JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

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Food Safety: Importance of Composition for Assessing Genetically Modified Cassava (*Manihot esculenta* Crantz)

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ABSTRACT: The importance of food composition in safety assessments of genetically modified (GM) food is described for cassava (*Manihot esculenta* Crantz) that naturally contains significantly high levels of cyanogenic glycoside (CG) toxicants in roots and leaves. The assessment of the safety of GM cassava would logically require comparison with a non-GM crop with a proven "history of safe use". This study investigates this statement for cassava. A non-GM comparator that qualifies would be a processed product with CG level below the approved maximum level in food and that also satisfies a "worst case" of total dietary consumption. Although acute and chronic toxicity benchmark CG values for humans have been determined, intake data are scarce. Therefore, the non-GM cassava comparator is defined on the "best available knowledge". We consider nutritional values for cassava and conclude that CG residues in food should be a priority topic for research.

KEYWORDS: *genetically modified food, food composition, comparative approach, cassava, Manihot esculenta (Crantz), cyanogenic glycoside, history of safe use, Codex Alimentarius Commission, food safety standards*

INTRODUCTION

Cassava (*Manihot esculenta* Crantz) is one of a number of crop plants receiving a great deal of attention from international bodies and research groups because of its importance in food security. Cassava, the major food and feed crop for nearly a billion people and their animals, is produced in tropical and subtropical parts of the world and ranks eighth among the major food crops, on the basis of consumption per capita per day.[1] It is the fourth most important crop grown in developing countries.[1] The roots are consumed for their high starch content; unfortunately, they contain high levels of cyanogenic glycoside toxicants (CG). These toxicants are the focus of this paper. The roots are also deficient in adequate levels of protein as well as some vitamins and minerals. This is a confounding factor in the evaluation of the safety of the crop. The knowledge of and need for improvement of cassava are of great importance. Conventional breeding to address improved cassava productivity and nutrition has had little success because of its complex genetic makeup; therefore, biotechnology offers a promising research tool for meeting that goal.[2] The current focus of research through collaboration among international and national institutions is on disease resistance, improved nutritional quality, and improved poststorage harvest of roots.[3] Research on reduction of the level of CG using recombinant DNA (rDNA) techniques has been carried out by several groups with impressive reductions in CG concentration.[4]

The safety assessment of crops with new characteristics developed by genetic modification presents a challenge. The introduction of food from genetically modified (GM) crop plants raised increased interest in the comparative assessment of food composition as an important method to confirm the relative safety of new food. The safety assessment of GM cassava is considered in this study according to the internationally accepted comparative compositional safety assessment approach to illustrate the importance of food composition.

SAFETY/RISK ASSESSMENT OF GM FOOD

The comparative safety assessment approach for safety and nutritional assessment of products from GM crops focuses on determining similarities and differences between the compositions of the GM food and the conventional counterpart. It is regarded as the starting point of an assessment based on comparison with safety information of the comparator isoline.[5] Should there be differences, these are further investigated to determine exposure and characterize risks to human and animal health. The compositional comparison approach is regarded as a sensitive method compared with traditional toxicological testing that is less sensitive because of many difficulties with testing whole food.[6]

Several international bodies[6−12] contributed to the development of the requirements for safety/risk assessment of GM crops. The work of the first and second Codex Alimentarius Commission (CAC) Ad Hoc Inter-Governmental Task Force on Foods Derived from Modern Biotechnology in 1999−2003 and 2004−2009 is significant in this respect as it is the reference guideline for many countries including South Africa.[13]

The focus of this study on cassava food safety and compositional assessment is the identification of those components characteristic of cassava as a food source and

Special Issue: Safety of GM Crops: Compositional Analysis

Received: March 14, 2013
Revised: July 30, 2013
Accepted: July 30, 2013
Published: July 30, 2013

then an examination of the effect of genetic and environmental variability. The food safety requirements of the comparator form the main part of this study.

