Chapter

Toxicity Potential of Cyanogenic Glycosides in Edible Plants

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Abstract

Cyanogenic glycosides are natural phytotoxins produced by over 2000 plant species, many of which are consumed by humans. The important food crops that contain cyanogenic glycosides include cassava (*Manihot esculenta*), sorghum (*Sorghum bicolor*), cocoyam (*Colocasia esculenta* L. and *Xanthosoma sagittifolium* L.), bamboo (*Bambusa vulgaris*), apple (*Malus domestica*), and apricot (*Prunus armeniaca*). Cyanogenic glycosides and their derivatives have amino acid-derived aglycones, which spontaneously degrade to release highly toxic hydrogen cyanide (HCN). Dietary cyanide exposure has been associated with several health challenges such as acute cyanide poisoning, growth retardation, and neurological disorders. This chapter will introduce general cyanogenesis principles, highlight major food plants with lethal cyanide levels, and provide epidemiological-based health conditions linked to cyanide intake. Furthermore, strategies for elimination of cyanogens from food crops, such as processing technologies, will be discussed. Finally, the chapter will analyze the role of cyanogenic plants in ensuring food security among resource-poor communities.

Keywords: cyanogenic glycosides, cyanogens, phytotoxins, detoxification, food safety

1. Introduction

Many plant species that are grown for food contain phytotoxins in different parts of the plant. Natural toxins are usually secondary metabolites produced by plants for defensive purposes against threats such as bacteria, fungi, insects, and predators [1]. They may also occur in food plants because of natural selection and new breeding methods that enhance protective mechanisms of the crops [2]. The most common natural toxins found in food plants include lectins in beans, glycoalkaloids in potatoes, and cyanogenic glycosides in cassava, bitter apricot seed, bamboo shoots, and flaxseeds [3]. A review of several natural toxins in food plants commonly consumed in the world, including the toxicological effects associated with the ingestion of these toxins, shows that cyanogenic glycosides are the most important and extensively studied group of phytotoxins [4].

Cyanogenic glycosides are chemical compounds that release hydrogen cyanide (HCN) and are common in certain families such as the Fabaceae, Rosaceae, Leguminosae, Linaceae, and Compositae [2]. Approximately 25 cyanogenic glycosides, which are mostly found in the edible parts of plants, have been identified [4]. The potential toxicity of cyanogenic glycosides and their derivatives largely depends on their ability to release hydrogen cyanide. Dietary cyanide exposure

may result in acute poisoning and has also been associated with the etiology of several chronic diseases [5]. Therefore, the presence of cyanogenic glycosides in food and fodder presents a significant social and economic problem in many parts of the world, particularly in developing countries. In Africa, consumption of insufficiently processed cassava (*Manihot esculenta* Crantz) has been associated with cyanide poisoning, tropical ataxic neuropathy (TAN) disease, and konzo [6, 7]. In 1992, the death of three people in Nigeria was attributed to cyanide intake from cyanogenic glycosides of cassava [5], and a decade ago five Nigerians died of cyanide poison after reportedly eating a meal prepared with cassava flour.

Cyanogenic glycosides found in plants are not toxic on their own. However, when cell structures of plant are disrupted, cyanogenic glycoside will be brought together with the corresponding hydrolytic β-glucosidase enzyme. Subsequently, the glycoside degenerates to a sugar and a cyanohydrin that rapidly decomposes to hydrogen cyanide and an aldehyde or a ketone [8]. In bitter almonds and peach stones, cyanogenic glycoside, amygdalin, is converted to glucose, benzaldehyde, and toxic hydrogen cyanide. In edible plants, cyanide levels are reduced significantly during the processing to an accepted Food and Agricultural Organization (FAO)/World Health Organization (WHO) level of 10 mg HCN/kg dry weight [9]. However, when poorly processed lethal concentrations of the cyanogens may be obtained in the final edible products.

2. Cyanogenic glycosides in food plants

Cyanogenic glycosides are a structurally diverse class of secondary metabolites that are mostly used by plants as a defense against various threats such as bacteria, fungi, insects, and predators [1]. The compounds consist of α-hydroxynitrile aglycones attached to a sugar moiety (Vetter, 2000) and are widely distributed in the plant kingdom [10]. Cyanogenic glycosides are common in certain families such as the Fabaceae, Rosaceae, Leguminosae, Linaceae, and Compositae, and their constituents provide a useful tool for taxonomic identification [2]. Several important food plants are known to synthesize cyanogenic glycosides; for example, linamarin in cassava and butter bean, dhurrin in sorghum and macadamia nut, and amygdalin in almond, peach, sweet cherry, and sour cherry [2, 11].

2.1 Biosynthesis of cyanogenic glycosides

In plants, cyanogenic glycosides are derivatives of five amino acids (valine, isoleucine, leucine, phenylalanine, and tyrosine) and the non-proteinogenic amino acid, cyclopentenyl glycine. Linamarin and lotaustralin are derived from valine, isoleucine, and leucine, while dhurrin is derived from tyrosine. Amygdalin and prunasin are derived from phenylalanine [12]. The biosynthesis of various cyanogenic glycosides in different plants has been described, and the most extensively reported are dhurrin in sorghum and linamarin in cassava [10]. The generic biosynthetic pathway for the production of cyanogenic glycosides from amino acids is shown in **Figure 1**.

The first two steps of biosynthetic production of cyanogenic glycoside are catalyzed by a cytochrome P450 enzyme through two successive N-hydroxylations of the amino group of the parent amino acid. The α-hydroxynitrile (cyanohydrin) is then generated following the decarboxylation and dehydration of aldoxime and nitrile, respectively [14]. The final step that produces cyanogenic glycoside involves glycosylation of the cyanohydrin moiety, and the process is catalyzed by UDPG-glycosyltransferase [10].

