African Journal of Pharmaceutical Research and Development
Available online at https://ajopred.com
Vol. 18 No.2; pp. 760-783 (2026)

Original Research Article

PHYTOCHEMISTRY, PHARMACOLOGY, NUTRITIONAL COMPOSITION, AND SOCIO-ECONOMIC SIGNIFICANCE OF KOLANUT [*Cola nitida* (Vent.) Schott & Endl. and *Cola acuminata* (P. Beauv.) Schott & Endl.] IN NIGERIA AND WEST AFRICA: A SCOPING REVIEW

OLUWATOYIN ISHOLA[1,*], ELIJAH OLUWATOSIN OLOPADE[2], BARNABAS OLUWATOMIDE OYEYINKA[3], JENNIFER OGOCHUKWU DIKE[4], BASIL MBAH[5], HASSANAT MUJAHIDAH ABDUL-FATAI[6], ADESEWA BALQIS ADEKUNLE[7]

1. Department of Biochemistry, Faculty of Life Sciences, Kaduna State University, Kaduna, Nigeria.
2. Department of Biochemistry, Faculty of Science, Adeleke University, Ede, Nigeria.
3. Biomedicinal Research Centre, Forestry Research Institute of Nigeria, Ibadan, Nigeria.
4. Department of Medical Laboratory Science, Faculty of Health Sciences, Imo State University, Owerri, Nigeria.
5. Department of Chemistry, Faculty of Physical Sciences, Ahmadu Bello University, Zaria, Nigeria.
6. Department of Pharmacology and Toxicology, Faculty of Pharmaceutical Sciences, Usmanu Danfodiyo University, Sokoto, Nigeria.
7. Department of Biochemistry and Molecular Biology, Faculty of Science, Obafemi Awolowo University, Ile-Ife, Nigeria.

ABSTRACT

Kolanut, the seed of Cola species (family Malvaceae), is an economically, culturally, and pharmacologically important crop across Nigeria and West Africa, yet no synthesis has mapped its phytochemical, pharmacological, nutritional, agronomic, and socio-economic evidence base or weighed how consistent that evidence is. This review maps peer-reviewed and grey-literature evidence on kolanut's phytochemistry, fatty acid profile, pharmacological and toxicological activity, nutritional composition, and socio-economic significance, and classifies this evidence by study type and confidence level. Following the Arksey and O'Malley scoping-review framework and PRISMA-ScR guidance, 82 sources were identified through PubMed, Google Scholar, ScienceDirect, SpringerLink, AJOL, Scopus, and Web of Science. Kolanut consistently contains alkaloids, flavonoids, tannins, phenols, cardiac glycosides, terpenes, steroids, and saponins, with anthraquinones and phlobatannins generally absent. Caffeine, theobromine, catechin, and epicatechin are well characterized. Reported antioxidant activity is frequently comparable to, or exceeds, standard antioxidants. Pharmacological studies document antidiabetic, antimicrobial, antimalarial, and hepatoprotective activity, mostly from rodent and in vitro models, alongside toxicological signals at high or chronic doses. Species-specific fatty acid data remain sparse. Confidence is high for phytochemical and antioxidant findings, moderate for pharmacological findings, and limited for fatty acid composition and dose-response translation to humans. Kolanut is phytochemically rich and socio-economically important, but evidence remains unevenly distributed and largely preclinical. Species-specific fatty acid data, human trials, and dose-response studies are priorities for future research.

ARTICLE INFO

Received 24 July, 2026
Accepted 28 August, 2026
Published 31 August, 2026

KEYWORDS

Cola acuminata,
Cola nitida,
Kolanut,
Phytochemicals,
Antioxidant activity,
Nigeria

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***Corresponding author:** oluwatoyinishola2024@gmail.com; +234 810 244 0103
https://doi.org/10.59493/ajopred/2026.2.6 ISSN: 0794-800X (print); 1596-2431 (online)

INTRODUCTION

Kolanut is the seed of trees in the genus *Cola* (family Malvaceae, subfamily Sterculioideae), of which *Cola nitida* and *Cola acuminata* are the two species most widely cultivated and consumed in West Africa [1,2]. The genus contains well over 100 described species, but only a small number — principally *C. nitida*, *C. acuminata*, and to a lesser extent *C. anomala*, *C. gigantea*, and *C. millenii* — are of recognized economic and pharmacological importance [3]. Members of the wider family Sterculiaceae/Malvaceae to which *Cola* belongs have long been recognized as a pharmacologically active plant group,[4] and ethnobotanical inventories have repeatedly flagged *Cola* species as productive starting points for pharmacological research precisely because of their deep embeddedness in indigenous medicinal knowledge systems [5]. Historically, *C. nitida* has dominated formal export trade while occurring across a broad West and Central African range,[6] whereas *C. acuminata* is more commonly retained for local consumption, traditional medicine, and ceremonial use [2,7,8].

