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### Cyanide in cassava: unveiling health risks in the lens of unsustainable food systems in Sub-Saharan Africa – a systematic review

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Objective: Cassava (Manihot esculenta Crantz) remains a vital staple crop across Sub-Saharan Africa (SSA), sustaining millions of livelihoods. However, its consumption poses a significant public health concern due to the presence of cyanogenic glycosides. This systematic review synthesizes evidence on the health impacts of cyanide exposure from cassava consumption in SSA and examines how these risks are shaped by structural vulnerabilities in food systems. Methods: A comprehensive literature search was conducted across four databases: PubMed, Scopus, JSTOR, and AJOL. Retrieved publications were organized using Mendeley Desktop. The review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Two independent reviewers carried out the search and screening processes, with any disagreements resolved through discussion with a third reviewer. The review included human epidemiological studies—observational, interventional, and clinical—that examined the health impacts of dietary cassava intake among populations in SSA. The keywords used in the search included cassava, cyanide, hydrogen cyanide, linamarin, lotaustralin, cyanogenic glycosides, konzo, health risk, acute poisoning, toxicity, tropical ataxic neuropathy, and neurological disorder. The initial search was conducted in January 2025 and updated on 24th June 2025.

Results: The review identified 45 relevant studies, with the majority conducted in the Democratic Republic of Congo (n = 18), followed by Mozambique (n = 10), Tanzania (n = 7), and Nigeria (n = 6). Urinary thiocyanate levels often exceeded the World Health Organization's safety threshold of 350 µmol/L, reaching up to  $1,730 \mu mol/L$ , particularly among individuals affected by konzo. These adverse health outcomes were often compounded by armed conflict, drought, poor infrastructure, and protein-deficient diets. Climate-related stressors, such as El Niño events and prolonged dry spells may further intensify reliance on cassava, resulting in the consumption of inadequately processed roots. Residual Hydrogen Cyanide (HCN) concentrations in cassava products varied widely depending on the processing method. Among these, the wetting method consistently achieved the greatest reductions, lowering HCN levels to as little as 4 ppm.

Conclusion: Cyanide exposure from cassava remains a significant public health concern in SSA, particularly in areas with fragile food systems and limited

access to safe processing methods. Strengthening food system resilience, expanding access to safer cassava cultivars (e.g., biofortified cassava varieties), and promoting effective processing methods such as wetting, are essential strategies for reducing cassava-related health risks.

KEYWORDS

cassava, cyanide, food systems, food safety, konzo, Sub-Saharan Africa

#### 1 Introduction

Cassava (*Manihot esculenta* Crantz) is the world's fourth most important staple food, following rice, wheat, and maize, and serves as a dietary staple for over one billion people worldwide (Adebayo, 2023). Its resistance to drought, ability to thrive even in poor soils, and flexibility to be planted and harvested nearly year-round, underscore its critical role in food security, particularly in drought-prone and nutrient-depleted regions like Sub-Saharan Africa (SSA). Cassava occupies a pivotal role in the agricultural landscape of Africa, where it is the second most crucial staple crop after maize, with the highest per capita consumption occurring in SSA (Hood et al., 2023). On average, individuals in SSA consume  $\sim$ 300 g of cassava daily, contributing up to 37% of the region's dietary energy intake (Bamigboye, 2023). However, beyond its contributions to food security, cassava presents complex trade-offs.

As a region, SSA grapples with complex challenges, including climate change, declining agricultural productivity, and increasing food insecurity. In this context, cassava has emerged as a resilient and indispensable crop that is promoted as a drought-tolerant crop [Food and Agriculture Organization of the United Nations (FAO), 2022] that sustains livelihoods across diverse landscapes. Recent trends, particularly between 2010 and 2023, show that cassava production in SSA is on the rise, driven by its growing significance as a food security crop amidst worsening climate variability, declining yields of traditional cereals like maize and rice, and increasing population pressures (FAOSTAT, 2025; Otekunrin, 2024)

Nutritionally, cassava is a source of starch, delivering 160 kcal/100 g when consumed raw, while its protein (<2%), fat (<1%), and micronutrient content (<1%) are minimal (Salvador et al., 2014). Due to its wide consumption as a staple food in SSA, where vitamin A deficiency remains a significant public health problem (UNICEF, 2023), biofortification programmes have successfully developed biofortified cassava varieties enriched with pro-vitamin A that have proven efficacy in improving serum retinol in school children (Talsma et al., 2016) and acceptable by consumers (Bechoff et al., 2018). As cassava broadens, it will likely continue to be promoted, increasing access and consumption in many SSA societies.

Despite the resilience and potential that cassava possesses, the utilization of cassava and its products is to some extent compromised by cyanide. Cyanogenic glycosides, primarily linamarin and lotaustralin which exist in the ratio 97:3 (Lykkesfeldt and Lindberg Møller, 1994) are natural constituents of cassava that present a real threat to human health (Rivadeneyra-Domínguez and Rodríguez-Landa, 2020). Cassava is considered bitter if its cyanide concentrations exceed 100 mg/kg, and sweet if cyanide

levels are below 100 mg/kg (Fukushima et al., 2016). Consumption of inadequately processed bitter cassava results in enzymatic hydrolysis to release Hydrogen Cyanide (HCN), a potent toxin with deleterious effects on physiological functions. Cumulative exposure to cyanide has been linked to a range of adverse health outcomes, including acute poisoning and chronic neurological conditions such as tropical ataxic neuropathy and konzo—a paralytic neurological disease primarily linked to cyanide exposure and commonly affecting children and women of reproductive age (Siddiqi et al., 2020; Alitubeera et al., 2019; Oluwole and Oludiran, 2013).

Importantly, the choice to grow bitter cassava is not always accidental or a result of limited knowledge. In many SSA communities, farmers intentionally cultivate bitter varieties due to their higher yield potential, better storability, and suitability for processing into flour (Imakumbili et al., 2019; Oluwole et al., 2007). Moreover, environmental factors such as soil characteristics and crop management practices—including poor weeding, piecemeal harvesting, and the age of the plant at harvest—can influence cassava root bitterness and subsequently increase cyanogenic glucoside production (Imakumbili et al., 2019). Additionally, bitter cassava serves as a natural deterrent to pests, livestock, and theft, as its toxicity discourages unwanted harvesting or consumption before proper processing (Kapinga et al., 1997; Chiwona-Karltun et al., 1998). This suggests that cyanide exposure from cassava and cassava-related products is still prevalent in SSA (Forkum et al., 2025). This health risk is further compounded by the fragility of food systems in the region, encompassing production, processing, storage, distribution, and consumption. These components are often fragmented, under-resourced, and vulnerable to a range of stressors, including climate variability, land degradation, socioeconomic inequality, and political instability (Ulimwengu, 2024; Bjornlund et al., 2022). Such systemic weaknesses hinder the adoption of safe cassava processing practices such as adequate fermentation, wetting, drying, or soaking needed to reduce cyanide levels in cassava. Hence, populations remain at risk of chronic or acute cyanide exposure. Despite such systemic challenges, reliance on cassava continues to grow.