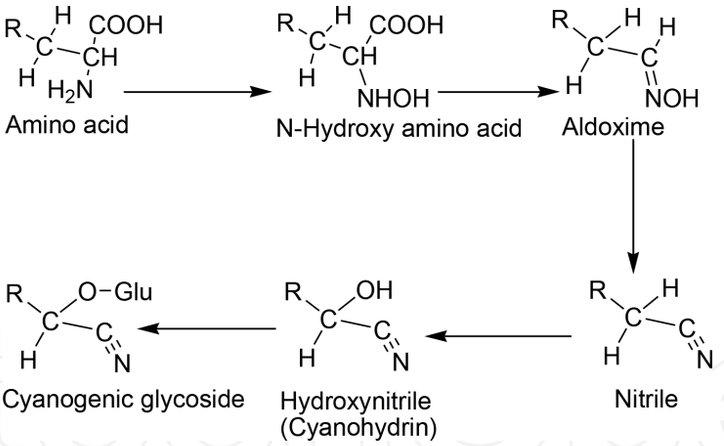

Figure 1.
The biosynthetic pathway for cyanogenic glycosides from its precursor amino acid [13].

2.2 Cyanogenesis

Cyanogenesis is the ability of some plants to synthesize cyanogenic glycosides to form hydrogen cyanide via cyanohydrin intermediate [15, 16]. The hydrolysis of the cyanogenic glycosides is accomplished by the β-glucosidase enzymes, which facilitate the cleavage of the carbohydrate moiety of the cyanogenic glycoside to yield corresponding cyanohydrins which further decompose to release hydrogen cyanide and an aldehyde or ketone [17] as illustrated in **Figure 2**. The final step that produces the toxic compound, HCN, is catalyzed by hydroxynitrile lyase enzyme, which is widespread in cyanogenic plants [16].

The cyanogenic glycosides linamarin (α-hydroxybutyronitrile-β-D-glucopyranoside) and lotaustralin (ethyl linamarin) are distributed in cassava cell vacuoles, while the enzyme linamarase is found in the cell wall [18]. The hydrolysis of linamarin in cassava starts with the disruption of the root tissue during

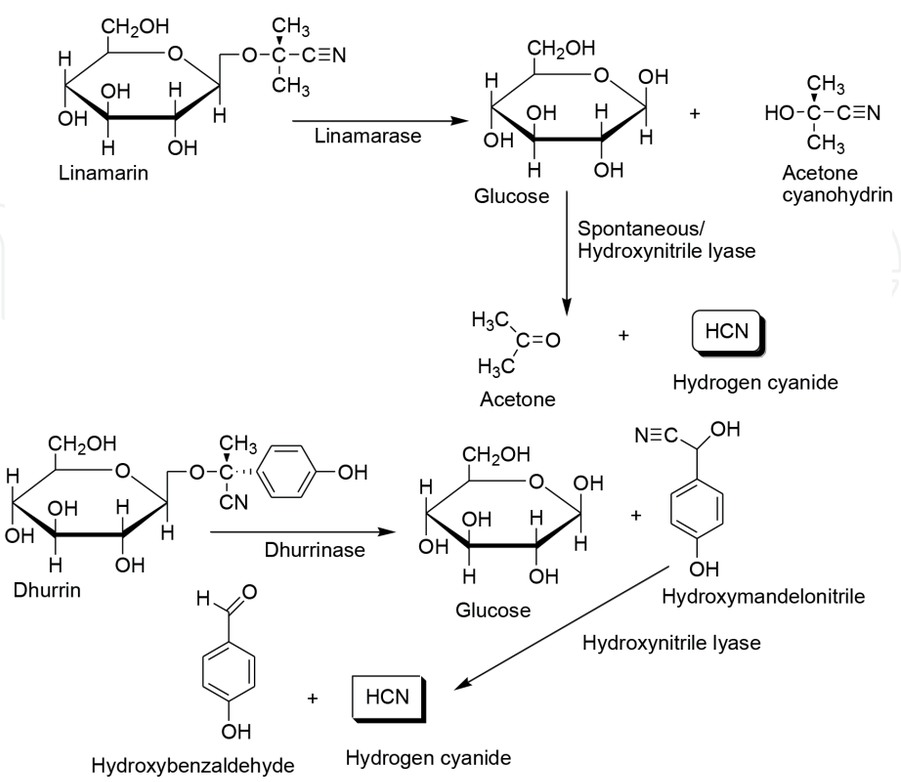

Figure 2.
Enzymatic hydrolysis of cyanogenic compounds, linamarin, and dhurrin.

processing or chewing to release the endogenous enzyme (linamarase), which catalyzes the hydrolysis of linamarin to glucose and acetone cyanohydrins. During processing factors such as reduced moisture and increased temperature facilitate the spontaneous conversion of cyanohydrins to toxic hydrogen cyanide and the corresponding ketone, acetone [19].

In sorghum, the cyanogenic glycoside dhurrin (4-hydroxymandelonitrile-β-D-glucopyranoside) and the enzyme β-glucosidase (dhurrinase) are stored in separate plant compartments. However, when the plant tissue is crushed, the enzyme and substrate dhurrin are brought in contact. The hydrolysis of dhurrin is then initiated by dhurrinase, which hydrolyzes the cyanogenic glycoside to form hydroxymandelonitrile and glucose. In acidic conditions or in the presence of hydroxynitrile lyase, the intermediate compound, hydroxymandelonitrile, further decomposes to generate hydrogen cyanide and hydroxybenzaldehyde [19] as shown in **Figure 2**. In food plants, cyanogenic glycosides are not toxic on their own. However, when cell structures of a plant are disrupted, cyanogenic glycosides will be brought together with the corresponding β-glucosidase enzyme to liberate a toxic compound, HCN.