In Nigeria, kolanut occupies a place that extends well beyond nutrition: it is chewed as a mild central nervous system stimulant, presented at naming ceremonies, weddings, funerals, and reconciliation rites, and traded as a significant agricultural commodity across Yoruba, Igbo, Hausa, and other cultural contexts [1,9,10,11,12,13]. Beyond its cultural significance, kolanut has attracted growing scientific interest as a source of bioactive secondary metabolites. Preliminary phytochemical screens across numerous studies on *C. acuminata* and *C. nitida* converge on a consistent profile of alkaloids, flavonoids, tannins, phenols, cardiac glycosides, terpenes, steroids, and saponins in the seed, with anthraquinones and phlobatannins typically absent [2,14,15,16]. Several of these compound classes are pharmacologically important, having reported anti-inflammatory, antimicrobial, hypoglycaemic, antimalarial, and antioxidant activities, which has motivated a substantial parallel body of work evaluating the free-radical scavenging and lipid-peroxidation-inhibiting capacity of kolanut extracts using assays such as DPPH, nitric oxide (NO) scavenging, thiobarbituric acid reactive substances (TBARS), total antioxidant capacity (TAC), and ferric reducing antioxidant power (FRAP) [17,18,19].

The purine alkaloids caffeine and theobromine, together with catechin, epicatechin, and procyanidins B1 and B2, are among the best-characterized bioactive constituents of kolanut and have been directly implicated in both its stimulant properties and its antioxidant capacity [3,20]. Caffeine and total phenolic content have additionally been shown to vary geographically across West African production zones, with comparative data available from Côte d'Ivoire alongside the Nigerian literature [21]. A growing pharmacological literature, generated largely by research groups working with hot-water or ethanolic kolanut infusions, has additionally reported antidiabetic, cardioprotective, hepatoprotective, neuroprotective, and antimalarial activities in rodent models,[24,25,26,27,28,29,30] with two broader narrative reviews of *Cola* pharmacology available for general background [22,23]. At the same time, a smaller but important toxicological literature documents adverse effects of chronic or high-dose kolanut consumption on reproductive hormones, hepatic enzymes, and renal function, underscoring the need to interpret kolanut's pharmacological promise alongside dose-dependent safety considerations [31,32,33,34,35,36,37,38,39].

Two prior narrative reviews have summarized *Cola* phytochemistry and pharmacology at the whole-genus level [3,23]. Unlike those reviews, the present work applies an explicit evidence-hierarchy and narrative confidence-rating framework — classifying every included theme as high, moderate, or limited confidence based on replication, cross-study consistency, and study-design type — so that readers can see not only what has been reported about kolanut, but how strongly each claim is supported and where the evidence is thin.

In parallel, the fatty acid and volatile/semi-volatile phytochemical composition of kolanut oil is of interest both nutritionally and industrially, given ongoing global efforts to identify plant oils with favourable unsaturated-to-saturated fatty acid ratios as alternatives to palm oil and other high-saturated-fat industrial oils. However, detailed gas chromatography-mass spectrometry (GC-MS) and gas chromatography-flame ionization detection (GC-FID) characterization specific to *C. acuminata* oil is comparatively rare in the accessible literature; more granular fatty acid and non-fatty-acid compositional data exist for the related, less-studied species *C. gigantea* and *C. millenii*, which offer a useful comparative reference point [40,41].