■ CONSIDERATIONS FOR COMPOSITIONAL ASSESSMENT OF FOODS FROM GM CROPS

Components To Be Analyzed. OECD consensus documents for safety of food and feed components have been developed as guidelines for comparative assessments by the OECD Task Force for the Safety of Novel Foods and Feeds (OECD Task Force). The food components identified for comparison are agreed on by members (as well as invited nonmembers) and selected on the basis of their suitability, cultural differences, preparation differences, consumption patterns for different regions, and analytical methods. The consensus documents also include valuable information on history of safe use.[14] The OECD Task Force aims to reach consensus on "searchlight" components of interest rather than a "filling a bucket" approach.[15,16] The proposed key compositional components are useful not only for GM compositional purposes but also for conventional techniques.

Cassava provides an example to illustrate choices of nutrients and antinutrients for analysis. According to the OECD cassava consensus document,[14] the proposed components to be measured in fresh roots for human food include proximates, starch, fatty acids, amino acids, minerals (calcium, phosphorus, magnesium, and iron), vitamins (β-carotene, ascorbic acid, thiamin, riboflavin, and niacin), CG, and hydrocyanic acid (HCN). The components proposed for fresh leaves include all those for roots except starch but include, in addition, tannins and phytic acid. The choice of components for analysis is based on a large concentration of starch in the roots, which is an important source of energy where cassava is a staple food. The protein content of roots (crude protein, 1.5−4.7 g/100 g dry matter) is low. Cassava leaves are a valuable source of protein (14.7−36.4 g/100 g dry matter), β-carotene, vitamin C, and minerals (iron and calcium)[14,17] where cassava is the staple food. CG and HCN are obvious choices for safety assessment, because levels in roots are as high as 2561.7 mg HCN/kg dry weight.[18] In whole leaves 4073 mg/kg dry weight has been reported.[19] The recommended time of harvesting for comparison is set at 12 months, because most of the nutritional data are available at this age of the plant.[14]

Processed cassava products are not included in the current OECD consensus document because of the wide range of processing and preparation methods and products consumed. Insufficient compositional data are available for all processed products. This may be a limitation in the OECD document as different processing methods can profoundly reduce the levels of CGs and HCN as well as nutrients present in the final product.[20−22] Data on the composition of the processed products are important in the establishment of the safety of cassava.

Genetic and Environmental Variability. The GM crop, the nearest isoline control, and a number of conventional varieties or hybrids are normally included in the same field trials. The purpose is to review differences between the components of the test substance (GM crop) and components of the nearest isoline comparator against the background of the range of values found in the edible varieties of the crop under different environmental conditions. The results from such trials can be further compared with information reported in recognized databases and publications such as the OECD consensus documents and the International Life Sciences Institute Crop Composition Database (ILSI database). Differences, whether genetic or environmental in origin, could be identified in this way. For example, the information on maize components shows the impact of genetics and the environment on the nutritional and metabolite components.[23−25] Data from the ILSI database are valuable because a wide range of geographies, years, and conventional varieties of soybean, cotton, and maize are presented in a searchable format.[26] These are the GM crops that multinational companies mainly invest in. Such information on cassava has not yet been included in the ILSI database perhaps because of the current small scale of trials in this early phase of the development of GM cassava.

Cassava is known to grow under extreme environmental conditions[27,28] and has been called the drought, war, and famine crop.[28] Cyanide content and nutrient composition of cassava vary not only between cultivars but also with agricultural practices and environmental conditions such as drought and soil nutrient supply.[29] The OECD consensus document for cassava indicates the ranges of constituents in the raw product. This is the first international source of a set of compositional data for cassava obtained from peer-reviewed publications.[14] However, regular updating of the OECD information would contribute to its validity.

History of Safe Use. Defining the comparator for the comparative safety assessment approach is of critical importance. The comparator in the safety assessment is normally selected to be a conventional counterpart grown and harvested under the same conditions.[6] A conventional counterpart is defined as "a related plant variety, its components and/or products for which there is experience of establishing safety based on common use in food" (p 8).[6] The ideal comparator should be the parental isogenic line according to Codex Alimentarius (p 16).[6] Such a comparator should have a "history of safe use" to make a statement on the safety of the GM food.

