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Review

Rising African cassava production, diseases due to high cyanide intake and control measures

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Abstract: Cassava is the staple food of tropical Africa and its production, averaged over 24 countries, has increased more than threefold from 1980 to 2005, and the population has more than doubled over that time compared with a 1.5 times increase worldwide. Agriculturally, cassava performs very well but the roots and leaves contain cyanogenic glucosides that are dangerous to human health. These cyanogens sometimes produce acute intoxication leading to death, they exacerbate goitre and cretinism in iodine-deficient regions, cause konzo and are implicated in the occurrence of tropical ataxic neuropathy and stunting of children. Konzo is an irreversible paralysis of the legs with many thousands of cases, mainly amongst children, in Mozambique, Tanzania, Democratic Republic of Congo, Cameroon, Central African Republic and probably other tropical African countries. Attempts to alleviate cassava cyanide toxicity have included the development of an information network and distribution in developing countries of picrate kits, which measure total cyanide in cassava and urinary thiocyanate. A simple wetting method that reduces total cyanide in cassava flour three- to sixfold has been successfully field tested and is being introduced in Mozambique. Transgenic technology shows promise in increasing the rate of loss of cyanide from roots during processing. World health and agricultural bodies should pay more attention to emerging health problems associated with toxicity of cyanogens in cassava.

Keywords: cyanide; cassava; poison; konzo; TAN; rising cassava production

INTRODUCTION

Cyanide is a very effective poison of animals, insects and plants. The lethal dose range for humans of hydrogen cyanide taken by mouth for a 60 kg adult amounts to 30–210 mg of HCN. The lethal dose is proportional to body weight.[1,2] It is therefore not surprising that more than 2000 plants use cyanide to protect themselves from animals and marauding insects.[3] These plants produce a cyanogenic glycoside and an enzyme that catalyses its hydrolysis to a cyanohydrin, which is then hydrolysed in a second reaction to HCN. This second hydrolysis occurs spontaneously and in some cases is catalysed by a second enzyme made by the plant. The cyanogenic glycoside and the hydrolytic enzyme must occur in different parts of the plant cell, otherwise the plant itself would be poisoned.[4] With cassava the cyanogenic glucoside is linamarin (and a small amount of lotaustralin – methyl linamarin), which is located in the plant cell vacuole, and the enzyme is linamarase, which is located in the cell wall.[5] If the plant cell is ruptured by a chewing insect then linamarase immediately hydrolyses linamarin to form acetone cyanohydrin, which is unstable above pH 5 and hydrolyses to HCN and acetone. The chewing insect is effectively deterred by the plant.

Linamarin is present in large amounts in the leaves and the peel of the roots (900–2000 mg HCN equivalents kg^{-1} fresh weight = ppm)[6] and the leaves also contain a second enzyme called hydroxynitrile lyase, which catalyses the hydrolysis of acetone cyanohydrin to produce HCN and acetone.[7] In some varieties of cassava the interior of the roots (parenchyma) contains only a small amount of cyanide. This is called sweet cassava, which may be boiled and eaten, as is normal in the South Pacific.[2] However, in Amazonia (the original source of cassava) and in Africa different varieties have a range of total cyanide contents in the parenchyma from very low to very high (1–1550 ppm).[6] Naturally occurring acyanogenic cassava has never been observed.[2] Since linamarin is bitter,[8] high-cyanide cassava roots

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containing >100 ppm cyanide are normally bitter and are called bitter cassava. One such variety in Nigeria is called 'chop and die'. If the plant is stressed by insect attack or by drought it normally makes more linamarin.[9] For example, the average cyanide content of cassava flour increased during drought in northern Mozambique from 45 to >100 ppm.[6,10]

The cassava plant is by far the most important human food source that uses cyanide as a defence mechanism. Cassava is the third most important food source in the tropics after rice and maize and is the staple food of about 600 million people. The use of cassava as a food source is increasing particularly in Africa, because it yields well even in poor soil without fertilizer, is drought resistant[11] and the root can be left in the ground for up to 3 years as a reserve source of food. In a drought the leaves drop off, the plant is kept alive by its large roots, and when the rains come the leaves sprout again. The roots are very starchy with lower protein content compared with other tropical root crops, and the young cassava leaves (after processing) are used in Africa as a good source of vitamins and protein.[2]

