta	*Zonocerus variegatus*, wild pigs, baboons, porcupines, rats and game [85–87].
Pteridium aquilinum	Deer, sheep and some insects [88–89].
Simmondsia chinensis	Desert rodents [90].
Sorghum bicolor	*Locusta migratoria* [91–92].
Trifolium repens	Slugs, snails and weevils [71, 73, 93–96].

same behaviour when both cyanogenic and acyanogenic *Trifolium repens* are available together (Ellis Davies, personal letter 22 November 1977 and two photographs, copyright of the Welsh Plant Breeding Station), but not with *Lotus corniculatus* [80], in spite of strong circumstantial evidence to the contrary [81]. Following further field experiments, we found that cyanogenesis in *L. corniculatus* and *T. repens* is remarkably effective against casual herbivores [72].

Table 7 shows some examples of this type of chemical defence in other cyanogenic species, including food plants. Some of the animals involved, particularly insects in tropical and subtropical regions, can do immense damage to food crops that are not adequately protected.

Nearly all the experiments and field observations to date have been with one or a small number of plant species. On a larger scale, a close correlation was found between the distribution of cyanogenic individuals and insects eating the 800 plants of 108 species sampled in a neotropical sandy region near Rio de Janeiro [97]. Furthermore, in subsites, there was a seasonal correlation, cyanogenic individuals and insects being commoner during the summer. It was concluded that plant defence against insects was the best explanation for the distribution of the cyanogenic plants.

In my early experiments in cyanogenesis [68, 74], slugs and snails were sometimes observed to bite through the stems of cyanogenic plants, but eat no more. Later the molluscs would return to eat the bitten-off stems and leaves. By that time cyanogenesis would have been completed, following from osmotic shock, and the plant material would have become palatable. Whether this is deliberate behaviour by these gasteropods has not been determined, but it does parallel the processing of cyanogenic foods by humans.

Another type of pre-ingestive food processing has been observed, this time by lepidopteran larvae. The caterpillars of several species drain the leaves of their foodplants of the defensive latex and so avoid having their mouthparts clogged by the drying latex [98–99].

DISCUSSION

This is by no means the first occasion on which the importance of cyanogenesis both in human food and in human diet has been emphasised [e.g. 39, 100–101]. What is novel is the statistical analysis of the existing data, with the revelation that a grossly disproportionate number of the most important human food plants is cyanogenic. Furthermore, it is now possible to attempt to explain how this came about.

There are now sufficient examples of plant defence by cyanogenesis for us to conclude that cyanogenesis is an important system of chemical defence for plants. From this mass of information, collected for a multitude of different purposes, a coherent picture showing the reason for so many food plants being cyanogenic can be developed. A potential food plant has to be nutritious, easy to grow and 'good' to eat. It is not difficult to imagine that a plant with few pests would be an attractive candidate for domestication. It is unlikely that our ancestors deliberately sought plants free of pests, but in the same way that before the arrival of large refrigerators certain grocery stores were noted for their good cheese, wine and dried fruit because, fortuitously, they had good cellars, so some food plants were preferred for cultivation because they were less eaten by animals and less attacked by fungi than others. The chemical defence involved, in an overwhelming number of cases, happened to be cyanogenesis. The apparent resistance of cassava to *Zonocerus variegatus*, wild pigs, baboons, porcupines and other game and of *Sorghum* to *Locusta migratoria* is a clear demonstration of the benefit of cyanogenesis to the plant and, presumably, to the primitive farmer. Concern today about the diseases and pests of food plants is irrelevant to the evolution of our staple foods. Monocultures are always subject to rapid evolution of pests, almost irrespective of the natural defences of the crop plant. Cassava, for example, shows the problem well [102–104]. The planting of monocultures on a large scale is a relatively recent farming practice and so, during the domestication of our staple foods, the increase of pests and diseases would have been scarcely noticeable.