Constable et al.[30] state that the concept of history of safe use is "hard to define since it relates to an existing body of information which describes the safety profile of a food, rather than a precise checklist of criteria" (p 2513) and that it should be regarded as a "working concept" (p 2513). They propose a profile consisting of the "period over which the traditional food has been consumed, the way it has been prepared and used and at what intake levels, its composition and the results of animal studies and observations from human exposure" (p 2513).[30] With a profile of the food in mind, which includes the "best available scientific knowledge" (p 11),[6] a judgment of the safety of the conventional counterpart can be made. Assuming that the conventional comparator has a reasonable history of safe use, the relative safety of the GM counterpart can be determined.

According to Wolt,[31] the concept of "food safety is not absolute, since it is a judgment, it is value laden... [that is] understood within the context of society, culture, politics, and economics" (p 2). Even with a concept of safety, risk is not negated because there is always a degree of risk.[31,32] The OECD describes safety vaguely as "reasonable certainty" of "no harm" (p 17).[8] A definition of *harm* should be considered with great caution because of different perceptions. The role of scientists in interacting with regulators and society to define harm needs consideration. Different regulatory bodies may judge safety differently. The extent of exposure of the population to a food containing high levels of a toxicant and recognized processing practices to reduce the level of the poisonous substances are important criteria in judging safety.

Historically, knowledge of food safety and nutritional values has developed through trial and error by selection and preservation of plant variants with desirable traits and human preference for taste and color.[33] Humans are aware of crop plant toxicants and antinutrients from traditionally gained knowledge and experience in cultivation and food preparation. Standard practices for preparation of food containing high levels of toxicants and antinutrients serve as a general guide to ensure safety of food.[14] Scientific investigation has shed more light on traditional knowledge and practices. Traditional knowledge is often the point of departure for future developments. The history of food use is therefore an important benchmark in the research and assessment of new products.

Domesticated crops such as maize, wheat, and rice have an extensive history of safe use, and information on nutrients and metabolites is well documented; therefore, these require no further discussion. Documented scientific knowledge of toxicants and antinutrients present in other crop plants (e.g., toxic amino acids, lectins, proteinase inhibitors, antigenic proteins, alkaloids, fibrous polysaccharides, saponins, and condensed tannins) is of particular importance in assessing food safety.[34] The CG toxicants, particularly as components of cassava, are important in a discussion on the concept of "history of safe use".

■ CASSAVA CYANOGENIC GLYCOSIDES

The CGs may have different functions in plants, including chemical defense, plant−insect interactions,[35] nitrogen storage,[36] and phagostimulants,[37] to name a few. CGs may also be intermediate compounds in the synthesis or breakdown of other plant metabolites without a specific eco-physiological role. Ganjewala et al.[38] quote the CG toxicants as a specific safety concern being produced in more than 2600 plant species. This list includes crop plants such as barley, sorghum, and cassava.

CG Biosynthesis and Catabolism. Progress has been made in unraveling the biosynthesis of CGs and their catabolism. Several reviews have documented the important findings from such research. A short overview of current knowledge of CG biochemistry is provided by Ganjewala et al.[38] (Figure 1).

The main CGs in cassava are linamarin and to a lesser extent lotaustralin. The aglycone consists of a reactive α-hydroxynitrile that is conjugated with either D-glucose or gentiobiose. Both CGs are derived from only two amino acid precursors, namely, L-valine and L-isoleucine, although L-leucine, L-phenylalanine, L-tyrosine, and a nonprotein amino acid, cyclopentenylglycine, are reported in other crops as precursors of CGs. Three phases in the biosynthesis have been identified. In the first, the precursor amino acid is converted to aldoxime by N-hydroxylation of the parent amino group. An enzyme from the cytochrome P450 family is involved. In the second, aldoxime is converted to cyanohydrins catalyzed by another cytochrome P450 enzyme. In the third, glycosylation occurs by a soluble enzyme uridinediphosphate (UDP) glycosyltransferase. Previous studies suggested that the enzymes are organized as a metabolon, which is defined as a "supramolecular complex of sequential metabolic enzymes and cellular structural elements"[39] ensuring channeling of precursor/substrates and intermediates. Ganjewala et al.[38] list a number of published research papers on gene identification and characterization in the biosynthetic pathway.