While various reviews have examined cassava toxicity and efforts to mitigate cyanide toxicity through cassava processing methods (Kuliahsari et al., 2021; Panghal et al., 2021; McMahon et al., 1995), specific cyanide-related health conditions such as konzo (Baguma et al., 2021; Rivadeneyra-Domínguez and Rodríguez-Landa, 2020; Cliff et al., 2011; Kashala-Abotnes et al., 2019; Nhassico et al., 2008; Aregheore and Agunbiade, 1991), as well as the safety of cassava and cassava-derived products (Forkum et al., 2025), remain persistent public health concerns. However, there is a critical gap in understanding how these

health risks are embedded within and perpetuated by the broader structural vulnerabilities of food systems in SSA. Therefore, the objective of this review was to synthesize existing evidence on the health risks associated with cyanide exposure from cassava consumption in SSA, and to examine how these risks are shaped and perpetuated by structural vulnerabilities within the region's food systems. The review aims to inform integrated, context-sensitive interventions that promote food safety, public health, and sustainable food systems.

### 2 Methods

This systematic review was conducted following guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA 2020) (Page et al., 2021). Given the nature of the research question and the diversity of study designs, the SPIDER framework (Sample, Phenomenon of Interest, Design, Evaluation, Research type) was employed to structure the review objectives and eligibility criteria, as it is particularly effective for synthesizing qualitative and mixed-methods research (Cooke et al., 2012). Table 1 shows the SPIDER framework and its application to this study.

### 2.1 Eligibility criteria

The inclusion and exclusion criteria were developed not only to ensure methodological rigor but also to align with the review's central theme: understanding the health risks of cassava consumption through the lens of unsustainable food systems in SSA. These criteria ensure that the selected studies reflect the human health consequences of systemic weaknesses in food systems within SSA. Table 2 shows the inclusion and exclusion criteria for the review.

### 2.2 Information sources and search strategy

A comprehensive literature search was conducted in the following electronic databases: PubMed, Scopus, Journal Storage (JSTOR), and African Journals Online (AJOL). Prior to the search, an academic librarian was consulted to assist in developing comprehensive search strategies, identifying relevant databases, optimizing keywords and subject heading selection, and ensuring rigorous adherence to the PRISMA guidelines. The search strategy used a combination of relevant keywords and concepts related to cassava and cyanide. The keywords used in the search included cassava, cyanide, hydrogen cyanide, linamarin, lotaustralin, cyanogenic glycosides, konzo, health risk, acute poisoning, toxicity, tropical ataxic neuropathy, and neurological disorder. A full search index and the Boolean search strings used for each database are shown in Table 3. To ensure comprehensive search, no restrictions or filters were placed on publication year, language or country during the search of various databases. The initial search was conducted in January 2025 and updated on 24th June 2025. Two independent reviewers performed the search and screening processes and resolved any disagreements through discussion or consultation with a third reviewer. Supplementary

TABLE 1 Summary of the SPIDER framework and its application to the study.

SPIDER element	Definition	Application to the study
Sample	Population or group of interest	Populations in Sub-Saharan Africa consuming cassava
Phenomenon of interest	The behaviors, experiences, or exposures being studied	Cyanide toxicity from cassava consumption
Design	Type of research design	Observational studies, case reports, outbreak investigations, clinical studies
Evaluation	Outcomes or measures of interest	Health outcomes such as konzo, neuropathy, cognitive impairment, and acute poisoning
Research type	Qualitative, quantitative, or mixed methods	Primarily quantitative studies, with some mixed methods approaches

TABLE 2 Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Human studies conducted in SSA.	<ul> <li>Animal or laboratory experiments or <i>in vitro</i> studies.</li> <li>Technical focus only: studies focused solely on genetic engineering, breeding or agronomic practices.</li> </ul>
Studies investigating health outcomes associated with cassava consumption and cyanide exposure (e.g., konzo, neuropathy, acute poisoning)	Studies conducted outside SSA     Lack of relevance to cassava as a crop
Observational studies, clinical studies, case reports, and outbreak investigations	Articles not addressing health impacts of cassava or cyanide exposure
Study reporting primary data with quantitative or mixed-methods analysis	Review articles, editorials, opinion pieces, or non-peer-reviewed sources
Publications in English	Non-English publications
No restriction on publication year	

data illustrating cassava production trends were obtained from FAOSTAT (2025).

### 2.3 Study selection and data extraction

All database search results were collated, stored, and managed in Mendeley desktop software (version 1.19.8). Multiple folders were created in Mendeley to contain the results of each database search, and then all the results were aggregated into a single folder with duplicates removed. The study selection process was conducted in two phases: an initial screening of titles and abstracts, followed by a full-text review of potentially eligible studies. Data from the included studies were extracted using a standardized data extraction form. The extracted data included: study characteristics (i.e., authors, publication year, study location, study population); cyanide exposure assessment (i.e., thiocyanate concentrations); residual HCN concentrations and cassava processing methods; reported health outcomes or adverse effects; and potential confounding factors.

TABLE 3 Search algorithms returning publications in the database search.