3. Food plants with cyanogenic compounds

Cyanogenic glycosides are present in over 100 families of flowering plants, and at least 2000 plant species are known to contain this class of natural toxins. In addition to high plants, they are also found in some species of ferns, fungi, and bacteria [16]. Cyanogenic glycosides are amino acid-derived constituents of plants produced as secondary metabolites and are used as a defensive mechanism against various threats such as bacteria, fungi, insects, and other predators. There are wide variations in the levels of cyanogenic glycosides in plants due to genetic and environmental factors such as location, season, and soil types [3]. **Table 1** shows the types of cyanogenic glycosides commonly found in major edible plants.

Approximately 25 cyanogenic glycosides have been reported in different cyanogenic food plants, and **Figure 3** shows structures of examples of cyanogenic glycosides commonly found in edible plants.

3.1 Cassava

Cassava (*Manihot esculenta* Crantz) is a perennial crop that originated from South America and was introduced in Africa by the Portuguese explorers during

Species	Family	Vegetative part	Source of HCN
Cassava (*Manihot esculenta*)	Euphorbiaceae	Leaves, tuber peel, and parenchyma	Linamarin Lotaustralin
Sorghum (*Sorghum bicolor*)	Poaceae	Fruits (seeds), shoot tips, and leaves	Dhurrin
Cocoyam (*Colocasia esculenta* and *Xanthosoma sagittifolium*)	Araceae	Leaves and roots	Dhurrin
Bamboo (*Bambusa vulgaris*)	Poaceae	Stem and sprouts	Taxiphyllin
Apple (*Malus domestica*)	Rosaceae	Seeds and fruits	Amygdalin
Apricot (*Prunus armeniaca*)	Rosaceae	Kernels	Amygdalin Prunasin

Table 1.
Cyanogenic glycosides in major edible plants.

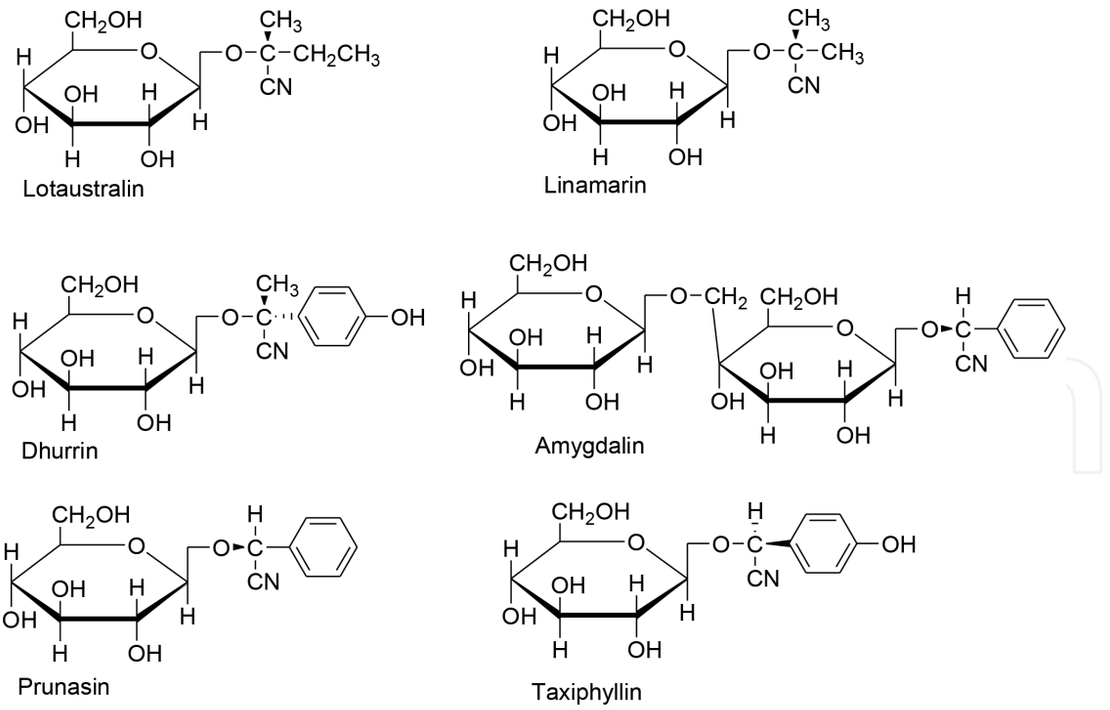

Figure 3.
Structures of cyanogenic glycosides found in major edible plants [20].

the sixteenth and seventeenth centuries. The crop is a staple food in most African communities and has economic value in Africa, South America, and Southeast Asia. The crop is widely cultivated in the tropics, and a total area of over 18 million ha is grown to cassava [21], and over half a billion of the world's population depend on cassava as their major staple [22]. Africa is the largest producer of cassava in the world and accounts for over 53% of the global production [23]. According to the Food and Agriculture Organization, cassava is ranked third, after rice and corn, as the most important source of calories in the tropics [23]. The tuberous roots of the crop have high carbohydrate content, which makes cassava a good source of calorie for over half a billion people in the world. Additionally, cassava leaves are rich in proteins, vitamin C, vitamin A, and dietary fiber. Cassava is one of the world's most important tuberous food crops, with annual global production estimated at 252 million metric tons (MT) in 2011. **Table 2** shows the production trend among the top five producing countries in the world according to the Food and Agriculture Organization statistics [23].