Unlike most other animals, humans had the ability to process foods, grinding and steeping followed by cooking. In this way the cyanogenic glycosides that, by cyanogenesis, were deterrents to the herbivores in the wild state could be removed effectively while at the same time sweetening the taste from the rather bitter flavour of raw cyanogenic plant material (as is known for bitter almonds and cassava). Selective breeding has also been used in attempts to improve the taste and reduce the toxicity of food plants. Sometimes this can be done, othertimes not (e.g. [105]). There is, however, the danger that removal of the defence compound opens up the crop to an increase in pest pressure (e.g. [106]).

We already know that some progenitors of food plants are cyanogenic, e.g. *Triticum monococcum* [4], *Manihot* spp. [107] and *Saccharum spontaneum* [17], and others still exist in the wild. The explanation outlined above predicts that at least one of the wild ancestors of a cyanogenic food plant will have been cyanogenic. I am now seeking to test for cyanogenesis as many as possible of the extant wild relatives of the most important food crops.

Acknowledgements—I am most grateful to Lincoln Brower, Paul Alan Cox, Timothy Johns, Miriam Rothschild, David Seigler and William Louis Stern for their constructive comments on an earlier draft of this paper. In the interests of brevity, I have not incorporated all the caveats suggested. For this I apologise, as I do for errors and false assumptions I may have made.

REFERENCES

1. Gibbs, R. D., *Chemotaxonomy of Flowering Plants.* McGill-Queens U.P., Montreal, 1974.
2. Harrison, S. G., Masefield, C. B., Wallis, M. and Nicholson, B. E., *Oxford Book of Food Plants.* Oxford University Press, Oxford, 1969.
3. Erb, N., Zinsmeister, H. D. and Nahrstedt, A., *Planta Medica*, 1981, **41**, 84.
4. Pitsch, Ch., Keller, M., Zinsmeister, H. D. and Nahrstedt, A., *Planta Medica*, **1984**, 388.
5. Erb, N., Zinsmeister, H. D., Lehmann, G. and Nahrstedt, A., *Phytochemistry*, 1979, **18**, 1515.
6. Pourmohseni, H., Ibenthal, W.-D., Machinek, R., Reemberg, G. and Wray, V., *Phytochemistry*, 1993, **33**, 295.
7. Michely, D., Zinsmeister, H. D., Roth, E. and Nahrstedt, A., *Zeitschrift für Lebensmittel Untersuchung Forschung*, 1983, **177**, 350.
8. Dunstan, W. R. and Henry, T. A., *Philosophical Translations of the Royal Society A*, 1902, **199**, 399.
9. Dunstan, W. R. and Henry, T. A., in *Annual Report for* 1906, The British Association for the Advancement of Science, 1906, p. 145.
10. Dunstan, W. R. and Henry, T. A., *Philosophical Translations of the Royal Society B*, 1903, **72**, 85.