Database	Algorithm
PubMed	(("Cassava" [All Fields] OR "Manihot esculenta" [All Fields] OR "Cyanogenic glycosides" [All Fields] OR "Linamarin" [All Fields] OR "Lotaustralin" [All Fields] OR "Hydrogen cyanide" [All Fields] OR ("Cyanide" [All Fields] AND "Cassava" [All Fields])) AND ("Konzo" [All Fields] OR "Tropical ataxic neuropathy" [All Fields] OR "Neurological disorder" [All Fields] OR "Acute poisoning" [All Fields] OR "Toxicity" [All Fields]))
Scopus	(TITLE-ABS-KEY ("cassava") OR TITLE-ABS-KEY ("Manihot esculenta") OR TITLE-ABS-KEY ("cyanogenic glycoside*") OR TITLE-ABS-KEY ("linamarin") OR TITLE-ABS-KEY ("lotaustralin") OR TITLE-ABS-KEY ("hydrogen cyanide") OR (TITLE-ABS-KEY ("cyanide") AND TITLE-ABS-KEY ("cassava"))) AND (TITLE-ABS-KEY ("tropical ataxic neuropathy") OR TITLE-ABS-KEY ("tropical disorder*") OR TITLE-ABS-KEY ("acute poisoning") OR TITLE-ABS-KEY ("acute poisoning") OR TITLE-ABS-KEY ("health risk*") OR TITLE-ABS-KEY ("toxicity"))
JSTOR	((cassava) AND ("health risk")) ((cassava) AND (toxicity)) ((cassava) AND (cyanide)) ((cassava) AND (konzo)) ((cassava) AND ("acute poisoning")) ((cassava) AND ("tropical ataxic neuropathy")) ((cassava) AND ("neurological disorder")) ((Linamarin) OR (Lotaustralin))
AJOL	cassava AND "health risk" cassava AND toxicity cassava AND cyanide cassava AND konzo cassava AND "acute poisoning" cassava AND "tropical ataxic neuropathy" cassava AND "neurological disorder" Linamarin OR Lotaustralin

### 2.3.1 Risk of bias and quality assessment of included studies

A comprehensive quality appraisal was conducted for all studies included in this review, following the PRISMA 2020 guidelines. Study quality was assessed using the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies [National Heart, Lung, and Blood Institute (NHLBI), 2013] and the JBI Critical Appraisal Checklist for Case Series [Joanna Briggs Institute (JBI), 2017], depending on study design. Each study was independently evaluated by two reviewers to minimize bias. Any discrepancies were resolved through discussion and consensus. Table 4 summaries the quality rating score.

#### 2.4 Data synthesis and analysis

The findings from the included studies were synthesized based on geographical distribution (country of study population), cyanide exposure levels reported (e.g., in  $\mu$ mol L<sup>-1</sup>), reported health

TABLE 4 Summary of the quality rating score.

Score range	Percentage of criteria met	Quality rating	Interpretation
0-4 (NIH tool) / 0-4 (JBI tool)	0-49	Low	Study has significant methodological concerns; high risk of bias
5–9 (NIH tool) / 5–7 (JBI tool)	50–79	Moderate	Study meets many criteria but has some limitations; moderate risk of bias
10–14 (NIH tool) / 8–10 (JBI tool)	80-100	High	Study meets most or all criteria; low risk of bias

outcomes (e.g., konzo, tropical neuropathy, acute poisoning), and their underlying factors such as processing methods and HCN concentrations in cassava products. A geographic map and tabular summaries were used as appropriate to the data. The findings have been reported following the PRISMA statement, including a flow diagram of the study selection process, tabular summaries of study characteristics (design, population, and key findings), and narrative syntheses, highlighting patterns, contradictions and gaps, as appropriate.

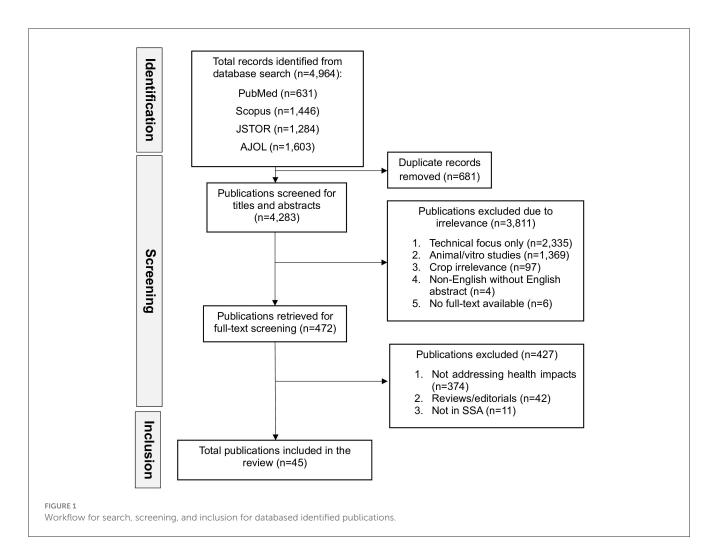
### **3 Results**

### 3.1 List of included publications

The initial database search identified a total of 4,964 records: PubMed (n=631), Scopus (n=1,446), JSTOR (n=1,284), and AJOL (n=1,603). After removing 681 duplicate records, 4,283 unique records were screened for titles and abstracts. From this pool, 472 publications were retrieved for full-text screening. Records were excluded at this stage based on irrelevance to the topic, that is, purely technical focus, use of animal or *in vitro* models, lack of relevance to cassava as a crop, non-English language, or unavailability of the full text. Following full-text screening, 426 publications were excluded for not addressing health impacts, being review articles or editorials, or being conducted outside SSA. Finally, 45 studies met the inclusion criteria and were included in the final review (Figure 1).

#### 3.1.1 Quality appraisal of included studies

Out of the 45 studies, 24 were appraised using the JBI Critical Appraisal Checklist for Case Series tool and 21 using the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies tool (Table 5). Most studies (n=26,58%) were rated as having moderate quality, while 19 studies (42%) were rated as high quality. No study was rated as low quality. Among the JBI-assessed studies, quality scores ranged from 67% to 90%, with most studies meeting 8 or 9 out of 10 criteria. For the NIH-assessed studies, scores ranged from 62% to 80%, with most studies meeting 8 or 9 out of 14 criteria. Common limitations included lack of clarity in participant selection, absence of blinding, and limited reporting on confounding factors.



### 3.2 Geographical scope of included publications

Figure 2 illustrates the frequency of included publications by the country where the studies were conducted. The Democratic Republic of Congo (DRC) had the highest frequency of publications (n=18), followed by Mozambique (n=10), Tanzania (n=7), and Nigeria (n=6). Other countries such as Malawi, Uganda, Zambia, and Cameroon each contributed only one study. This distribution highlights a concentration of research activity in regions with a high burden of cassava-related cyanide exposure, particularly in Central and East Africa.