Kolanut's importance is not confined to its chemistry and pharmacology. Agronomic and genetic studies document substantial intraspecific and interspecific variability in kola germplasm across Nigeria, Ghana, Côte d'Ivoire, and Cameroon, with direct implications for the bioactive-compound content of nuts reaching market [10,42,43,44,45]. Postharvest handling, curing, and storage practices — developed largely through indigenous knowledge to counter weevil infestation and fungal spoilage — materially affect the

quality and composition of nuts consumed and traded [46,47,48,49,50]. Ethnobotanical and socio-economic scholarship further situates kolanut as a crop of major cultural, ceremonial, and livelihood significance, generating income for farmers, processors, and traders across multiple West African countries while serving indispensable roles in marriage, chieftaincy, hospitality, and conflict-resolution rites [7,9,11,12,13,51,52,53].

Given this scattered and heterogeneous evidence base — spanning analytical chemistry, pharmacology and toxicology, nutrition science, plant genetics and agronomy, and ethnobotany/economics — a structured scoping review is needed to (i) consolidate what is known about the phytochemical, fatty acid, pharmacological, nutritional, agronomic, and socio-economic profile of kolanut, (ii) explicitly compare and critically weigh this evidence rather than merely enumerate it, (iii) clarify where the strongest and weakest parts of the evidence base lie, and (iv) identify concrete directions for future primary research, including GC-MS and GC-FID studies specific to *C. acuminata* seed oil grown in Nigeria's diverse agroecological zones, and dose-response toxicological studies relevant to habitual human consumption levels.

MATERIAL AND METHODS

Protocol and reporting

This review followed the five-stage scoping-review framework originally proposed by Arksey and O'Malley[54] and subsequently refined by Levac, Colquhoun, and O'Brien:[55] (i) identifying the research question, (ii) identifying relevant studies, (iii) study selection, (iv) charting the data, and (v) collating, summarizing, and reporting results. Reporting followed the PRISMA extension for Scoping Reviews (PRISMA-ScR) checklist [56]. Consistent with standard scoping-review methodology, no formal risk-of-bias scoring of individual studies was undertaken; instead, a narrative confidence-rating approach, described below, was used to communicate the relative strength of evidence across themes.

Research questions

The review addressed six linked questions: (1) What classes of phytochemicals and specific GC-MS-identified compounds have been reported in *Cola* species used as kolanut? (2) What is the reported fatty acid composition of kolanut seed oil, and how does it compare across *Cola* species? (3) What antioxidant assays have been applied to kolanut extracts, and what potency (IC50) values have been reported relative to standard antioxidants? (4) What pharmacological activities and toxicological/safety signals have been documented for kolanut in preclinical and human-relevant studies? (5) What agronomic, genetic, postharvest, ethnobotanical, and socio-economic factors shape kolanut's composition, quality, and significance in Nigeria and West Africa? (6) How strong, internally consistent, and translatable to human health is the assembled evidence base, and where does it disagree?

Eligibility criteria

Inclusion criteria: peer-reviewed original research articles, reviews, technical reports, and relevant grey literature (institutional reports, government/FAO-type technical papers), published predominantly in English, reporting qualitative or quantitative phytochemical screening, GC-MS phytochemical profiling, GC-FID/GC-MS fatty acid composition, in vitro or in vivo pharmacological/toxicological activity, proximate/nutritional/mineral composition, agronomic or genetic characterization, postharvest/storage data, or ethnobotanical/socio-economic data on any part (seed, leaf, bark, pod, root) of *Cola* species used as kolanut, with priority given to *C. acuminata* and *C. nitida* and comparative inclusion of *C. gigantea*, ***C. millenii***, *C. anomala*, and other congeners.

Exclusion criteria: studies focused exclusively on *Garcinia kola* (bitter kola, a taxonomically distinct genus) without direct comparative data on *Cola* species; non-peer-reviewed sources lacking retrievable full text; duplicate or overlapping datasets from the same research group where a fuller version existed; and studies on *Cola* species with no plausible relevance to kolanut phytochemistry, pharmacology, nutrition, agronomy, or socio-economics. Grey-literature sources (institutional reports, theses, technical bulletins) were retained only where their content could be corroborated against, or was materially complementary to, the peer-reviewed literature; formal grey-literature appraisal frameworks such as AACODS (Authority, Accuracy, Coverage, Objectivity, Date, Significance), of which the WHO's quality-control guidance for medicinal plant materials is a relevant domain-specific example,[57] provide a template for this kind of judgement, though a full AACODS scoring exercise was not separately tabulated here.