Country	Annual cassava production quantity (million metric tons)				
	2007	2008	2009	2010	2011
Nigeria	43.41	44.58	36.82	42.53	52.40
Brazil	26.54	26.70	24.40	24.50	25.45
Indonesia	19.99	21.59	22.04	23.92	24.01
Thailand	26.92	25.16	30.09	22.21	21.91
Ghana	10.22	11.35	12.23	13.50	14.24
Others	99.35	102.62	109.87	110.25	114.20
World	226.43	232.00	235.45	236.11	252.21

Table 2.
Major cassava-producing countries in the world.

Despite the nutritional and economic benefits obtained from cassava, almost all parts of the plant contain cyanogenic glycosides, which limits the potential utilization of the plant as food for human and animal consumption. Each part of the cassava plant (leaves, stem, root) contains high levels of cyanogenic glycosides, mainly linamarin and lotaustralin with the former being the most predominant cyanogen at the ratio of 9:1 [17]. The biosynthesis of the major cyanogenic glucoside in cassava, linamarin, occurs in leaves and is then transported to the tuber [24]. Cassava leaves and the cortex or peel of the roots contain large quantities of cyanogenic glycosides (900–2000 mg HCN/kg dry matter) [8], while the tuberous parenchyma has approximately 20-fold lower levels. Studies have found that cassava roots contain a total cyanide content of 10–500 mg/kg of dry matter [25] although higher contents have also been reported, particularly in bitter cultivars. All cassava varieties are known to contain cyanogenic compounds, and cyanide levels depend on factors such as variety, plant age, soil condition, fertilizer application, and environmental conditions [25].

3.2 Cocoyam

Cocoyam generally refers to two members of the Araceae family, namely, *Colocasia esculenta* (L.) Schott and *Xanthosoma sagittifolium* (L.) Schott. The plant is native to Central and South America where it has been cultivated and consumed for centuries but has since been naturalized in most tropical regions including sub-Saharan Africa [26]. Cocoyam is an important staple for most rural communities in many developing countries of Africa, Asia, and the Pacific. In sub-Saharan Africa, the most cultivated species, *Colocasia esculenta*, is extensively grown for livelihood by small-scale resource-poor farmers with minimal input.

For the last 3 decades, Africa's annual cocoyam output of about 10 MT has consistently been higher than other regions [9]. The continent's contribution to the global cocoyam output is presented in **Table 3**. The mean global production in the 2003–2012 decade was more than double the mean production obtained in the years between 1983 and 1992, which could principally be attributed to increased production in Africa. The major cocoyam-producing countries in Africa are Nigeria, Ghana, and Cameroon, which contributed about 68% of the global mean output between 2003 and 2012.

Edible cocoyam is a nutrient dense tuber crop that can be processed into flour and used to make mashed meal or porridge. The tubers can also be consumed baked or boiled. Cocoyam is rich in carbohydrates; as a result, it is an important source of

Producer	1983–1992		1993–2002		2003–2012	
	Mean[a]	%[b]	Mean	%	Mean	%
World	4.88		8.04		10.72	
Africa	2.74	56.26	5.88	73.13	8.25	76.96
China	1.20	24.62	1.40	17.47	1.61	15.04
Cameroon	0.49	10.14	0.88	10.98	1.40	13.02
Ghana	1.01	20.64	1.53	19.04	1.57	14.62
Nigeria	0.52	10.61	2.60	32.36	4.28	39.91

[a]*Mean production in million tons over 10 years.*
[b]*Percentage of contribution to global mean.*

Table 3.
Contributions of top producers to global cocoyam output in the last 3 decades [9].

calorie for millions of people in the tropical and subtropical regions [27]. In addition to carbohydrates, cocoyam contains other nutrients such as protein, vitamins, carotenoids, and minerals [28]. Apart from the nutrient composition of cocoyam tuber, antinutritional compounds such as cyanogenic glycosides have been reported in the crops albeit in lower concentrations (21.0–171.3 mg/kg dry matter) [29, 30] than other food plants.

3.3 Bamboo shoot

Fresh immature bamboo shoots are consumed as vegetable in some Asian countries, and they contain appreciable quantities of vitamin C, carbohydrates, and protein [31]. Apart from the nutritive value, bamboo shoots contain lethal concentrations of cyanogenic glycosides. The cyanogenic glycoside present in bamboo shoot is taxiphyllin, which quickly decomposes when exposed to boiling water. Cyanide contents of 1000–8000 mg HCN/kg have been reported [32]. Although cyanide content of bamboo shoot is much higher than that of cassava root, the cyanide content in bamboo shoots decreases substantially following harvesting and processing.

3.4 Sorghum

The plant sorghum [*Sorghum bicolor* (L.) Moench] belongs to the Poaceae family (tribe Andropogoneae) and is one of the most important crops in Africa, Asia, and Latin America. It is a very genetically diverse crop both in cultivated and wild species. About five sorghum's landraces are known, and the greatest variation within the sorghum genus is found in the Ethiopia-Sudan region, which is believed to be the origin of the plant. The most important global producers of sorghum are the United States of America, Nigeria, Sudan, Mexico, China, India, Ethiopia, Argentina, Burkina Faso, Brazil, and Australia [23]. Burkina Faso appears to be the world leader of sorghum production and consumption per inhabitant. There has been an increased demand for the crop in Africa over the last 50 years. Studies indicate that more than 35% of sorghum is grown directly for human consumption, while the rest is used primarily for animal feed, alcohol production, and industrial products [33]. Although sorghum is a widely grown cereal crop that resembles corn in general composition, it is an inferior crop due to the presence of cyanogenic glycosides, dhurrin and amygdalin, among other factors. The major cyanogenic glycoside in sorghum is dhurrin, and its content in shoot tips of seedlings is estimated at 30% dry weight. In young sorghum leaves, dhurrin and the enzymes responsible for its hydrolysis to hydrogen cyanide are localized in vacuoles and cytoplasm of plants, respectively. The compartmental separation of the enzyme and the substrate makes tissues free from cyanide in intact leaves. The levels of dhurrin decrease with plant age, and immature sorghum leaves contain higher concentrations of dhurrin than the mature ones [17].