### 3.2.1 Cassava production trends

Figure 3 illustrates increasing cassava production trends from 2000 to 2023 in selected countries. Notably, Nigeria and DRC demonstrated the most pronounced increases. Specifically, cassava production in DRC has shown a consistent and sustained rise since 2010. Although Nigeria experienced an overall substantial rise during the same period, production declined in 2013, 2019, and 2020.

### 3.3 Urinary thiocyanate concentration and associated health conditions

Urinary thiocyanate levels, a biomarker of cyanide exposure from cassava consumption, were reported in 28 of the 45 included studies (Table 6). The levels varied widely across populations, health conditions, and intervention periods. Several studies, particularly those conducted in the DRC, Mozambique, and Tanzania, reported extremely high thiocyanate levels, far above the World Health Organization's safety threshold of 350 µmol/L for urinary thiocyanate. The highest concentrations were observed in individuals diagnosed with konzo - a neurological disorder linked to cyanide toxicity. For instance, Tshala-Katumbay et al. (2001) reported concentrations of 1,128 µmol/L among individuals with konzo in the DRC, while Mlingi et al. (1991) reported a mean value of 1,730  $\mu$ mol/L at the onset of a konzo outbreak in Tanzania. Similarly, Tylleskär et al. (1992) found levels of 757 µmol/L in affected children compared to 50 µmol/L in unaffected peers. In addition, neurological conditions (e.g., tropical ataxic neuropathy), cognitive impairment, and acute intoxication events were reported.

Several studies demonstrated the impact of interventions aimed at improving cassava processing. For example, Banea et al. (2013) reported a reduction from 930  $\mu$ mol/L pre-intervention to 150

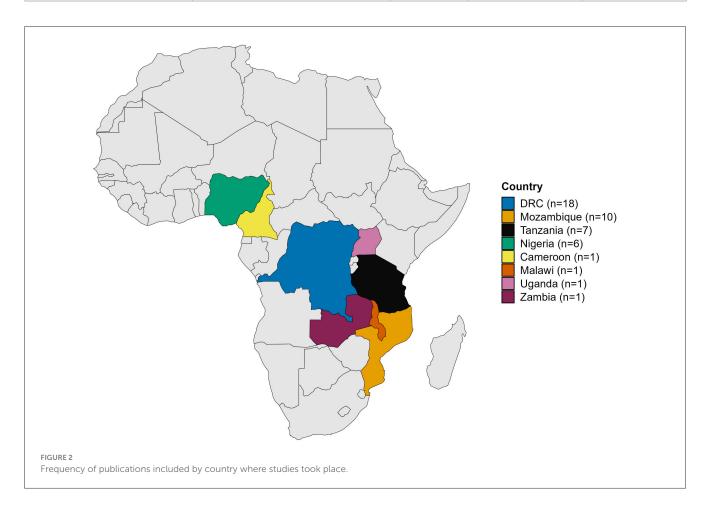
TABLE 5 Quality appraisal of all included studies using JBI Critical Appraisal Checklist for Case Series and NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.

References	Study design	Tool	Criteria met (%)	Quality rating
Osuntokun et al. (1968)	Clinical case series	JBI	6/9 (67%)	Moderate
Osuntokun et al. (1969)	Observational cross-sectional survey	NIH	8/13 (62%)	Moderate
Makene and Wilson (1972)	Clinical case series	JBI	7/10 (70%)	Moderate
Ministry of Health (1984)	Observational cross-sectional	NIH	8/13 (62%)	Moderate
Cliff et al. (1985)	Case series	JBI	9/10 (90%)	High
Cliff et al. (1986)	Observational cross-sectional	NIH	8/13 (62%)	Moderate
Howlett et al. (1990)	Observational cross-sectional	NIH	10/14 (71%)	Moderate
Mlingi et al. (1991)	Case series	JBI	8/10 (80%)	High
Tylleskär et al. (1991)	Cross-sectional epidemiological	NIH	8/13 (62%)	Moderate
Akintonwa and Tunwashe (1992)	Case series	JBI	6/9 (67%)	Moderate
Howlett et al. (1992)	Case series	JBI	8/10 (80%)	High
Tylleskär et al. (1992)	Cross-sectional analytical	NIH	8/13 (62%)	Moderate
Essers et al. (1992)	Clinical case series	JBI	8/10 (80%)	High
Mlingi et al. (1992)	Observational study with case series	JBI	9/10 (90%)	High
Tylleskär et al. (1993)	Case series	JBI	7/9 (78%)	Moderate
van Heijst et al. (1994)	Clinical case series	JBI	8/10 (80%)	High
Banea-Mayambu et al. (1997)	Observational case series	JBI	9/10 (90%)	High
Cliff and Nicala (1997)	Longitudinal clinical case series	JBI	8/9 (89%)	High
Cliff et al. (1997)	Observational case series	JBI	8/10 (80%)	High
Cliff et al. (1999)	Cross-sectional observational	NIH	9/13 (69%)	Moderate
Banea-Mayambu et al. (2000)	Cross-sectional comparative observational	NIH	9/13 (69%)	Moderate
Chiwona-Karltun et al. (2000)	Cross-sectional observational	NIH	9/13 (69%)	Moderate
Tshala-Katumbay et al. (2001)	Case series	JBI	8/10 (80%)	High
Onabolu et al. (2001)	Cross-sectional ecological	NIH	9/13 (69%)	Moderate
Bonmarin et al. (2002)	Epidemiological case series	JBI	7/10 (70%)	Moderate
Ernesto et al. (2002)	Observational case series	JBI	8/10 (80%)	High
Mwanza et al. (2003)	Clinical case series	JBI	8/10 (80%)	High
Cardoso et al. (2004)	Observational case series	JBI	7/10 (70%)	Moderate
Okafor (2004)	Cross-sectional biochemical exposure	NIH	8/13 (62%)	Moderate
Ciglenecki et al. (2011)	Case series	JBI	8/10 (80%)	High
Chabwine et al. (2011)	Epidemiological case series	JBI	8/10 (80%)	High
Diasolua Ngudi et al. (2011)	Cross-sectional observational	NIH	9/13 (69%)	Moderate
Banea et al. (2012)	Case series	JBI	9/10 (90%)	High
Banea et al. (2013)	Case series	JBI	9/10 (90%)	High
Oluwole and Oludiran (2013)	Cross-sectional geospatial ecological	NIH	8/10 (80%)	High
Bumoko et al. (2014)	Cross-sectional observational	NIH	9/13 (69%)	Moderate
Banea et al. (2015a)	Case series	JBI	9/10 (90%)	High
Banea et al. (2015b)	Cross-sectional survey	NIH	9/13 (69%)	Moderate
Bumoko et al. (2015)	Cross-sectional observational	NIH	9/13 (69%)	Moderate
Nhassico et al. (2015)	Case series	JBI	9/10 (90%)	High
Kambale et al. (2017)	Cross-sectional observational	NIH	9/13 (69%)	Moderate