Information sources and search strategy

Sources were identified through PubMed, Google Scholar, ScienceDirect, SpringerLink, Scopus, Web of

Science, and Africa Journals Online (AJOL), supplemented by citation tracking (backward and forward snowballing) from retrieved articles and institutional/grey-literature sources. Searches combined the population terms ("*Cola acuminata*" OR "*Cola nitida*" OR "kolanut" OR "kola nut" OR "*Cola gigantea*" OR "*Cola millenii*") with concept terms ("phytochemical*", "GC-MS", "fatty acid*", "antioxidant*", "DPPH", "proximate composition", "pharmacology", "toxicity", "agronomy", "genetic diversity", "postharvest", "ethnobotany", "socio-economic") using Boolean operators, in the representative form: ("*Cola acuminata*" OR "*Cola nitida*" OR "kolanut" OR "kola nut") AND ("phytochemical*" OR "GC-MS" OR "fatty acid*" OR "antioxidant*" OR "pharmacology" OR "toxicity" OR "agronomy" OR "ethnobotany").

Searches covered all records available in the databases and sources listed above up to the time of writing, restricted predominantly to English-language sources, with no lower date limit applied so as to capture foundational methodological and toxicological references.

Study selection process

The study-selection process followed the PRISMA-ScR flow shown in Figure 1. Database searching identified 341 records, supplemented by 28 additional records from citation snowballing and institutional/grey-literature sources (369 records total). After removal of duplicates, 302 unique records remained and were screened at title and abstract level; 176 were excluded at this stage for falling outside the *Cola* genus or lacking compositional or bioactivity data, leaving 126 full-text articles assessed for eligibility. Of these, 44 were excluded following full-text review — 14 for reporting agronomic or genetic data with no compositional information, 10 for lacking retrievable full text, 8 as duplicate datasets from the same research group, and 12 for being non-peer-reviewed or thesis abstracts without a corresponding full report. This left 82 sources meeting the eligibility criteria and forming the evidentiary basis of this review, subsequently charted by evidence theme as summarized in Figure 1.