3.5 Fruits and fruit kernels

Most fruits and fruit kernels contain the potentially toxic cyanogenic glycoside compound, amygdalin. The contents of amygdalin in fruit seeds vary significantly among varieties and environmental conditions [34]. The following sections will highlight two important sources of amygdalin: apple and apricot fruits.

3.5.1 Apple (Malus domestica)

Apple seeds contain appreciable amounts of amygdalin, a cyanogenic glycoside composed of cyanide and sugar. When metabolized in the digestive system, this

chemical degrades into highly poisonous hydrogen cyanide. Studies have reported that amygdalin content in apple seeds ranged from 1 to 4 mg/g, while that of apple juice was reported to be between 0.001 and 0.08 mg/ml [34].

3.5.2 Apricot fruits (Prunus armeniaca)

Apricot fruits are widely cultivated in Central Asia, Africa, America, and Europe. There are two varieties of apricot kernels: bitter and sweet. Bitter apricot kernels contain a considerably high amount of the cyanogenic glycoside amygdalin and thus are unsafe for consumption. On the other hand, sweet varieties are safe for human consumption because of their low level of cyanogens [35]. The concentration of hydrogen cyanide in apricot kernels varies widely (49–4000 mg/kg), depending on whether the skin was included or not during cyanide determination. Ingestion of raw or improperly processed apricot kernels with high cyanide levels can cause serious acute problems that could lead to death [2].

4. Food processing technologies

Incidences of health conditions associated with dietary intake of cyanogens can be prevented or reduced by effective removal of cyanogenic compounds in food plants prior to consumption. Food plants are traditionally processed using various methods that vary widely depending on geographical location and ethnicity of communities [36]. The main aims of the food processing techniques are to reduce toxicity and improve palatability and storability. The main processing techniques used worldwide for most food plants include drying, boiling/cooking, soaking/wetting, fermentation, and/or a combination of the processes [8]. For example, processing techniques and stages used for production of snacks and main dishes from cassava roots are summarized in **Figure 4**.

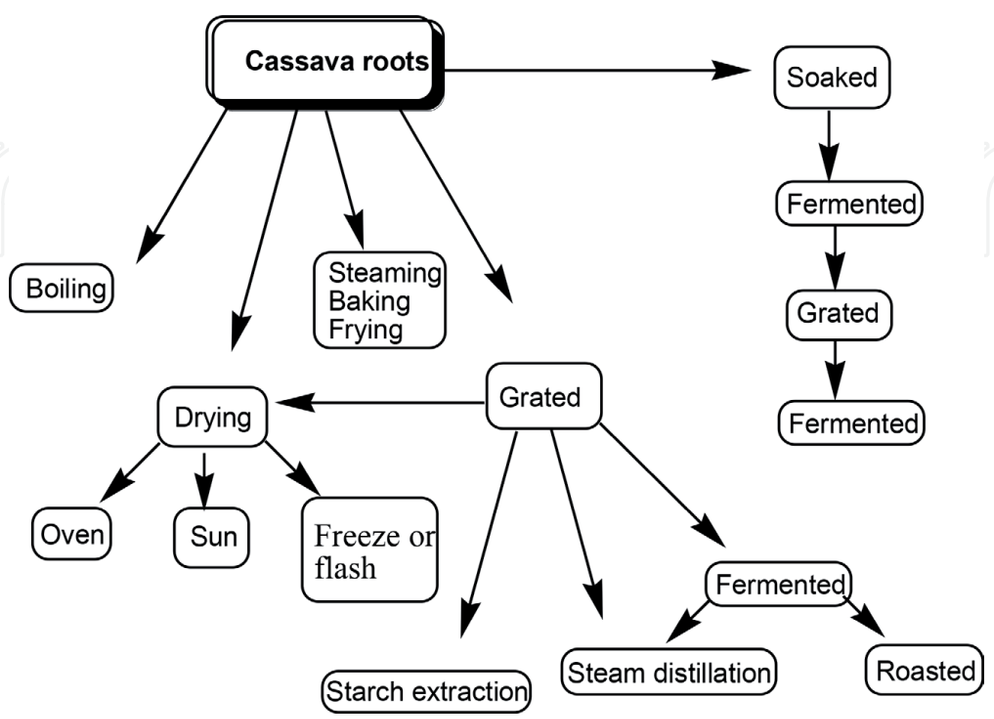

Figure 4.
Common cassava processing methods used worldwide.

4.1 Drying

Drying is one of the most appropriate processing methods for removal of cyanogenic glycosides in food plants. This is a mass transfer process which removes water from the product by evaporation and keeps the product free from microorganisms. There are several drying methods that can be employed to reduce cyanogens from food products, and they include the use of sun, oven, freeze, and superheated steam. Studies have reported that in bamboo shoots around 80% cyanogenic glycoside reduction was obtained after vacuum freeze-drying for 24 hours at −50°C. On the other hand, superheated steam drying at 120–160°C afforded significant decomposition of taxiphyllin, which causes bitterness in bamboo shoots [37], while oven-drying after grating at 60°C for 8 hours led to very high reduction of cyanogen content of up to 95% [38].

In eastern and southern Africa, cassava is traditionally processed into flour by sun drying the peeled roots followed by pounding and sieving or heap fermentation. However, because this process does not allow enough contact between linamarase and linamarin, total cyanogen content of 59 ppm of HCN equivalents has been reported in processed products, which is higher than the WHO safe level of 10 ppm [39]. The high levels of residual cyanogens can be attributed to the drying process, which restricts the contact between the endogenous enzymes linamarase and cyanogenic glucoside and promotes the retention of cyanohydrin and free cyanide in dried cassava.