(Continued)

TABLE 5 (Continued)

References	Study design	Tool	Criteria met (%)	Quality rating
Kashala-Abotnes et al. (2018)	Cross-sectional observational	NIH	9/13 (69%)	Moderate
Alitubeera et al. (2019)	Cross-sectional outbreak investigation	NIH	9/13 (69%)	Moderate
Siddiqi et al. (2020)	Cross-sectional outbreak investigation	NIH	9/13 (69%)	Moderate
Kabamba et al. (2023)	Cross-sectional observational	NIH	9/13 (69%)	Moderate



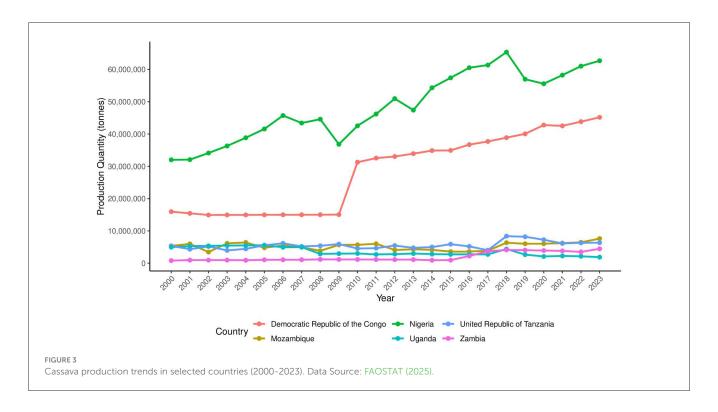
 $\mu mol/L$  post-intervention. Comparable declines were observed in Nhassico et al. (2015) (from 530  $\mu mol/L$  to 180  $\mu mol/L$ ) and Banea et al. (2015a) (from 444  $\mu mol/L$  to 191  $\mu mol/L$ ). In contrast, populations with safer cassava processing practices or lower cassava consumption exhibited significantly lower thiocyanate levels. For instance, Chiwona-Karltun et al. (2000) and Onabolu et al. (2001) reported levels as low as 50  $\mu mol/L$  and 17  $\mu mol/L$ , respectively, in non-endemic or low-consumption areas (Table 6).

# 3.4 Cassava processing methods and residual hydrogen cyanide (HCN) concentrations

Table 7 shows substantial variability in residual Hydrogen Cyanide (HCN) concentrations across different cassava processing

methods and duration. Raw bitter cassava roots contained the highest HCN levels, with concentrations reaching 327 ppm (Ministry of Health, 1984). In contrast, properly processed cassava flour showed significantly reduced HCN levels, depending on the method and duration of processing. Sun-drying alone reduced HCN levels to between 30 and 95 ppm, while heap fermentation was more effective, lowering concentrations to as low as 17–28 ppm (Cardoso et al., 2004; Ernesto et al., 2002). The combination of heap fermentation and sun-drying further reduced HCN to <10–20 ppm, particularly under lab-controlled fermentation conditions for 6 d (Chabwine et al., 2011).

Studies involving wetting methods (i.e., 2h sun and 5-h shade exposure) as a cassava processing intervention consistently achieved the lowest HCN levels. (eg.,) Banea et al. (2012, 2013, 2015a) and Nhassico et al. (2015) reported reductions from preintervention levels of 22–74 ppm to post-intervention levels of 4–25 ppm. In contrast, studies that documented unspecified or shortened processing methods consistently reported higher cyanide levels.



Bumoko et al. (2015); Kambale et al. (2017); and Kabamba et al. (2023) all recorded ranges between 30 and 200 ppm.

#### 4 Discussion

### 4.1 Cassava's dual role in food security and cyanide-related health risks

This systematic review highlights the persistent public health risks associated with cyanide exposure from cassava consumption in SSA, despite the crop's critical role in regional food security. The findings reveal a complex interplay between agricultural practices, processing methods, and structural vulnerabilities within food systems that collectively shape the health outcomes of cassava consumers. In countries like the DRC and Mozambique, cassava was a critical staple, especially during periods of conflict, drought, or economic hardship. However, in these contexts, cassava plays a dual role: while it is a resilient and accessible food source, it also poses significant health risks due to its high cyanogenic glycoside content, particularly in bitter varieties. These risks were amplified when cassava was consumed without adequate processing, which remains common in many resource limited settings like SSA.

Despite the availability of effective processing methods such as wetting and heap fermentation, their adoption remains limited due to weaknesses and disruptions in SSA's food systems. For instance, wars and conflicts profoundly disrupt agricultural activities, food distribution, and household food security (Weldegiargis et al., 2023; Muriuki et al., 2023), forcing communities to rely heavily on inadequately processed cassava (Cliff et al., 1997). Socio-economic stress often forces households to rely on shortened or informal processing methods, which are less effective at detoxifying cassava. Moreover, the intentional cultivation of bitter varieties due to their

pest resistance, storability, and yield further complicates efforts to reduce cyanide exposure (Imakumbili et al., 2019; Chiwona-Karltun et al., 1998; Kapinga et al., 1997). These food system challenges have intensified in recent years across SSA, exacerbated by climate change impacts such as prolonged dry spells, El Niño events, and cyclones (World Food Programme, 2024; United Nations Office for the Coordination of Humanitarian Affairs, 2022), all of which further entrench the over-reliance on cassava as a food security crop.

### 4.2 Geographical distribution of cyanide-related health risks

The burden of cassava-related health risks was concentrated in a few countries, most notably the DRC, Mozambique, Tanzania, and Nigeria. However, the absence of epidemiological data from other high cassava-consuming countries, such as Ghana and Malawi (Adebayo, 2023), may not necessarily indicate a lack of risk. In some cases, this may reflect weak surveillance systems to detect sub-lethal cyanide exposure or milder neurological symptoms that are not present as overt clinical cases. Nonetheless, it may also reflect the absence of key contributing factors such as wars and conflicts or the widespread use of safer processing practices, as observed in Malawi (Chiwona-Karltun et al., 2000). Furthermore, many of the studies included in this review are decades old, suggesting either a decline in research interest possibly due to reduced funding-or a genuine reduction in incidence, potentially linked to increased awareness and improved cassava processing practices. This gap highlights the urgent need for renewed investment in research and the strengthening of

TABLE 6 Urinary thiocyanate concentrations and related health conditions reported in the included studies.