Because of its agricultural advantages and potential to feed rapidly increasing populations, cassava is increasingly popular with farmers particularly in countries of tropical Africa. Also households under stress from HIV/AIDS are switching from high-input to low-input farming systems that involve cassava.[12] It is difficult to understand how cassava can be promoted without giving proper consideration to the fact that it contains a cyanogen (linamarin) that liberates poisonous cyanide in the body.[13] It is the object of this paper to note the extent of increased production of cassava in Africa, the danger to health of the cyanogens that it contains and the contributions of an information network, cassava cyanide analysis kits, new methods of processing and gene technology towards reducing human cyanide intake.

RESULTS AND DISCUSSION

Effects of cyanide from cassava on humans

Consumption of cassava and cassava products containing large amounts of cyanide can cause acute intoxication, with symptoms of dizziness, headache, nausea, vomiting, stomach pains, diarrhoea and sometimes death.[14,15] Since the lethal dose of cyanide is proportional to body weight, children tend to be more susceptible to outright poisoning than adults. In regions where there is iodine deficiency, which causes goitre and cretinism, cyanide intake from cassava exacerbates these conditions.[16] In West Africa (particularly Nigeria), Tanzania, Uganda, Kenya, the West Indies and tropical Asia there is a disease called tropical ataxic neuropathy (TAN), which generally occurs in older people who have consumed a monotonous cassava diet over years. TAN is progressive and causes unsteady walking, produces loss of sensation in hands, loss of vision, deafness and weakness. Until recently long-term cyanogen intake was linked with the occurrence of TAN[17,18] but recent work has shown that the situation may be more complex.[19]

In eastern, southern and central Africa there is a disease called 'konzo', which causes irreversible paralysis of the legs, particularly in children and in women of child-bearing age. It is an upper motor neurone disease of sudden onset.[20–22] Konzo is persistent in some districts of Nampula Province of Mozambique[10] and larger outbreaks and epidemics occur as a result of droughts and war.[23] The linamarin content of cassava flour more than doubles during drought,[6,10] which leads to outbreaks of konzo; most recently there were more than 100 cases in Nampula and Zambezia Provinces due to drought in 2005.[24] The recent five-year civil war in the Democratic Republic of Congo (DRC) caused millions of deaths and forced people to live off the land and eat bitter cassava roots from the bush without processing, which caused many thousands of konzo cases in DRC. There have been more than 2000 cases of konzo in Mozambique since 1980 and a similar number of cases in Tanzania; konzo occurs in Cameroon and the Central African Republic and may also be present in other eastern, southern and central African countries.

When cassava is eaten, most of the ingested cyanide is converted into thiocyanate, a reaction catalysed by the enzyme rhodanese, which uses up part of the pool of S-containing essential amino acids methionine and cysteine/cystine.[17,25,26] These amino acids are essential in the diet because they can only be obtained from the food consumed.[26] A shortfall of these S-containing amino acids would limit protein synthesis and could cause stunting of growing children, as was found in a study of children in DRC.[27]

Average daily consumption of cassava and cyanide diseases

The average daily per capita consumption in 2005 of fresh and dried cassava obtained from FAO statistics[28] is given in Table 1 in descending order. Of the first 18 entries only one is not from Africa, namely Thailand, in seventh place. Nigeria, the world's largest producer of cassava, has twice the daily per capita consumption of Indonesia and nearly three times that of Brazil. The much lower per capita intake of cassava and hence of total cyanide in Brazil and Indonesia compared with these tropical African countries shows the greater diversity of the diet in Brazil and Indonesia.