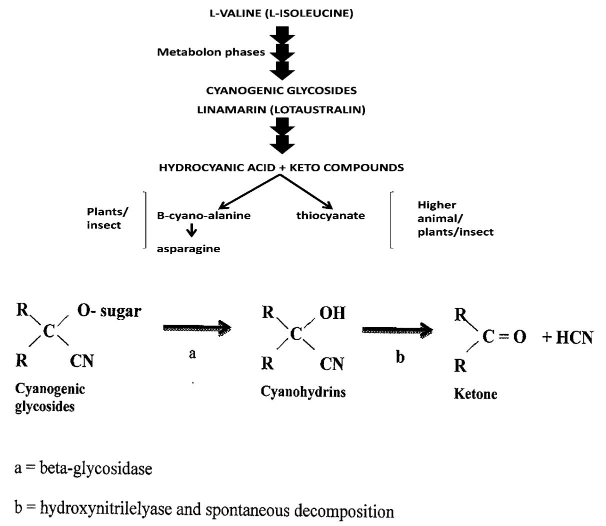

Figure 1. Schematic pathways of biosynthesis and catabolism of cassava cyanogenic glycosides.

Cyanogenic glycosides are catabolized to α-hydroxynitriles (cyanohydrins) and sugars by β-glycosidases followed by dissociation at a pH above 6 into HCN and a ketone or aldehyde, which is acetone in the case of linamarin. At low pH, the α-hydroxynitrile degradation is catalyzed by α-hydroxynitrilelyase, resulting in the release of HCN (Figure 1). HCN is detoxified by two separate routes. The first route leads to the formation of asparagine. The second route leads to the formation of a thiocyanate catalyzed by rhodanese. The CGs and their breakdown products cyanohydrins and HCN are jointly known as cyanogens. Genes encoding some of the enzymes of CG catabolism have been cloned and characterized. Detection of CGs has been made possible by chromatographic procedures and enzyme immunoassay methods, however, with some limitations.[38] Ganjewala et al.[38] conclude that despite the progress in unraveling the biochemistry of CGs, more knowledge is needed for a complete understanding of the regulatory mechanisms that control CG biosynthesis and catabolism.

In their review of the biochemistry of cassava, Ganjewala et al.[38] refer to ongoing research to reduce the levels of CG. One such study followed a complementary approach whereby the hydroxynitrilelyase enzyme is expressed in cassava roots to accelerate cyanogenesis and cyanide volatilization during food processing.[4]

CG Toxicity. CG toxicants are enzymatically metabolized to produce HCN. Intoxication occurs from ingestion of raw cassava or partially processed foods. Acute cyanide intoxication has been well described. In short, cyanide has an influence on the electron transport chain in respiration, leading to a decrease in utilization of oxygen and production of ATP. It clinically manifests in central nervous system and cardiovascular disturbances that could result in coma and death. In addition, consumption of cassava and its products resulted in konzo (an irreversible paralysis of the legs) and tropical ataxic neuropathy (TAN), a chronic condition noticed in elderly persons.[40] Goiter and cretinism could be aggravated by cyanide from cassava, especially in areas of endemic iodine deficiency.[40] The competitive inhibition of iodine uptake is caused by thiocyanate, a metabolite of ingested cyanide, similar in size

 dx.doi.org/10.1021/jf401153x | J. Agric. Food Chem. 2013, 61, 8333−8339

to the iodine molecule.[40] The association between chronic exposure to CGs and the above-mentioned diseases is confounded by nutritional deficiencies in populations on a restricted diet of mainly cassava. The occurrence of CG poisoning has been described in detail in a recent document by the Joint FAO/World Health Organization Expert Committee on Food Additives (JECFA).[40] JECFA refrains from making any association between chronic symptoms and nutritional deficiencies.