11. Butler, G. W., *Phytochemistry*, 1965, **4**, 127.
12. Tjon Sie Fat, L. A., *Koninkl. Nederl. Akad. Wetensch.*, 1977, **80**, 227.
13. Dziewanowska, K., Niedźweidź, I., Chodelska, I. and Lewak, S., *Physiologia Végétale*, 1979, **17**, 687.
14. Lieberei, R., in *Cyanide Compounds in Biology*, ed. D. Evered and S. Harnett. Wiley, Chichester (Ciba Foundation Symposium 140), 1988, p. 247.
15. Puentes de Diaz, A. M., Galdames Portus, M. I. and Freitas da Silva, M., *Acta Amazonica*, 1978, **8**, 679.
16. Honig, D. H., Hockridge, M. E., Gould, R. M. and Rackis, J. J., *Journal of Agricultural and Food Chemistry*, 1983, **31**, 272.
17. Seigler, D. S., Coussio, J. D. and Rondina, R. V. D., *Journal of Natural Products*, 1979, **42**, 179.
18. Brünnich, J. C., *Journal of the Chemical Society Transactions*, 1903, **83**, 788.
19. Jaffe, W. C., *Acta Cientia Venezolana*, 1950, **1**, 62.
20. Montgomery, R. D., *West Indian Medical Journal*, 1964, **13**, 1.
21. Hérissey, H., *Journal de Pharmacie et Chimie*, 1906, **24**, 350.
22. Abrol, Y. P., *Indian Journal of Biochemistry*, 1967, **4**, 54.
23. Rabaté, J., *Bulletin de la Société de Chimie Biologique Paris*, 1935, **15**, 385.
24. Kofod, H. and Eyjólfsson, R., *Phytochemistry*, 1969, **8**, 1509.
25. Nahrstedt, A., *Phytochemistry*, 1970, **9**, 2085.
26. Chandra, A. and Nair, M. G., *Phytochemical Analysis*, 1993, **4**, 120.
27. Plouvier, V., *Comptes Rendues Académie des Sciences, Paris*, 1964, **259**, 665.
28. Plouvier, V., *Comptes Rendues Academie de Science, Paris*, 1974, **279**, 1689.
29. Dahler, J. M., McConchie, C. A. and Turnbull, C. G. N., *Australian Journal of Botany*, 1995, **43**, 619.
30. Jensen, S. R. and Nielsen, B. J., *Acta Chemica Scandinavica*, 1973, **27**, 2661.
31. Nahrstedt, A., *Phytochemistry*, 1975, **14**, 1339.
32. Hegnauer, R., *Pharmaceutica Acta Helvetiae*, 1971, **46**, 585.
33. Spencer, K. C. and Seigler, D. S., *American Journal of Botany*, 1984, **71**, 1444.
34. Tjon Sie Fat, L. A., *Konink. Nederl. Akad. Wetensch.*, 1978, **81**, 347.
35. Schwarzmaier, U., *Chemische Berichte*, 1976, **109**, 3379.
36. Schwarzmaier, U., *Phytochemistry*, 1977, **16**, 1599.
37. Spencer, K. C. and Seigler, D. S., *Journal of Agricultural and Food Chemistry*, 1983, **31**, 794.
38. Eyjólfsson, R., *Acta Chemica Scandinavica*, 1970, **25**, 1898.
39. Poulton, J. E., in *Handbook of Natural Toxins Vol.* 1 *Plant and Fungal Toxins*, ed. R. F. Keeler and A. T. Tu. Marcel Dekker, Basel, 1983, p. 117.
40. Halstrom, F. and Moller, K. D., *Acta Pharmacologica et Toxicologica*, 1945, **1**, 18.
41. Coop, I. E. and Blakely, R. L., *New Zealand Journal of Science and Technology A*, 1949, **30**, 277.