A study made in Nampula Province in Mozambique showed that an estimated maximum cassava flour intake of children in an area prone to konzo was 700–900 g fresh flour per child per day and in a non-konzo area was 20–140 g fresh flour per child per day.[26] The estimated high consumption rates of cassava flour for children in a konzo-prone area are being approached by the daily per capita consumption of fresh cassava plus dried cassava in countries such as Angola, Mozambique and DRC, in two of which there have been recent outbreaks of konzo and for the

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Table 1. Daily per capita consumption in 2005 of fresh and dried cassava[28]

Country	Daily per capita consumption (g)
Angola	787
Mozambique	680
DRC	653
Congo	637
Ghana	546
Liberia	390
Thailand	383
Tanzania	373
Guinea	352
Central African Republic	347
Uganda	328
Benin	323
Nigeria	294
Malawi	282
Togo	274
Madagascar	252
Cote d'Ivoire	237
Cameroon	233
Indonesia	146
Brazil	105

third (Angola) we have no information. This shows the very great dependence of these African countries on cassava as a staple food and underlines the importance of paying attention to the cyanogens that it contains. By contrast, the consumption rate of cassava flour in a non-konzo area of 20–140 g is similar to that found in Indonesia and Brazil (see Table 1) where, as expected, there are no reports of the occurrence of konzo.

Effects on populations of rapidly increasing cassava consumption

A calculation of the ratio of consumption in 2005 divided by consumption in 1990 shows the highest value for Malawi (12.8), followed by Senegal (3.3), Guinea (2.4) Sierra Leone (2.3) and Angola (2.0). In Malawi cassava consumption increased from 22 g per capita per day in 1990 to 282 g per capita per day in 2005, while maize consumption decreased over the same period from 345 to 316 g per capita per day. In Senegal and Sierra Leone increased cassava consumption has occurred over the same period and appreciable reductions occurred in consumption of rice paddy. Reduction in consumption of maize in Malawi and rice in Senegal and Sierra Leone and increased consumption of cassava present a problem because of the cyanogens present in cassava and also its nutritional inferiority as compared with maize and rice.[2]

The five countries listed above all showed large increases in production of cassava over the same 15-year period.[29] Cassava is now grown in districts in these countries where it was not grown formerly and where there has been little or no experience of correct methods of processing to remove cyanogens. It is important that the introduction of cassava into new regions is accompanied by efforts to educate the people in correct methods of processing of cassava to remove cyanogens, rather than simply ignoring the dangerous aspects of this crop.[13]

Rising cassava production and population growth in Africa

In Table 2 there is a comparison between cassava production and population growth for the 25-year period from 1980 to 2005 for the major cassava-producing countries in tropical Africa. The data for the top four world producing countries of cassava are included for comparison. We note that for 24 African countries that produce cassava the mean 2005/1980 ratio for cassava production of 3.07 is high and the population 2005/1980 ratio of 2.08 is also high compared with major non-African cassava producers. By contrast, the second to fourth largest world producers of cassava – Brazil, Indonesia and Thailand respectively – have much lower rates of population growth (which approximate to the world average) and only modest increases in cassava production. It is likely that the high rate of population increase in these tropical African countries is a major cause of increased cassava production, which highlights the need for proper health safeguards against cyanide diseases.

Measures to control cyanide intake

Cassava Cyanide Diseases Network (CCDN)

In 2001 a free information network called the Cassava Cyanide Diseases Network was established to include all those who were interested and concerned with the problems of cyanide diseases from consumption of cassava. The declared object of the CCDN is to work together to eliminate cyanide poisoning, konzo and TAN. The network has grown to more than 250 members from 35 countries worldwide and produces a newsletter called *CCDN News*.[31]

Simple methods for measurement of total cyanide in cassava and thiocyanate in urine

In 1995 a new simple picrate kit method that can be used by non-chemists was developed to determine

Table 2. Comparisons of cassava production and population growth from 1980 to 2005

Country/world	Cassava production[29] Ratio 2005/1980	Population[30] Ratio 2005/1980
Mean of 24 cassava-growing African countries[a]	3.07	2.08
Nigeria	3.61	1.99
Brazil	1.14	1.54
Indonesia	1.42	1.50
Thailand	1.02	1.35
World	1.70	1.46

[a] The 24 African countries are Angola, Benin, Cameroon, Central African Republic, Chad, Congo, Cote d'Ivoire, DRC, Guinea, Ghana, Kenya, Liberia, Madagascar, Malawi, Mozambique, Niger, Nigeria, Senegal, Sierra Leone, Tanzania, Togo, Uganda, Zambia and Zimbabwe.