References	Country	Summary of study population	Mean urinary thiocyanate level		Health condition diagnosed or studied	
Osuntokun et al. (1968)	Nigeria	9 patients aged 19-61 years	N/A		Tropical ataxic neuropathy	
Osuntokun et al. (1969)	Nigeria	384 individuals over 10 years	N/A		Tropical ataxic neuropathy	
Makene and Wilson (1972)	Tanzania	Adults (8 patients and 19 controls)	N/A		Tropical ataxic neuropathy	
Ministry of Health (1984)	Mozambique	17 affected and 17 control families	N/A		Spastic paraparesis (Konzo)	
Cliff et al. (1985)	Mozambique	1983: 31 children, 30 from	Cassava (Paraparesis)	84 mmol/mol*	Spastic paraparesis (Konzo)	
		neighboring area, and 28 urban children	Control (no cassava and paraparesis)	9 mmol/mol*		
Cliff et al. (1986)	Mozambique	375 school children	Children with clonus	125 mmol/mol*	Neurological dysfunction	
			Children without clonus	70 mmol/mol*	(ankle clonus)	
Howlett et al. (1990)	Tanzania	39 cases of affected individuals	N/A		Konzo	
Mlingi et al. (1991)	Tanzania	2,100 inhabitants (4 individuals	At onset	1,730 μmol/L	Konzo	
		with konzo	After 1 year	178 μmol/L		
Tylleskär et al. (1991)	DRC	134 konzo cases; 40 households; 152 other individuals	N/A	'	Konzo	
Akintonwa and Tunwashe (1992)	Nigeria	3 individuals (ages 8, 17, and 18) from the same family	0.40-0.7 mg/I	#	Acute intoxication	
Essers et al. (1992)	Mozambique	7 individuals, aged 6-32 (women and children)	51 mmol/mol*		Konzo	
Howlett et al. (1992)	Tanzania	28,500 inhabitants, with 116 konzo cases	N/A		Konzo	
Tylleskär et al. (1992)	DRC	77 adults and 31 children (affected); 46 children (unaffected)	Children (affected)	757 μmol/L	Konzo	
			Children (unaffected)	50 μmol/L		
Mlingi et al. (1992)	Tanzania	95 individuals (28 men, 37	Drought year (1988)	1120 μmol/L	Konzo	
		women, 30 children)	Normal year(1989)	68 μmol/L	Acute intoxication	
Tylleskär et al. (1993)	Tanzania	2 male patients (age 19 and 25 years)	N/A		Konzo	
van Heijst et al. (1994)	Tanzania	20 patients (age 11–39 years)	N/A		Tropical neuropathy	
Cliff and Nicala (1997)	Mozambique	9 patients (7 children and 2 adult women)	N/A		Konzo	
Cliff et al. (1997)	Mozambique	384 total cases	Schoolchildren	207 μmol/L	Konzo	
Banea-Mayambu et al.	DRC	298 individuals across 5 villages	Dry season (savanna)	593 μmol/L	Konzo	
(1997)			Wet season (Savanna)	359 μmol/L	1	
Cliff et al. (1999)	Mozambique	397 school children	Children with clonus	244 μmol/L	Ankle clonus	
			Children without clonus	154 μmol/L	Konzo	
Banea-Mayambu et al.	DRC	502 children (0–36 months)	North (safe processing)	50 μmol/L	Stunting	
(2000)			South (short processing)	757 μmol/L	-	
Chiwona-Karltun et al. (2000)	Malawi	176 women farmers	50 μmol/L		No reported cases of konzo or intoxication	
Onabolu et al. (2001)	Nigeria	1272 school children	Area A (TAN-edemic)	73 μmol/L	Tropical Ataxic Neuropathy	
			Areas C (North-low cassava 17 μmol/L consumption)			
Tshala-Katumbay et al. (2001)	DRC	2,723 inhabitants, with 55 konzo cases	1128 μmol/L		Konzo	

(Continued)

TABLE 6 (Continued)

References	Country	Summary of study population	Mean urinary thiocyanate level		Health condition diagnosed or studied	
Bonmarin et al. (2002)	DRC	237 confirmed Konzo cases	N/A		Konzo	
Ernesto et al. (2002)	Mozambique	30 schoolchildren per site from 5 communities	Terrene-A (sun drying	384 μmol/L	Konzo	
		communities	Mujocojo (heap fermentation)	225 μmol/L		
Mwanza et al. (2003)	DRC	21 Congolese patients	N/A		Konzo	
Cardoso et al. (2004)	Mozambique	School children from four sites, 30 samples per site	Niboia (>cassava consumption)	351 μmol/L	Konzo	
			Munhacuco ( <cassava consumption)<="" td=""><td>58 μmol/L</td><td></td></cassava>	58 μmol/L		
Okafor (2004)	Nigeria	85 individuals (40 Gari	Cassava consumers	62 μmol/L	Acute intoxication	
		processors, 25 cassava consumers and 20 smokers	Gari processors	148 μmol/L		
Chabwine et al. (2011)	DRC	61 individuals	129 μmol/L	+	Konzo	
Ciglenecki et al. (2011)	Cameroon	469 individuals (children under 15 and women of reproductive age)	N/A		Konzo	
Diasolua Ngudi et al. (2011)	DRC	3,015 individuals across 487 households	N/A		Konzo	
Banea et al. (2012)	DRC	Total population of 2,206 (50	Pre-intervention	332 μmol/L	Konzo	
		konzo cases identified)	Post-intervention	130 μmol/L		
Banea et al. (2013)	DRC	Total population of 1,315 (61 Konzo cases identified)	Pre-intervention	930 μmol/L	Konzo	
			Post-intervention	150 μmol/L		
Oluwole and Oludiran (2013)	Nigeria	150 farmers	N/A		Ataxic polyneuropathy	
Bumoko et al. (2014) DRC	DRC	40 children (21 konzo, 19 non-konzo)	Konzo children	Max ~1,032 μmol/L	Konzo     Cognitive impairment	
			Non-konzo children	Max~ 688 μmol/L		
Bumoko et al. (2015)	DRC	210 children (123 konzo, 87	Konzo children	519 μmol/L	Konzo	
		non-konzo)	Non-konzo children	388 μmol/L		
Banea et al. (2015a)	DRC	4,588 individuals, with 144 konzo	Pre-intervention	444 μmol/L	Konzo	
		cases	Post-intervention	191 μmol/L		
Banea et al. (2015b)	DRC	22,793 individuals, with 172 konzo cases	N/A		Konzo	
Nhassico et al. (2015)	Mozambique	Population of 6,190 (77 Konzo	Pre-intervention (Cava)	530 μmol/L	Konzo	
		cases and 50 school children and 50 women sample per village	Post-intervention (Cava)	180 μmol/L		
Kambale et al. (2017)	DRC	209 children (122 konzo, 87	Konzo children	522 μmol/L	Konzo	
		non-konzo)	Non-konzo children	385 μmol/L		
Kashala-Abotnes et al.	DRC	114 mother-child dyads (children	Children	617 μmol/L	Konzo	
(2018)		aged 12-48 months)	Mothers	818 µmol/L		
Alitubeera et al. (2019)	Uganda	98 probable cases (11 months to 75 years)	N/A		Acute intoxication	
Siddiqi et al. (2020)	Zambia	32 confirmed konzo cases (children aged 6-14 years and females ≥15 years	281 μmol/L (median value)		Konzo	
Kabamba et al. (2023)	DRC	406 adult participants (203 household couples)	950 μmol/L		Neurocognitive impairmen	