4.2 Boiling/cooking

The effectiveness of boiling/cooking on cyanogen removal from various plant food products shows that the method achieves different results depending on the processing duration and part of the plant species. Several studies have reported that cooking and boiling are among the most effective practices for reducing cyanogenic compounds from food plants. These processes appear to promote the rupture of cell walls, which allow translocation of cell contents including antinutrients and toxic substances [39]. A study on bamboo plant showed that cyanogenic glycoside in the shoots of *Bambusa vulgaris* were reduced by 67.84–76.92% after boiling for 10 minutes. Boiling the shoots for an additional 10 minutes further achieved up to 87% reduction in cyanogen content [37]. Similar studies in cassava reported that the efficacy of the boiling method for cyanogen reduction is substantially improved when small-sized cassava pieces are boiled in a large volume of water [40].

However, some studies have reported that boiling can only reduce cyanogen content by 50%, and therefore, it is not an effective method for cyanide removal. The inefficiency of this processing method is attributed to the high temperatures. It is reported that at an elevated temperature of 100°C, linamarase, a heat-labile β-glycosidase, is denatured, and linamarin cannot then be hydrolyzed into cyanohydrin and subsequent HCN. A study by Cooke and Maduagwu [41] reported that bound glucosides were reduced to 45 to 50% after 25 min of boiling. Free cyanide and cyanohydrin in boiled cassava roots are found at very low concentrations.

4.3 Soaking/wetting

Like most processing methods, soaking or wetting of harvested crops helps to improve the shelf life of the food products. Additionally, processing improves the safety and quality of the products. For example, a study reported that cassava flour and to a lesser extent *gari* stored under ambient conditions retained cyanogens over long periods [25]. However, if flour is mixed with water and the resultant wet

flour left in the shade for 5 hours at about 30°C to allow HCN gas to escape, the total cyanide content is reduced three to sixfold. In Africa, the wetting method is commonly practiced in villages around Uvira in South Kivu Province of the Democratic Republic of Congo (DRC) where sporadic incidences of cyanide poisoning and Konzo have been reported [42]. An improved wetting study that reduced processing time to 2 hours was found to be equally effective in removing cyanogens. However, flour samples dried at temperatures above about 80°C lead to denaturing of linamarase, and the wetting method becomes ineffective.

In Malawi, soaking of cassava roots is mostly practiced in the lakeshore areas of northern Malawi and Nkhotakota in the central region, where cassava roots are soaked peeled or unpeeled [36]. A comparative study of the two soaking methods showed that soaking of peeled roots was more effective in reducing levels of cyanogens than soaking unpeeled roots [36]. In the former case, flours of negligible cyanogen contents were obtained, and the residual cyanogen contents were below the maximum FAO/WHO limit. Soaking of unpeeled cassava roots was found to be ineffective as its products gave values above the FAO/WHO recommended limit of 10 mg HCN eq./kg dry matter. The study showed that inclusion of the peel during processing led to high retention of cyanogens in the pulp.

4.4 Fermentation

Fermentation is one of the ancient methods of food preservation and became widely accepted in many cultures due to its nutritional value and variety of sensory attributes. Fermentation enhances the nutritive value of food through biosynthesis of vitamins and essential amino acids and degradation of antinutrients [39]. In the African region, fermentation by lactic acid bacteria is one of the most practiced processing methods. Fermentation is done with grated or soaked cassava roots, which could be peeled or unpeeled [36]. The process results in a decrease in pH of the food material during processing.

In western Africa and southern America, cassava parenchyma is ground, grated, or crushed into small pieces to disrupt many plant cells and allow good contact between linamarin and linamarase. The moist mash is then left to ferment for several days, the water-soluble cyanogens is squeezed out, and the residual HCN gas is removed by roasting. This process significantly reduced the cyanogen content of the product (*gari* or *farinha*) [39].

5. Health conditions associated with cyanide exposure

Cyanide, one of the most rapidly acting poisons, exists in many forms. The most common are hydrogen cyanide and cyanide salts such as potassium cyanide, sodium cyanide, and calcium cyanide. Cyanide salts can react with acids and subsequently release HCN. In most developing countries, cyanide intake through food consumption is normally high since processed foods with residual levels of cyanogenic substances are a predominant diet among communities. However, cyanide toxicity appears to be a rare form of poisoning among the general population particularly in developed countries. Cyanide exposure occurs relatively frequently in individuals through a variety of modes including inhalation, ingestion, and dermal absorption. In food plants, ingestion of cyanogenic compounds is the most common form of cyanide exposure. The potential toxicity of cyanogenic plants is largely dependent on their ability to produce lethal concentrations of hydrogen cyanide when exposed to humans. The toxic compound, HCN, is formed following the hydrolysis of potentially toxic compounds, cyanogenic glycosides. The conversion process is initiated

by the breakdown of the cyanogenic compounds upon disruption of the plant cells that occur during crushing of the edible plant material either during consumption or during processing of the food crop. The residual cyanogens in food products are the primary source of cyanide toxicity to humans when broken down in the gastrointestinal tract to form cyanide [43]. Generally, small quantities of cyanide are naturally detoxified by cellular enzymes and thiosulfates present in many tissues to form relatively harmless thiocyanate, which is excreted in the urine [44].

Human exposure to cyanide from consumption of food products with considerable amounts of cyanogenic glycosides is associated with health complications such as acute intoxications, chronic toxicity, neurological disorders, growth retardation, and goiter. The following sections will provide the epidemiological information, etiology, and prevalence of health conditions attributed to the toxic effects of cyanogenic glycosides in edible plants.