total cyanide in cassava products such as flour.[32] This was tested in Mozambique in 1996 and works well as a simple field test, with a 10-level colour chart from 0 to 800 ppm, and accurately by elution of the picrate paper with water and measurement of absorbance in a spectrophotometer.[32,33] An average result of 45 (37) ppm (range10–200 ppm) was obtained from 80 cassava flour samples from Nampula Province of Mozambique in a year of normal rainfall.[33] The method was improved and adapted to determine the total cyanide content of cassava roots,[34] and total cyanide in other cyanide-containing plants.[35] The average total cyanide content of cassava flour from the same locations in Nampula Province during drought increased to >100 ppm in 1997–8.[6,10] The World Health Organization safe level for cyanide in cassava flour is 10 ppm.[36]

A simple picrate kit method to determine thiocyanate in urine[37] was field tested in Mozambique in 1999. Since ingested linamarin is converted to thiocyanate in the body and excreted in the urine,[17,38] urinary thiocyanate analysis measures cyanide intake over previous days. High mean levels of 225–385 μmol thiocyanate L^{-1} were obtained in school children, consistent with the occurrence of konzo. Twenty-seven new konzo cases were observed and mean cyanide levels of >100 ppm were obtained in cassava flour.[10]

Since 1996, simple picrate cassava cyanide kits allowing 100 analyses and needing only water to operate have been produced at the Australian National University and given away free to health and agricultural workers in developing countries. Since 1999, a urinary thiocyanate kit has been added. More than 350 kits have been given away in developing countries and 150 kits have been sold in first world countries. This policy has helped many workers in tropical Africa to measure the total cyanide content of cassava and its products for the first time. This has made people aware of the problem but has not in itself helped to reduce cyanogen levels in their staple food.

Processing of cassava roots

Because the cassava root deteriorates in air in just a few days in the tropics and it also contains cyanogens, it must be processed to produce a stable and hopefully low-cyanide product that can be stored for many months.[2] Processing methods were developed by trial and error hundreds of years ago by indigenous people in Amazonia (the source of cassava) for the preparation of farinha.[39] Gari in West Africa is produced by a similar process. Because of the extensive literature on this subject reviewed by Padmaja,[40] it is not useful to attempt a review of all methods here, but rather to focus on some of the major processing methods used in tropical Africa, where there are considerable health problems associated with cyanide residues in cassava products. Some processing methods remove nearly all the cyanogens,[39,41] but others leave large amounts behind in the flour.[6,33,42] The simplest process, called sun drying, involves peeling the root and drying in the sun. It is then ground up in a wooden pestle and mortar and sieved to produce white cassava flour. This removes two-thirds to three-quarters of the cyanide.[41,42] In another method, called heap fermentation, a small heap of peeled cassava roots is left in the shade for 3–5 days, allowing fermentation inside the heap. The roots are then sun dried, pounded and sieved, producing a white grey flour. This method removes twice as much cyanogen as sun drying and is used by women processors in northern Mozambique when cyanide levels are high during drought.[6] However, although an improvement over sun drying, heap fermentation still leaves unacceptably high levels of cyanogen in the flour especially during drought, and does not stop the occurrence of konzo in eastern, southern and central Africa.[6]

In West Africa the major processed cassava product is gari. To make gari the peeled root is ground up using a mechanical grinder and placed in a hessian bag for 2–3 days; there is extensive hydrolysis of linamarin to hydrogen cyanide catalysed by linamarase as well as lactic fermentation, which reduces the pH to about 4. Excess water is squeezed out in a press and the product is roasted by heating over a wood fire in a metal pan with continuous stirring, which removes HCN and water and produces gari. The total cyanide content of gari is in the range 0–40 ppm, with an average of 20 ppm,[43–45] which is still twice the WHO safe level of 10 ppm.[36] There are no reports of the occurrence of konzo in West Africa west of Cameroon, which is consistent with the assessment that konzo occurs after very high cyanide intake over a relatively short period. By contrast, TAN (or a similar syndrome) has been reported from West Africa (especially Nigeria), Tanzania, Uganda, Kenya, the West Indies and various parts of tropical Asia, amongst mainly older poor people who have consumed cyanide from cassava (mainly gari) over many years.[18]