As the intention of this paper is to highlight the importance of food composition as a cornerstone in the comparative approach to safety assessment, mere reference to malnutrition would suffice.

Processing of Cassava. Processing of the cassava crop into various forms of products may or may not sufficiently reduce the levels of toxicants.[20,21,41,42] Cassava is processed into a wide variety of different food and feed products. According to the OECD consensus document,[14] the roots are first peeled followed by various processes to produce approximately eight end products, including peel meal, toasted flour, flour (pressing, drying, and milling), fermented starch, dried native starch, gari (a fermenting and roasting process), dried chips/snacks, and fresh root meal. Young shoots and leaves are processed into a few other products.[14] There are at least 80 types of processed cassava in Africa grouped into peeled and unpeeled products.[21] The peels contain about 5 times higher concentrations of cyanohydrins than the pulp. Peeling and soaking of the roots seems to produce flour with negligible cyanogenic content. Cardoso et al.[41] compared the percentage retention of cyanide by different processing methods. They concluded that processes commonly used in eastern and southern Africa such as heap fermentation and sun-drying of cassava parenchyma (pulp) did not adequately remove cyanide in a normal year and were completely inadequate in a dry year due to increased levels of CG because of low rainfall. The levels of CGs in certain areas such as Mozambique are also of concern.[29] Therefore, there is a great need for improved processing methods in Africa.

Cassava Safety: Perceptions. Safety in the context of cassava is illustrated by a study on farmers' perception of the toxicity of and reasons for farming with cassava.[43] A percentage of farmers interviewed in Tanzania and Nigeria were consuming raw cassava, both sweet and bitter, in areas with and without neurological syndromes. This group had never seen anybody die from eating raw cassava and did not ascribe any adverse effects to consumption of cassava, except for one farmer, who noticed minor acute ailments.

The levels of cyanogenic compounds in this study ranged from 8 to 1063 HCN equiv/kg dry weight cassava in Nigeria and from 22 to 244 HCN equiv/kg dry weight cassava in Tanzania. In Nigeria, the concentration ranges were 47−1064 mg HCN equiv/kg in an endemic area for ataxic polyneuropathy and 8−614 mg HCN equiv/kg dry weight in a nonendemic area. In Tanzania, the concentration ranges of cyanogenic compounds were 27−117 mg HCN equiv/kg dry weight in the endemic area for konzo and 22−244 mg HCN equiv/kg dry weight in the nonendemic area. The altitude at which the plants are grown seems to have an effect on the levels of cyanogens, with reduced levels at high altitudes and vice versa for low altitudes. Preference for bitter cassava was because of higher yield, resistance to pests,[45] and reduced theft of produce.[46] Except for the lowest level of toxicant exposure in the range for Nigeria, all other exposure levels were higher than the recommended level of 10 mg HCN/kg in cassava flour (see the text above within brackets and Safety Standards for CGs). According to Oluwole et al.,[43] most of the farmers from Nigeria and Tanzania plant cassava for subsistence and as a cash crop only. The introduction of improved processing practices to reduce levels of CG would be a major endeavor. Codex is considering a guideline of practices to reduce the presence of HCN in cassava and cassava products.[44]

Determining Cyanogen Content. Cyanogenic glycosides (e.g., linamarin) and their breakdown products, cyanohydrins and free HCN, are jointly known as cyanogens. The cyanogen content of a food is expressed in terms of the HCN released by hydrolysis. Not all CGs will be hydrolyzed during processing; therefore, total cyanogenic potential is expressed as HCN equivalents. Total HCN content consists of all cyanogenic glycoside, cyanohydrins, and "free" HCN. To conform to Codex maximum levels (mg/kg), the levels found must be converted stoichiometrically to total (potential) HCN concentrations. Following complete metabolism/hydrolysis, 1 g of linamarin (relative molecular mass = 247) could theoretically generate 109.3 mg of HCN (equivalent to 105.2 mg of cyanide).[40] Codex is currently considering suitable analytical methods that could determine total HCN by measuring all potential contributors to the formation of HCN.[44,47]