5.1 Acute toxicity

Acute cyanide poisoning occurs when the cyanide level exceeds the limit an individual can detoxify, and therefore the natural detoxification mechanisms are overwhelmed [44]. In humans, the cyanide ion (CN^-) has a strong affinity to the trivalent iron (Fe^{3+}) of the cytochrome oxidase and is readily absorbed from the intestinal and respiratory tracts [45]. A typical cherry red venous blood is seen in cases of acute cyanide poisoning because of the failure of the oxygen-saturated hemoglobin to release its oxygen at the tissues since the enzyme cytochrome oxidase is inhibited by the cyanide [44]. Thus, cyanide inhibits cytochrome oxidase preventing oxygen utilization leading to cytotoxic anoxia. This causes a decrease in the utilization of oxygen in the tissues. Additionally, increases in blood glucose and lactic acid levels and a decrease in the ATP/ADP ratio are observed, indicating a shift from aerobic to anaerobic metabolism [46].

Acute cyanide exposure mainly adversely affects the central nervous system (CNS) and the cardiovascular, endocrine, and respiratory systems. In humans, the clinical signs of acute cyanide intoxication can include rapid respiration, drop in blood pressure, dizziness, headache, stomach pains, vomiting, diarrhea, mental confusion, cyanosis with twitching, and convulsions followed by terminal coma and death. There is great variability of lethal doses reported in the literature. However, the mean lethal dose by mouth of cyanide in human adults is estimated to be in the range of 50 to 200 mg, and if untreated death is rarely delayed more than 1 hour [47].

5.2 Chronic toxicity

Persistent and prolonged exposure to low levels of cyanide is known to produce symptoms that are different from those observed in acute exposures described above. Chronic exposure to lower cyanide concentrations has been associated with several health conditions especially among cassava-eating populations. Health manifestations such as malnutrition, congenital malformations, neurological disorders, and myelopathy have been attributed to chronic cyanide toxicity [48]. Reports have also shown that goiter, the swelling of the thyroid glands, has occurred in communities where the levels of cyanogenic glycosides in cassava diets are greater than 10–50 mg/kg food [48].

5.3 Neurological effects

Although the entire human body is affected by dietary cyanide exposure, adverse effects on the central nervous system are the most prevalent because of

the high metabolic demand for oxygen in neurons and its control of respiratory function. Thus, the stimulation of carotid and aortic bodies contributes to the poor functions of the central nervous system and respiratory system.

Chronic human exposure to cyanide has been studied in African regions where populations consume large amounts of cyanide-containing cassava root. Neurological findings among the affected individuals include symmetrical hyperreflexia of the upper limbs, symmetrical spastic paraparesis of the lower limbs, spastic dysarthria, diminished visual acuity, peripheral neuropathy, cerebellar signs, and deafness [6]. Cyanide intake from a cassava-dominated diet is a contributing factor in two forms of nutritional neuropathies, tropical ataxic neuropathy described from Nigeria, and epidemic spastic paraparesis described from Mozambique, Tanzania, and Zaire [49, 50].

5.3.1 Tropical ataxic neuropathy

The term tropical ataxic neuropathy refers to several neurological disorders caused by many factors including toxiconutritional agents. The syndrome, first reported in Jamaica in 1897 and named tropical ataxic neuropathy in 1959, describes several neurological symptoms effecting the mouth, eyesight, hearing, or gait. In the African population, TAN is predominantly prevalent among the elderly population of mostly older males and females. TAN is mostly attributed to cyanide intake due to constant consumption of foods derived from cassava with high levels of cyanogenic compounds [48]. Studies conducted in West Africa particularly Nigeria, Tanzania, Uganda, Kenya, the West Indies, and tropical Asia have reported that cases of TAN generally occur in older people who have consumed a monotonous cassava diet over the years.

5.3.2 Konzo

Konzo, which means "bound legs" in Yaka language of Kwango region in the Democratic Republic of Congo, was first described in 1938 by an Italian missionary doctor. It is a distinct neurological disease with selective upper motor neuron damage and is characterized by an abrupt onset of an irreversible, non-progressive and symmetrical spastic paraparesis [50]. The disease is mostly associated with high dietary cyanogen consumption from poorly processed roots of bitter cassava combined with a protein-deficient diet low in sulfur amino acids [43]. Studies have found that cassava processing methods that involve shortcuts, as practiced during times of war and famine, exacerbate the health condition among the communities. Since its first description in the DRC, Konzo epidemics have been reported from many cassava-consuming areas in rural Africa. The disease has extended beyond DRC borders, and it remains a serious health problem among African communities that subsist on cassava [48]. In sub-Saharan Africa, at least seven countries have reported the outbreaks of Konzo, and they include the Democratic Republic of Congo, Mozambique, Tanzania, Central African Republic, Angola, Cameroon, and Zambia. In most of the affected countries, the epidemics were preceded by food shortages and several weeks of exclusive consumption of poorly processed bitter cassava roots, resulting in high dietary cyanide exposure, which was confirmed by high levels of thiocyanate in serum and urine [50].

5.4 Goiter and cretinism

Goiter and cretinism are common diseases in most developing countries because of low intake of iodine (<100 μg/day) among communities. Populations that exclusively depend on cassava as a staple food have shown high incidences of endemic goiter and cretinism. Several studies have reported that populations with very low

iodine intake and correspondingly high thiocyanate levels showed severe endemic goiter. The endocrine effect may be due to formation of thiocyanate, a lesser toxic metabolite of cyanide. Thiocyanate is known to block iodine uptake in the body and compete with iodide ion (I^-) as a substrate for the thyroid peroxidase, thereby decreasing the iodination of tyrosine to form iodotyrosine by the thyroid gland. Consumption of food products with residual cyanogenic glycosides even at a very low concentration can cause iodine deficiency leading to goiter [43].