New wetting method to remove cyanide from flour

Preliminary experiments showed that the total cyanide content of dry cassava flour remained constant for more than 6 months under ambient laboratory conditions. At 100% relative humidity at room temperature the cyanide level fell by about 30% per week. On mixing many different cassava flour samples with water and standing at 30 °C for 5 h, on average about two-thirds of the cyanide was lost.[46] At low linamarase concentration little HCN was lost, but losses increased greatly if exogenous linamarase was added. Water rapidly swelled the flour and the linamarase present catalysed hydrolysis of linamarin to acetone cyanohydrin, which hydrolysed spontaneously at pH > 6 to HCN. Thirty cassava flour samples from Nampula Province showed an average loss of five-sixths of their cyanide. With larger (500 g) samples of flour it was necessary to spread out the wet flour in a thin layer for 5 h so that the HCN gas could escape readily.[47]

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The method was field tested in Nampula and Zambezia Provinces during a period of drought in 2005, when more than 100 new cases of konzo were examined. Rural women filled a bowl with flour, spread it out evenly and marked the level on the bowl. Water was added with mixing until the wet flour came up to the same mark. The wet flour was spread in a thin layer not more than 1 cm thick on a basket and left in the shade for about 5 h for HCN gas to escape. As is traditional, the wet flour was mixed with boiling water to produce a stiff porridge. In a blind taste test local volunteers tasted stiff porridge made from untreated and from treated flour. About 60% preferred the stiff porridge made from treated flour, presumably because it lacked the bitter taste of linamarin still present in the untreated flour.[24] A project for the rehabilitation of konzo sufferers and prevention of konzo is in progress under the auspices of the Mozambican Red Cross and funded by the Australian Agency for International Development (AusAID) in konzo-prone districts of Nampula Province in Mozambique; a similar initiative has just been funded for work in the Mtwara Region of southern Tanzania. In order to advertise the simple wetting method to remove cyanide from flour amongst rural women, a laminated coloured poster, originally produced by Dr Dulce Nhassico in Portuguese, has been modified and made available for free in various languages, especially African languages.[48] Some work is also in progress in DRC. As a result of these initiatives it is hoped that the wetting method will be widely adopted in those areas in eastern, southern and central Africa where konzo occurs and that this may lead to a great reduction in konzo and other diseases associated with chronic cyanide intoxication.

Transgenic technology

Although very low cyanide cassava root parenchyma has been analysed,[49] acyanogenic root parenchyma has never been seen in nature.[2] This has now been achieved in transgenic plants.[50,51] In the plant, the first step in the synthesis of linamarin from valine is catalysed by two closely related P450 enzymes. The genes that code for these P450 enzymes were isolated by Anderssen *et al*.[52] Using antisense technology the expression of the genes coding for the P450 enzymes were inhibited and in this way linamarin synthesis was blocked. Leaf linamarin content was reduced between 60% and 94% and the root linamarin content to <1% of wild-type levels. However, these antisense plants failed to produce roots unless reduced nitrogen (ammonia) was present in the soil. This interesting result suggested that linamarin synthesized in the leaves was transported to roots and was used there as a source of reduced nitrogen. Thus the inhibition of linamarin synthesis in these transgenic plants may reduce plant yields. A further possible problem would be the need for strategies to control animal and insect attack of transgenic cassava with lowered linamarin in its leaves, since this serves as a natural defence mechanism.[53]

Cassava leaves contain the enzyme hydroxynitrile lyase (HNL), which catalyses the hydrolysis of acetone cyanohydrin to acetone and hydrogen cyanide, but there is virtually no HNL present in cassava roots.[4] However, if cassava roots contained HNL then this would reduce the amount of residual acetone cyanohydrin present in gari, which constitutes most of the residual cyanogens present in gari.[54] Furthermore, acetone cyanohydrin is completely broken down to poisonous cyanide under the alkaline conditions of the gut, whereas it is estimated that less than one half of ingested linamarin is broken down to cyanide in the body.[38] Thus it would be advantageous to reduce greatly the amount of acetone cyanohydrin residues present in cassava products by the incorporation of HNL into cassava roots. This has now been achieved[7] through the production of transgenic cassava in which HNL was over-expressed in leaves (twofold increase) and in roots (13-fold increase).