 $N/A, not\ reported\ or\ measured; *\ Urinary\ SCN/creatinine; \#\ not\ thiocyanate,\ but\ urine\ cyanide\ levels.$ 

TABLE 7 Cassava processing methods and residual hydrogen cyanide (HCN) concentrations.

References	Cassava product	Processing method	Duration	Mean HCN (ppm)
Ministry of Health	Fresh roots (bitter)	Raw	N/A	327
(1984)	Dried roots (bitter)	Sun-drying	1-2 d	95
	Cassava flour	Sun-drying + pounding	1-2 d	40
Ernesto et al. (2002)	Cassava flour	Sun-drying	Not specified	46
		Heap fermentation	Not specified	28
Cardoso et al. (2004)	Cassava flour	Sun-drying	Not specified	30
		Heap fermentation	Not specified	17
Chabwine et al. (2011)	Cassava root	Heap fermentation + sun-drying	2–3 days fermentation, 1–2 days drying	20 (median value)
	Cassava root (lab-controlled)	Heap fermentation only	6 days	<10
Banea et al. (2012)	Cassava flour	Soaking (pre-intervention)	1-2 days	22
		Wetting (post-intervention)	2-hours sun / 5-hours shade	4-10
Banea et al. (2013)	Cassava flour	Soaking (pre-intervention)	1–2 ddays	43-74
		Wetting (post-intervention)	2-hours sun / 5-h shade	9-18
Banea et al. (2015a)	Cassava flour	Soaking + drying (Pre-intervention)	2 days soaking / 1-4 days drying	19-41
		Wetting (post-intervention)	2-hours sun / 5-hours shade	8-12
Nhassico et al. (2015)	Cassava flour	Soaking + drying and heap fermentation (pre-intervention)	1-2 days	17-64
		Wetting (post-intervention)	2-hours sun / 5-hours shade	9-25
Bumoko et al. (2015)	Cassava flour	Shortened processing (not specified)	Not specified	30-200
Kambale et al. (2017)	Cassava flour	Shortened processing (not specified)	Not specified	30-200
Kashala-Abotnes et al. (2018)	Cassava flour	Soaking + sun-drying	≤3 nights	52
Alitubeera et al. (2019)	Cassava flour	likely soaking and drying	Not specified; likely shortened	88
Siddiqi et al. (2020)	Cassava roots and leaves	Sun drying (main), soaking (less common)	Not specified; likely shortened	400 (median value)
Kabamba et al. (2023)	Cassava flour	likely soaking and sun-drying	Not specified; shortened	30-200

surveillance systems to capture both acute and chronic health effects of cyanide exposure in cassava-consuming populations.

### 4.3 Health risks associated with cyanide exposure

The review revealed a consistent association between cassava consumption and neurological conditions such as konzo and tropical ataxic neuropathy (TAN). Konzo is characterized by a sudden onset of non-progressive spastic paraparesis, leading to severe motor impairment and often resulting in irreversible disability (Kashala-Abotnes et al., 2019; World Health Organization, 1996; Tylleskär et al., 1991). In contrast, TAN presents as a progressive condition involving both sensory and motor deficits, while broader neuropathies may arise from prolonged, low-level cyanide exposure (Adamolekun, 2011).

Biomarker data, particularly urinary thiocyanate levels, provided strong evidence of chronic cyanide exposure in affected populations (Cliff et al., 2011). In several studies (Bumoko et al.,

2014, 2015; Tshala-Katumbay et al., 2001; Mlingi et al., 1992), levels exceeded WHO recommended safety limit of 350  $\mu mol/L$  (World Health Organization, 1996). In contrast, lower thiocyanate levels (<350  $\mu mol/L$ ) were typically observed in populations with access to adequately processed cassava, reduced reliance on cassava as a staple, or the use of low-cyanide cassava varieties. These findings highlight the effectiveness of targeted mitigation strategies in reducing cyanide exposure and preventing associated health outcomes.

### 4.4 Effectiveness of cassava processing methods and recent advances

Processing methods play a critical role in determining the residual HCN levels in cassava products. Raw bitter cassava roots were found to contain extremely high HCN concentrations, reaching up to 327 ppm (Ministry of Health, 1984). In contrast, more effective processing techniques, particularly heap fermentation and the wetting method consistently reduced HCN

levels to below the WHO's recommended safety limit of 10 ppm for cassava flour and dried cassava products (FAO/WHO, 2011). Post-intervention studies, particularly using the wetting method, demonstrated substantial reductions in HCN content, with some achieving levels as low as 4–10 ppm (Banea et al., 2012, 2013). However, the review also found that shortened or improperly applied methods, such as soaking for only 1–2 days, often resulted in dangerously high HCN levels—sometimes exceeding 400 ppm. These inadequate practices were frequently driven by time constraints, limited awareness, or lack of access to water. Such findings underscore the urgent need to promote improved cassava processing techniques, particularly the wetting method, and to strengthen community education on safe detoxification practices to reduce the risk of cyanide exposure.