42. Moran, E. A., *American Journal of Veterinary Research*, 1954, **15**, 171.
43. Christensen, H. E., *Registry of Toxic Effects of Chemical Substances*. National Institute of Occupational Safety and Health. DHEW Publication 191, 1976.
44. Towill, L. E., Drury, J. S., Whitefield, B. L., Lewis, E. B., Galyan, E. L. and Hammons, A. S. R., *Reviews of the Environmental Effects of Pollutants: V. Cyanide*. US Environmental Protection Agency, Cincinnati, 1978.
45. Conn, E. E., in *Toxicants Occurring Naturally in Foods* 2nd edn, Committee on Food Protection. National Academy of Sciences, Washington, 1973, p. 299.
46. Seigler, D. S., *Revista Latinoaméricana de Quimica*, 1981, **12**, 39.
47. Majak, W., *Canadian Journal of Animal Science*, 1987, **67**, 1133.
48. Majak, W., *Journal of Range Management*, 1992, **45**, 67.
49. Carter, J. H., McLafferty, M. A. and Goldman, P., *Biochemical Pharmacology*, 1980, **29**, 301.
50. Uwakwe, A. A., Monanu, M. O. and Anosike, E. O., *Plant Foods for Human Nutrition*, 1991, **41**, 117.
51. Westley, J., in *Cyanide Compounds in Biology*, ed. D. Evered, and S. Harnett. Wiley, Chichester, 1988, p. 201.
52. Nestel, B., in *Chronic Cassava Toxicity*, ed. B. Nestel and R. MacIntyre. International Development Research Centre, Ottawa, Canada, 1973, p. 11.
53. Wilson, J., in *Chronic Cassava Toxicity*, ed. B. Nestel and R. MacIntyre. International Development Research Centre, Ottawa, Canada, 1973, p. 121.
54. Wilson, J. and Matthews, D. M., *Clinical Science*, 1966, **31**, 1.
55. Montgomery, R. D., *American Journal of Clinical Nutrition*, 1965, **17**, 103.
56. Collomb, M., Quere, M. A., Cross, J. and Giordano, C., *Journal of Neurological Science*, 1967, **5**, 159.
57. Osuntokun, B. O., in *Chronic Cassava Toxicity*, ed. B. Nestel and R. MacIntyre. International Development Research Centre, Ottawa, Canada, 1973, p. 127.
58. Wilson, J., in *Cyanide Compounds in Biology*, ed. D. Evered and S. Harnett. Wiley, Chichester, 1988, p. 244.
59. Rosling, H., *Cassava Toxicity and Food Security*. University Hospital, Uppsala, Sweden, 1987.
60. Burgess, R. C., *Lancet*, 1946, **2**, 411.
61. Glander, K. E., Wright, P. C., Seigler, D. S., Randrianasolo, V. and Randrianasolo, B., *American Journal of Primatology*, 1989, **19**, 119.
62. Essers, A. J. A., Alsen, P. and Rosling, H., *Ecology, Food and Nutrition*, 1992, **27**, 17.
63. Ologhobo, A. D., Fetuga, B. L. and Tewe, O. O., *Food Chemistry*, 1984, **13**, 117.
64. Sundaresan, S., Nambisan, B. and Amma, C. S. E., *Indian Journal of Agricultural Sciences*, 1987, **57**, 37.
65. Pearsall, D. M., in *The Origins of Agriculture*, ed. C. W. Cowan and P. J. Watson. Smithsonian Institution Press, Washington, 1992, p. 173.
66. Crawford, G. W., in *The Origins of Agriculture*, ed. C. W. Cowan and P. J. Watson. Smithsonian Institution Press, Washington, 1992, p. 7.
67. Miller, N. F., in *The Origins of Agriculture*, ed. C. W. Cowan and P. J. Watson. Smithsonian Institution Press, Washington, 1992, p. 39.
68. Jones, D. A., *Nature, London*, 1962, **193**, 1109.
69. Jones, D. A., *Science*, 1971, **173**, 945.
70. Jones, D. A., in *Cyanide Compounds in Biology*, ed. D. Evered and S. Harnett. Wiley, Chichester (Ciba Foundation Symposium 140), 1988, p. 151.
71. Crawford-Sidebotham, T. J., *Heredity*, 1972, **28**, 405.
72. Compton, S. G. A. and Jones, D. A., *Biological Journal of the Linnaean Society*, 1985, **26**, 21.
73. Ennos, R. A., *Biological Journal of the Linnaean Society*, 1981, **15**, 75.
74. Jones, D. A., *Canadian Journal of Genetics and Cytology*, 1966, **8**, 556.
75. Nahrstedt, A., *Plant Systematics and Evolution*, 1985, **150**, 35.
76. Witthohn, K. and Naumann, C. M., *Zeitschrift für Naturforschung*, 1984, **39c**, 837.
77. Beesley, S. G., Compton, S. G. and Jones, D. A., *Journal of Chemical Ecology*, 1985, **11**, 45.
78. Jones, D. A., Parsons, J. and Rothschild, M., *Nature, London*, 1962, **193**, 52.
79. Nahrstedt, A., in *Phytochemical Diversity and Redundancy in Ecological Interactions*, ed. J. T. Romeo, J. A. Saunders and P. Barbosa. Plenum Press, New York, 1996, p. 217. (*Recent Advances in Phytochemistry*, Vol. 30).
80. Keymer, R. J., Ph.D. Thesis. University of Hull, 1978.
81. Jones, D. A., *Genetica*, 1972, **43**, 394.
82. Rehr, S. S., Feeny, P. P. and Janzen, D. H., *Journal of Animal Ecology*, **42**, 405, but see Seigler, D., Dunn, J. E., Conn, E. E. and Holstein, C. L., *Phytochemistry*, 1978, **17**, 445.
83. Majak, W., Bose, R. S. and Quinton, D. A., *Phytochemistry*, 1978, **17**, 803.
84. Georgiadis, N. J. and McNaughton, S. J., *Oikos*, 1988, **51**, 343.
85. Purseglove, J. W., *Tropical Crops: Dicotyledons 1*. John Wiley, New York, 1968.
86. Bernays, E. A., Chapman, R. F., Leather, E. M. and McCaffery, A. R., *Bulletin of Entomological Research*, 1977, **67**, 391.
87. Lal, S. S. and Maini, S. B., *Anz. Schädlingskde., Pflanzenschutz, Umweltschutz*, 1977, **50**, 138.