Roots processed from transgenic plants have threefold lower levels of residual acetone cyanohydrin compared with roots from untransformed plants.[7] Linamarin contents of the roots and leaves of these transgenic plants are the same as those of wild-type plants; hence these transgenic plants should retain their ability to deter animals and insects. Currently, transgenic cassava plants with HNL incorporated into the root seem to be the best prospect for removing acetone cyanohydrin from processed cassava products such as gari. The introduction of transgenic cassava into tropical countries of Africa may present some problems, because genetically modified organisms (GMOs) have proved to be controversial and GMO food aid has been banned by a number of southern African countries. A recent conference of African Union Ministers of Agriculture attempted to achieve a common African position on GMOs and is creating a taskforce to move this agenda forward.[55]

CONCLUSION

The cyanogens present in cassava and cassava products can cause acute intoxication leading sometimes to death, they exacerbate goitre and cretinism in iodine-deficient areas, cause konzo and are involved with TAN and stunting of children. The incidence of konzo alone in at least five African countries may in total be of the order of 100 000 persons. This health problem in tropical Africa is occurring alongside a rapid rise in cassava production and population that far exceeds the rise in cassava production and population of Indonesia and Brazil, two of the world's largest cassava producers. Furthermore, cassava is being introduced into new areas where people are not familiar with it and have little or no experience of the potential danger to human health of the cyanogens it contains, or of processing methods to remove the cyanide. It would be wrong for cassava to be promoted as a means to solve the food problems of tropical Africa,[13] without consideration being given to the considerable human health problems due to the cyanogens that it contains. The poorest of the poor in marginal agricultural areas in many parts of tropical Africa have very little other than cassava to eat. They live in double jeopardy because they must eat cassava or else starve, but if they consume cassava they may get acute intoxication and possibly konzo. Surely this health problem due to cyanide intake from consumption of cassava in tropical Africa requires attention from health and agricultural bodies of the world.

The control measures in place include: (1) the CCDN, which is an information network with 250 members;[31] (2) simple free kits to determine total cyanide in cassava and its products and urinary thiocyanate;[32–34,37] (3) a new wetting method to reduce the cyanide content of cassava flour three- to sixfold and its implementation in konzo-prone areas of Mozambique and Tanzania;[24,46,47] and (4) a new transgenic variety of cassava that promotes increased rate of removal of hydrogen cyanide during processing.[7] These complementary approaches deal with different aspects of the same problem. It is hoped that other new approaches may be forthcoming in the future to tackle this challenging health problem.

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REFERENCES

1 Montgomery RD, Cyanogens, in *Toxic Constituents of Plant Foodstuffs*, ed. by Liener IE. Academic Press, New York, pp. 143–160 (1980).

2 Bradbury JH and Holloway WD, *Chemistry of Tropical Root Crops: Significance for Nutrition and Agriculture in the Pacific*. *Australian Centre for International Agricultural Research, Monograph* No 6, Canberra, Australia (1988).

3 Jones DA, Why are so many plants cyanogenic? *Phytochemistry* **47**:155–162 (1998).

4 White WLB, Arias-Garzon DI, McMahon JM and Sayre RT, Cyanogenesis in cassava. *Plant Physiol* **116**:1219–1225 (1998).

5 Mkpong OE, Yan H, Chism G and Sayre RT, Purification, characterization and localization of linamarase in cassava. *Plant Physiol* **93**:176–181 (1990).

6 Cardoso AP, Mirione E, Ernesto M, Massaza F, Cliff J, Haque MR, *et al*, Processing of cassava roots to remove cyanogens. *J Food Comp Anal* **18**:451–460 (2005).

7 Siritunga D, Arias-Garzon D, White W and Sayre RT, Over-expression of hydroxynitrile lyase in cassava roots accelerates cyanogenesis and detoxification. *Plant Biotechnol J* **2**:37–43 (2004).

8 King NLR and Bradbury JH, Bitterness of cassava: identification of a new apiosyl glucoside and other compounds that affect its bitter taste. *J. Sci Food Agric* **68**:223–230 (1995).

9 Bokanga M, Ekanayake IJ, Dixon AGO and Porto MCM, Genotype–environment interactions for cyanogenic potential in cassava. *Acta Hortic* **375**:131–139 (1994).