Safety Standards for CGs. The international Codex standard for edible cassava flour intended for direct human consumption is based on a total HCN concentration of not more than 10 mg/kg (Codex Standard 176-1989)[48] and for gari a value of not more than 2 mg/kg as "free hydrocyanic acid" (Codex Standard 151-1989).[49] These standards (or maximum level, ML) by Codex were accepted because of the absence of acute toxicity symptoms. No adequate data for chronic exposure were available at that time. Codex also published standards for sweet[50] and bitter[51] cassava as guidelines for food standards by national legislation of the importing country. In a recent study by the JECFA,[40] health-based guidance values were proposed. An acute reference dose (ARfD) for linamarin of 0.9 mg/kg body weight per day (equivalent to 0.09 mg/kg body weight as cyanide) is based on increased skeletal defects in developing hamster fetuses following acute exposure of maternal animals. This applies to a diet containing CGs only as source of cyanide. A provisional maximum tolerable daily intake (PMTDI) for cyanide of 20 μg/kg body weight (0.02 mg/kg body weight) per day is based on a 13 week study showing that continuous exposure to sodium cyanide via drinking water caused a variety of effects related to male reproductive organs.[40] This standard is acceptable in the absence of long-term studies because of the acute nature of cyanide toxicity and the sensitivity of the effect on male reproductive organs. Ideally, the total amount of cyanide exposure through the dietary/water intake should be less than the two identified standards. JECFA's[40] estimates for maximum amounts of cassava or cassava products that can be consumed per day before the Codex standard of 10 mg total cyanide/day in cassava flour can be exceeded is 560 g/day for acute effects and 125 mg/day for chronic effects (p 309). JECFA[40] concludes that "more consumption data particularly for Africa would enable a better estimation of the global risk of dietary exposure to cyanogenic glycosides" (p 310). This need for more information was confirmed by the Codex Committee on Contaminants in Food[44] that identified, in addition to more "occurrence data on HCN in cassava and cassava product also information on processing (cooking) methods, consumption patterns, with a view to determine the need and feasibility to establish MLs for cassava (raw and processed) in future" (p 9)

UNINTENDED COMPOSITIONAL DIFFERENCES

Apart from the intended effects of genetic modification, there may be unintended differences in components of GM and non-GM crops. These are functions of genetic variables, environmental factors, agricultural practices, or genetic modification.

All methods of crop improvement have potential to cause unintended compositional changes, as described by an advisory group for the U.S. National Academy of Sciences.[33] The group contended that it was unlikely that all methods of GM, non-GM, and conventional breeding will have equal probability of unintended effects. They identified methods of induced mutagenesis as being the most genetically disruptive technique and thus the most likely to display unintended phenotypic changes. This was followed by biolistic transfer and then by *Agrobacterium* transfer of rDNA from distantly related species. *Agrobacterium* transfer of rDNA from closely related species was ranked less likely to cause unintended changes than any of the above methods, including conventional pollen-based crossing of distantly related species and/or embryo rescue.

Unintended effects have been reported from non-GM crop varieties at the point of commercialization, although this is rare.[52] Trace amounts of the unintended metabolite *cis*-15-octadecadionic acid, an isomer of linoleic acid not usually present in non-hydrogenated soybean oil but present in hydrogenated soybean oil and other food sources, were reported.[33,53] A number of examples of increased levels of toxicants have been reported, such as sporalins in celery (furanocoumarins), apparently owing to environmental factors or genetics.[54,55]

Plant breeders traditionally eliminate observed off-types during the evaluation process. However, agronomic/phenotypic assessments are not food safety assessments. Compositional analysis of conventionally produced food is often required only for labeling of processed food. For example, in South African legislation, the onus is on the seller to ensure food safety of fresh products.[56] South African food quality guidelines such as those for potatoes prescribe grading according to the amount of "green",[57] but quantifying the parameters that would designate a food "unfit for human consumption" is a controversial issue.