5.5 Growth retardation

In humans, low birth weights among children are a common health problem especially in developing countries. Chronic exposure to cyanogenic glycosides has been reported as a major contributing factor to this health problem. Growth retardation is particularly a serious problem in populations consuming foods with inadequate proteins especially diets that are low in sulfur-containing amino acids such as methionine and cysteine. Cyanide detoxification in the human body requires sulfur donors from sulfur-containing amino acids [43], and thus, dietary exposure to cyanide has been identified as one of the contributing factors to growth retardation among children [51].

6. Cyanide detoxification

Hydrogen cyanide whether ingested directly or released from cyanogens is readily absorbed in the blood by binding to iron in hemoglobin and quickly distributed to organs such as the liver, kidney, brain, and blood tissue. However, about 80

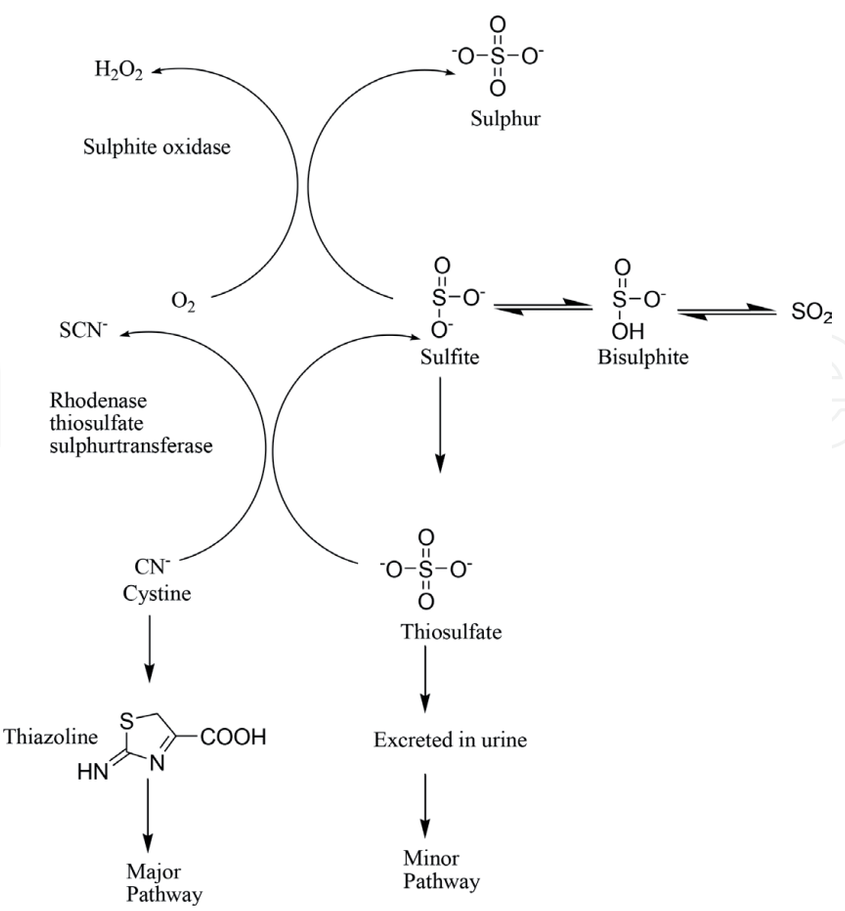

Figure 5.
Cyanide metabolism in the body [54].

percent of the absorbed cyanide is detoxified in the liver mainly by the mitochondrial enzyme rhodanese, which catalyzes the transfer of sulfur from a sulfate donor to cyanide, forming a less toxic metabolite, thiocyanate. There are two primary detoxification mechanisms of ingested cyanide in the body. The minor one involves methemoglobin in the red blood cells, which temporarily neutralize cyanide by reversible reaction [52]. The major pathway proceeds by the conversion of cyanide to a less toxic thiocyanate (SCN). This process is catalyzed by the enzyme rhodanese present in most tissues, by a reaction with sulfur [43], as shown in **Figure 5**. The two amino acids, cysteine and methionine, are the common source of sulfur [53]. The generated SCN is then slowly excreted through urine and sweat.

Other detoxification mechanisms exist and include the binding of hydroxocobalamin (vitamin B_{12}) to cyanide to form cyanocobalamin. Small quantities of cyanide along with CO_2 are eliminated through this pathway.

7. Conclusion

Cyanogenic glycosides are widely distributed in edible plants, and they play a major role in plant protection against herbivores, pathogens, and competitors. The presence of the potentially toxic compounds in food plants has also contributed to food security, particularly in the sub-Saharan African region. Most of the cyanogenic plants, such as cassava, have several agricultural advantages over other crops due to their outstanding ecological adaptation, low labor requirement, and high tolerance to extreme stress conditions such as drought and poor soils. Additionally, the cyanogenic compounds act as a deterrent against thieves and pests. However, several health disorders and diseases have been associated with consumption of food products with high quantities of residual cyanogens. Consequently, it is recommended that consumers should prepare foods properly before consumption in order to prevent adverse effects of cyanogenic glycosides in food plants. There are various traditional processing techniques that are relatively effective in removing cyanide from food plants, especially those involving grating and crushing. Generally, the efficiency of the technique largely depends on the duration of the process, material size, moisture, and temperature. In order to improve food safety, researchers have extensively studied mechanisms that accelerate cyanogenesis and cyanide volatilization during processing, which is a strategic step in detoxification of food plants. Therefore, effective processing technologies should be promoted among communities to enhance safety and organoleptic properties of products derived from cyanogenic food plants.

Conflict of interest

The author declares that there is no conflict of interest.

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