10 Ernesto M, Cardoso AP, Nicala D, Mirione E, Massaza F, Cliff J, *et al*, Persistent konzo and cyanide toxicity from cassava in northern Mozambique. *Acta Trop* **82**:357–362 (2002).

11 El-Sharkawy MA, Cassava biology and physiology. *Plant Mol Biol* **56**:481–501 (2004).

12 FAO Corporate Document Repository. [Online]. The impact of HIV/AIDS on the agricultural sector. Available: http://www.fao.org/DOCREP/005/Y4636E/y4636e05.htm [25 July 2008].

13 Madamombe I, Is cassava Africa's new staple food? *Africa Renewal* **20**:13 (2006).

14 Mlingi N, Poulter NH and Rosling H, An outbreak of acute intoxications from consumption of insufficiently processed cassava in Tanzania. *Nutr Res* **12**:677–687 (1992).

15 Akintonwa A, Tunwashe O and Onifade A, Fatal and non-fatal acute poisoning attributed to cassava – based meal. *Acta Hortic* **375**:285–288 (1994).

16 Delange F, Ekpechi LO and Rosling H, Cassava cyanogenesis and iodine deficiency disorders. *Acta Hortic* **375**:289–293 (1994).

17 Osuntokun BO, Cassava diet, chronic cyanide intoxication and neuropathy in Nigerian Africans. *World Rev Nutr Diet* **36**:141–173 (1981).

18 Osuntokun BO, Chronic cyanide intoxication of dietary origin and a degenerative neuropathy in Nigerians. *Acta Hortic* **375**:311–321 (1994).

19 Oluwole ASA, Onabolu AO, Cotgreave IA, Rosling H, Persson A and Link H, Incidence of endemic ataxic polyneuropathy and its relation to exposure to cyanide in a Nigerian community. *J Neurol Neurosurg Psychol* **74**:1417–1422 (2003).

20 Ministry of Health Mozambique, Mantakassa: an epidemic of spastic paraparesis associated with chronic cyanide intoxication in a cassava staple area of Mozambique. 1. Epidemiology and clinical and laboratory findings in patients. *Bull World Health Org* **62**:477–484 (1984).

21 Howlett WP, Brubaker GR, Mlingi N and Rosling H, Konzo, an epidemic upper motor neuron disease studied in Tanzania. *Brain* **113**:223–235 (1990).

22 Howlett WP, Konzo: a new human disease entity. *Acta Hortic* **375**:323–329 (1994).

23 Cliff J, Nicala D, Saute F, Givragy R, Azambuja G, Taela A, *et al*, Konzo associated with war in Mozambique. *Trop Med Int Health* **2**:1068–1074 (1997).

24 Muquingue H, Nhassico D, Cliff J, Sitoe L, Tonela A and Bradbury JH, Field trial in Mozambique of a new method for detoxifying cyanide in cassava products. *CCDN News* No. (6:):3–4 (2005).

25 Westley J, Mammalian cyanide detoxification with sulphane sulphur, in *Cyanide Compounds in Biology*. *Ciba foundation Symposium* 140, Wiley, Chichester, pp. 201–212 (1988).

26 Cardoso AP, Ernesto M, Nicala D, Mirione E, Chavane L, N'zwalo H, *et al*, Combination of cassava flour cyanide and urinary thiocyanate measurements of school children in Mozambique. *Int J Food Sci Nutr* **55**:183–190 (2004).

27 Banea-Mayambu JP, Tylleskar T, Tylleskar K, Gebre-Medhin M and Rosling H, Dietary cyanide from insufficiently processed cassava and growth retardation in children in the Democratic Republic of Congo. *Ann Trop Paediatr* **20**:34–40 (2000).

28 FAO [Online]. FAOSTAT. Available: http://faostat.fao.org/site/345/default.aspx [25 July 2008].

29 http://faostat.fao.org/site/340/default.aspx [23 October 2007].

30 *World Population Prospects*, The 2006 Revision UN, Department of Economic and Social Affairs, Table A8, NY (2007).