Morandini and Salamini[58] describe the complexity when permanent changes in the biochemical pathways may affect other pathways essential for producing critical nutrients. These could be a consideration when GM cassava crops with reduced concentrations of CGs and improved nutrient composition undergo compositional comparative assessments. Chassy[59] is of the opinion that it is unlikely that completely new toxicants will be formed as a result of genetic modification. The observed changes that have been noted to date are only in the levels of existing toxicants, including precursors or catabolic products. Should that be the case for cassava, the benchmark value for CG equivalents that includes all cyanogens in cassava flour should suffice. Other possible unintended changes of nutritional significance are already included in any safety assessment according to the OECD consensus document.

Nontargeted techniques that include genomics, transcriptomic profiling, proteomics, and metabolomics ("omics") are types of methodologies that opened up possibilities for in-depth comparative studies to gain a better understanding of the genomic and environmental effects on composition of crop plants. The use of metabolomics has been advocated as an approach to expand the range of metabolites that can be measured for potential unintended effects.[60] At this stage, interpretation of the vast amount of information is a challenge, and methodologies still need be standardized and validated and are qualitative and not fully reproducible. The need for such studies is still being considered. The current results from "omics" studies with single traits confirm the hypothesis that GM techniques are less disruptive to the genome than non-GM methods according to the analysis of Ricroch et al.[61] Nontargeted techniques should not be considered in the absence of targeted approaches. Harrigan et al.[62] suggest that "targeted assessments could easily facilitate a partnership with "omic" research conducting semitargeted profiling on pathways associated with toxic metabolites ...". Cassava may be a crop where such an approach would be beneficial. Harrigan et al.,[62] however, challenge the likelihood that metabolic profiling would provide "immediately interpretable data in safety assessments that would otherwise enhance rigorously quantitative assessments" (p 342).

DISCUSSION

The purpose of the study with cassava is to demonstrate the importance of crop components in food safety assessment of GM crops. A contentious issue is defining "history of safe use" that is applied to the comparator in a critical comparative analysis. Consumers are critical of the safety of GM food; therefore, the accountable and responsible regulatory authorities need convincing scientific evidence of safety. Much dietary exposure intake data need still be generated, especially for Africa, to be able to determine exposure through consumption of various cassava products. The terminology "history of safe use" for cassava and its products will remain a contentious issue until such time as more information is available and the need to establish new MLs for cassava (raw and processed) in the future has been confirmed. The current Codex standards are based on "best available knowledge" and could be considered a "working concept" for comparative purposes. In the absence of such information, any statement to the effect that non-GM cassava has a history of safe use must be considered debatable and misleading to consumers. The assessment of toxicity of toxicants is considered of great importance in all GM crops containing high levels of toxicants, and it is critically important to convey the correct message to consumers.

The question could still be asked: can GM cassava be regarded as safe? It is clear that many conventional foods, particularly cassava, cannot be regarded as without risk or completely safe. There is a reasonable expectation among the public that GM foods should be safe to eat. Yet this expectation has to be contextualized, considering that many conventional foods are not absolutely safe and that safety also depends on a variety of factors, including appropriate processing methods.

Strategies to improve safety of cassava could be two-fold. The challenge for researchers developing GM cassava would be to find a cassava variety to serve as starting point that would produce CG levels that could be processed to reduce the CG to below suggested Codex levels for processed food. This also requires research into processing methods and guidelines. Alternatively, research to produce GM cassava with reduced levels of CG to ensure that the PMTDI recommended by JECFA is not exceeded, particularly where cassava is a staple foodstuff, should receive priority attention. Such a GM variety could serve as benchmark for the nutritional improvement of cassava.

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Funding

We thank The South African National Research Foundation for funding the study.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We acknowledge the International Life Science Institute for initiating the study and the reviewers of the manuscript.

ABBREVIATIONS USED

CAC, Codex Alimentarius Commission; CG, cyanogenic glycoside; FAO, Food and Agriculture Organization of the United Nations; GM, genetically modified; GMO, genetically modified organism; HCN, hydrocyanic acid; JECFA, Joint FAO/WHO Expert Committee on Food Additives; OECD, Organization for Economic Cooperation and Development; rDNA, recombinant DNA; TAN, tropical ataxic neuropathy

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