In addition to traditional or conventional processing methods, recent innovations in cassava breeding and processing technologies offer promising solutions. Notably, bio fortified cassava varieties such as UMUCASS-38 (TMS 01/1371) and NR-8082, developed through collaborative efforts involving the [International Institute of Tropical Agriculture (IITA), 2012] and Harvest Plus, combine high yield, drought tolerance, and enhanced pro vitamin A content with low cyanogenic potential (Odoemelam et al., 2020). These varieties have been shown to contain cyanide levels of approximately 17.02  $\pm$  0.02 ppm (UMUCASS-38) and 18.01  $\pm$  0.01 ppm (NR-8082) in flour form, which are well below the WHO's safety threshold of 50 ppm for fresh cassava roots (FAO/WHO, 2011). Technologies such as hydraulic pressing, mechanical peeling, and grated fermentation have also been developed to enhance detoxification and reduce processing time [International Institute of Tropical Agriculture (IITA), 2012]. However, adoption of these innovations remains limited in many rural areas due to affordability constraints, weak extension services, and low awareness (Nweke et al., 2002). Cultural food preferences and the time-intensive nature of some improved methods may also hinder uptake. Expanding access to improved varieties, strengthening extension systems, and promoting behavior change communication are essential for scaling up safe cassava utilization.

### 4.5 Protein deficiency and nutritional vulnerability

Protein-deficient diets are a major underlying contributor to cyanide-related health risks. Many populations consuming bitter cassava lacked access to protein-rich foods that provide sulfur-containing amino acids, such as methionine and cysteine, critical for detoxifying cyanide into thiocyanate (Richie et al., 2023). Without sufficient intake of quality protein, the risk of conditions like konzo increased significantly (Tylleskär et al., 1995; Cliff et al., 1985; Ministry of Health, 1984). For instance, the [Integrated Food Security Phase Classification (IPC), 2022a] estimated that approximately 26.4 million people in the DRC experienced high levels of acute food insecurity (IPC Phase 3 or above) between July and December 2022, driven by widespread poverty, conflict, displacement, low agricultural production, high food prices, and poor infrastructure [Integrated Food Security Phase Classification

(IPC), 2022b]. For instance, in Malawi – a country where cassava is consumed – protein poverty is evident, as most dietary protein comes from cereals that are low in essential amino acids like lysine and tryptophan [International Food Policy Research Institute (IFPRI), 2020a,b; Muleya et al., 2022]. In addition, poor dietary diversity further contributes to deficiencies in micronutrients like selenium, calcium, and zinc, which are essential for neurological health and resilience to cyanide toxicity (Kurmi et al., 2023).

## 4.6 Cassava dependency and its implications for the broader food systems

This review also underscores how cassava toxicity reveals broader systemic vulnerabilities within SSA's food systems. In the context of worsening climate change, persistent conflict, economic fragility, and weak infrastructure, cassava remains one of the few accessible, drought-resilient crops, even when its consumption carries serious health risks. During the 2022/23 period, over 55 million people in 12 countries within the [Southern African Development Community (SADC), 2022] were food insecure. Additionally, 35 non-international armed conflicts were active across Africa in 2024 (Geneva Academy of International Humanitarian Law, and Human Rights, 2025). These persistent challenges reduce the viability of other staples, disrupt markets and agricultural production, and limit access to safe, nutritious diets. These pressures are unlikely to subside in the near future, reinforcing the chronic nature of cyanide toxicity. Strengthening food systems through continuous surveillance, support for diversified and climate-resilient agriculture, and the promotion of food sovereignty where communities control their food production and processing is essential for long term mitigation.

### 4.7 Strengths and limitations of the study

This review has several strengths that enhance the credibility and comprehensiveness of its findings. First, it employed a broad search strategy across multiple databases—PubMed, Scopus, JSTOR, and AJOL, ensuring the inclusion of country and regionspecific studies. Second, the methodological quality of all included studies was rigorously assessed using validated tools: JBI Critical Appraisal Checklist for Case Series and NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies. Third, the review adhered to the PRISMA guidelines, promoting transparency, reproducibility, and methodological rigor. Finally, the involvement of multiple reviewers in both the screening and risk of bias assessment processes helped enhance consistency and reduce the risk of selection bias. Despite these strengths, the review has a limitation. The exclusion of non-English language publications may have introduced language bias. However, to minimize this effect, studies with English titles and abstracts were screened for relevance, even if the full text was not available in English. While this approach helped reduce the risk of overlooking important studies, it may still have led to the omission of valuable data published in other languages.

### 5 Conclusion

This systematic review has underscored the ongoing public health threat posed by cassava cyanide toxicity in SSA, particularly in countries like the DRC and Mozambique, where the combined effects of conflict, drought, protein-deficient diets, and unsustainable food systems continue to undermine food and nutrition security. These challenges have intensified in recent years across SSA exacerbated by climate change phenomena such as prolonged dry spells, El Niño, and cyclones, along with global economic and political instability. Together, these factors reinforce reliance on cassava as a staple crop, increasing the risk of cyanide exposure, especially in communities lacking access to improved processing methods or safer cassava varieties.

While notable progress has been made through the development of low-cyanide cassava varieties (e.g., bio fortified cassava varieties) and improved processing innovations (e.g., wetting method), adoption remains uneven due to limited awareness, time constraints, inadequate extension support, cultural preferences, and water scarcity. Scaling up education on effective detoxification techniques such as wetting and heap fermentation and ensuring the availability and affordability of low-HCN cassava varieties are critical steps forward. Achieving this requires not only technical solutions but also broader support for food system transformation through research investment and community-led approaches that prioritize food sovereignty.

### Data availability statement

The original contributions presented in the study are included in the article, further inquiries can be directed to the corresponding author.

#### **Author contributions**

GO: Writing – review & editing, Conceptualization, Writing – original draft, Investigation, Formal analysis, Data curation, Methodology, Visualization. WM: Investigation, Writing – review & editing, Conceptualization, Writing – original draft, Visualization, Methodology, Data curation, Formal analysis. KM: Conceptualization, Writing – review & editing, Formal analysis, Methodology. TN-M: Conceptualization,

Supervision, Methodology, Writing – review & editing. AK: Visualization, Supervision, Writing – review & editing, Methodology, Conceptualization.

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### Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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