88. Cooper-Driver, G. A. and Swain, T., *Nature, London*, 1976, **206**, 604.
89. Schreiner, I., Nafus, D. and Pimental, D., *Ecological Entomology*, 1984, **9**, 69.
90. Sherbrooke, W. C., *Ecology*, 1976, **57**, 596.
91. Woodhead, D. and Bernays, E. A., *Nature, London*, 1977, **270**, 235.
92. Woodhead, D. and Bernays, E. A., *Entomology, Experimental Applications*, 1978, **24**, 123.
93. Horrill, J. C. and Richards, A. J., *Heredity*, 1986, **56**, 277.
94. Dritschilo, W., Krummel, J., Nafus, D. and Pimentel, D., *Heredity*, 1979, **42**, 49.
95. Burgess, R. S. L. and Ennos, R. A., *Oecologia*, 1987, **73**, 432.
96. Ellsbury, M. M., Pederson, G. A. and Fairbrother, T. E., *Journal of Economic Entomology*, 1992, **85**, 2467.
97. Kaplan, M. A. C., Figueiredo, M. F. and Gottlieb, O. R., *Biochemical Systems and Ecology*, 1983, **11**, 367.
98. Compton, S. G. A., *Ecological Entomology*, 1987, **12**, 115.
99. Compton, S. G. A., *South African Journal of Science*, 1989, **85**, 605.
100. Montgomery, R. D., in *Toxic Constituents of Plant Foodstuffs*, ed. I. E. Liener. Academic Press, New York, 1969, p. 143.
101. Nahrstedt, A., in *Phytochemistry and Agriculture*, ed. T. A. van Beek and H. Breteler. Clarendon Press, Oxford, 1993, p. 107.
102. Herren, H. R. and Neuenschwander, P., *Annual Review of Entomology*, 1991, **36**, 257.
103. Lozano, J. C. and Booth, R. H., *Diseases of Cassava* (*Manihot esculenta* Crantz). CIAT, Cali, Columbia, 1976.
104. Romanoff, S. and Lynam, J., *Ecology of Food and Nutrition*, 1992, **27**, 29.
105. Johns, T., in *Advances in Legume Systematics* 5: *The Nitrogen Factor*, ed. J. I. Sprent and D. McKey. Royal Botanic Gardens, Kew, 1994, p. 151.
106. Jones, D. A., Unattributed comment in *Chronic Cassava Toxicity*, ed. B. Nestel and R. MacIntyre. International Development Research Centre, Ottawa, Canada, 1973, p. 160.
107. Nassar, N. M. A. and Fichtner, S. S., *Canadian Journal of Plant Science*, 1978, **58**, 577.