31 Cassava Cyanide Diseases Network (CCDN). [Online]. Available: http://online.anu.edu.au/BoZo/CCDN/ [25 July 2008].

32 Egan SV, Yeoh HH and Bradbury JH, Simple picrate paper kit for determination of the cyanogenic potential of cassava flour. *J Sci Food Agric* **76**:39–48 (1998).
33 Cardoso AP, Ernesto M, Cliff J, Egan SV and Bradbury JH, Cyanogenic potential of cassava flour: field trial in Mozambique of a simple kit. *Intern J Food Sci Nutr* **49**:93–99 (1998).
34 Bradbury MG, Egan SV and Bradbury JH, Determination of all forms of cyanogens in cassava roots and cassava products using picrate paper kits. *J Sci Food Agric* **79**:593–601 (1999).
35 Haque MR and Bradbury JH, Total cyanide determination of plants and foods using the picrate and acid hydrolysis methods. *Food Chem* **77**:107–114 (2002).
36 FAO/WHO, *Joint FAO/WHO Food Standards Programme*, *Codex Alimentarius Commission* XII, Supplement 4, FAO, Rome (1991).
37 Haque MR and Bradbury JH, Simple method for determination of thiocyanate in urine. *Clin Chem* **45**:1459–1464 (1999).
38 Carlsson L, Mlingi N, Juma A, Ronquist G and Rosling H, Metabolic fates in humans of linamarin in cassava flour ingested as a stiff porridge. *Food Chem Technol* **37**:307–312 (1999).
39 Dufour DL, Cassava in Amazonia: lessons in utilization and safety from native peoples. *Acta Hortic* **375**:175–182 (1994).
40 Padmaja G, Cyanide detoxification in cassava for food and feed uses. *Crit Rev Food Sci Nutr* **35**:299–339 (1995).
41 Nambisan B and Sundaresan S, Effect of processing on the cyanoglucoside content of cassava. *J. Sci Food Agric* **36**:1197–1203 (1985).
42 Mlingi NLV and Bainbridge Z, Reduction of cyanogen levels during sun-drying of cassava in Tanzania. *Acta Hortic* **375**:233–239 (1994).
43 Oke OL, Eliminating cyanogens from cassava through processing: technology and tradition. *Acta Hortic* **375**:163–174 (1994).
44 Aletor VA, Cyanide in garri. 1. Distribution of total, bound and free hydrocyanic acid in commercial garri, and the effect of fermentation time on residual cyanide content. *Int J Food Sci Nutr* **44**:281–287 (1993).
45 Adindu MN, Olayemi FF and Nze-Dike OU, Cyanogenic potential of some cassava products in Port Harcourt markets in Nigeria. *J Food Comp Anal* **16**:21–24 (2003).
46 Bradbury JH, Simple wetting method to reduce cyanogen content of cassava flour. *J Food Comp Anal* **19**:388–393 (2006).
47 Cumbana A, Mirione E, Cliff J and Bradbury JH, Reduction of cyanide content of cassava flour in Mozambique by the wetting method. *Food Chem* **101**:894–897 (2007).
48 Denton I, Getting the konzo prevention message out. *CCDN News* No. (10:):4 (2007).
49 Bradbury JH, Egan SV and Lynch MJ, Analysis of cyanide in cassava using acid hydrolysis of cyanogenic glucosides. *J Sci Food Agric* **55**:277–290 (1991).
50 Siritunga D and Sayre RT, Generation of cyanogen-free transgenic cassava. *Planta* **217**:367–373 (2003).
51 Siritunga D and Sayre RT, Engineering cyanogen synthesis and turnover in cassava. *Plant Mol Biol* **56**:661–669 (2004).
52 Anderssen M, Bush P, Svendsen I and Moller B, Cytochromes P450 from cassava catalysing the first steps in the biosynthesis of the cyanogenic glucosides linamarin and lotaustralin. *J Biol Chem* **275**:1966–1975 (2000).
53 Taylor N, Chavarriaga P, Raemakers K, Siritunga D and Zhang P, Development and application of transgenic technologies in cassava. *Plant Mol Biol* **56**:671–688 (2004).
54 Onabolu AO, Oluwole OSA, Rosling H and Bokanga M, Processing factors affecting the level of residual cyanohydrins in garri. *J Sci Food Agric* **82**:966–969 (2002).
55 http://www.africaunion.org/root/au/Conferences/2008/february/rea/cama/Experts_GMOs.pdf [14 April 2008].

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