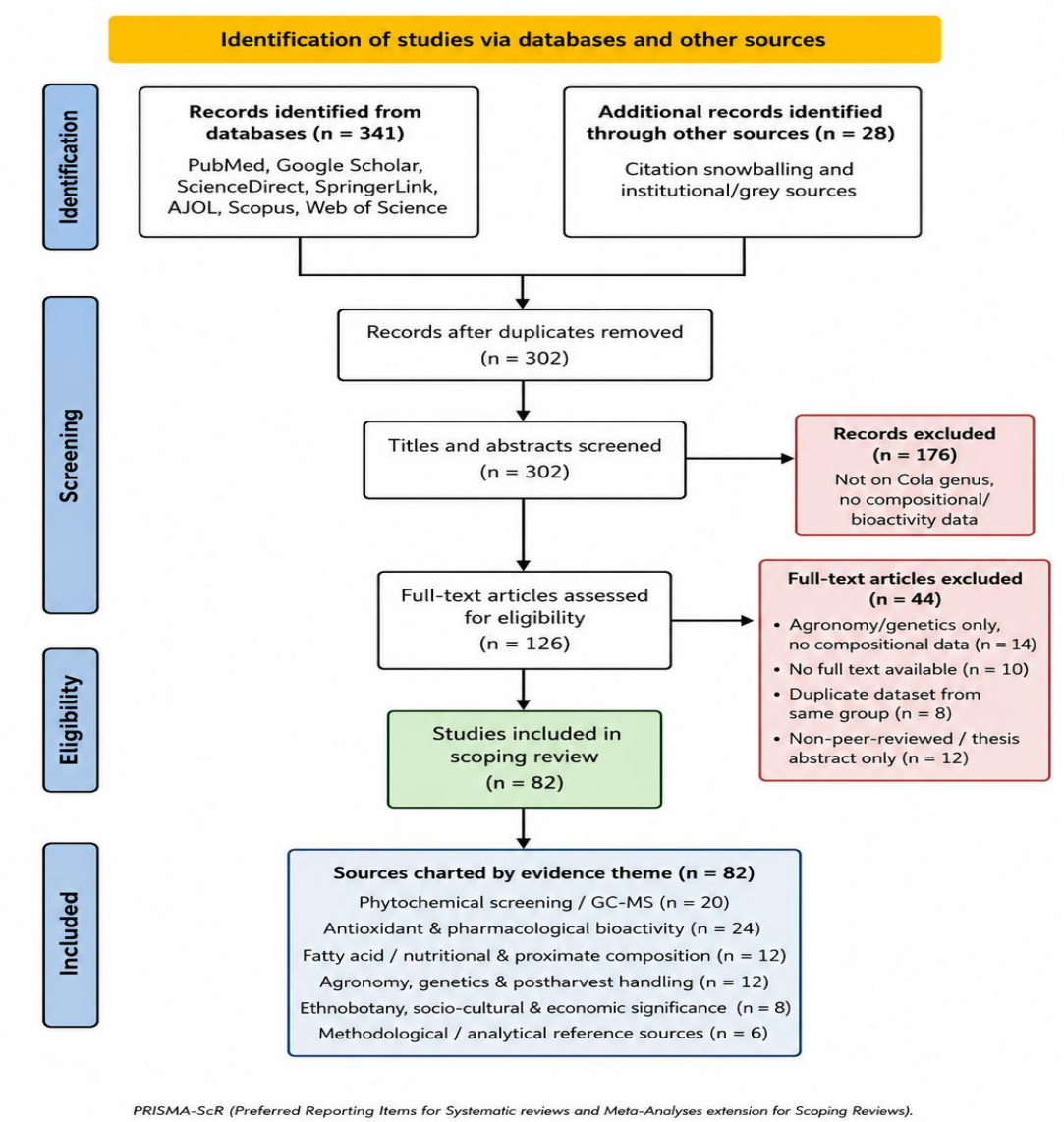


Figure 1. *PRISMA-ScR flow diagram of source identification, screening, eligibility assessment, and inclusion for this scoping review.*

Data charting and synthesis

For each included source, the following were charted: species and plant part studied, extraction solvent/method or study design (in vitro, in vivo, agronomic survey, socio-economic survey), analytical method (qualitative screening reagents, GC-MS, GC-FID, spectrophotometric antioxidant assay, HPLC, molecular marker analysis), and the principal quantitative or qualitative findings (percentage composition, retention times, IC50 values, genetic diversity indices, market/livelihood data). Data were synthesized narratively and organized thematically into phytochemical classes, GC-MS-identified compounds, fatty acid composition, antioxidant potential, pharmacological/toxicological activity, nutritional and proximate composition, agronomic/genetic/postharvest factors, and ethnobotanical/socio-economic significance, with results tabulated for comparison across studies.

Standard analytical and pharmacognostic reference methods

Because the included primary studies draw on a common set of standard analytical protocols, this review also cites the foundational methodological literature underlying those protocols, to aid readers assessing comparability across studies. Qualitative phytochemical screening across the included studies generally follows standard pharmacognostic reagent-based protocols [58,59,60,61]. Spectrophotometric antioxidant assays draw on established DPPH,[62] FRAP,[63] ABTS,[64] nitric-oxide-scavenging,[65] and TBARS/lipid-peroxidation[66] methods. Fatty acid extraction and quantification typically follow Bligh-and-Dyer-type lipid extraction[67] combined with GC-

FID/GC-MS derivatization, while proximate and mineral composition analyses generally follow AOAC International reference protocols [68]. Anticholinesterase inhibition assays follow Ellman's colorimetric method,[69] and total phenolic and flavonoid content are commonly quantified via Folin-Ciocalteu [70] and aluminium-chloride/flavonoid colorimetric methods,[71] respectively. Because assay conditions (solvent, incubation time, reference standard) vary somewhat between the original protocols and their adaptations in individual kolanut studies, IC50 values reported across studies are not strictly interchangeable, a point returned to later in the Results and Discussion.

Quality and confidence appraisal approach

Consistent with standard scoping-review methodology, no formal risk-of-bias instrument (e.g., ROBINS-I, SYRCLE) was applied to individual studies. To give readers a usable signal of evidence strength without overstating methodological rigor that was not formally assessed, each major evidence theme was assigned a narrative confidence rating of high, moderate, or limited. Ratings were assigned by the reviewer based on three considerations: (i) whether findings were replicated by more than one independent research group, (ii) whether the direction of effect was consistent across studies using different extraction solvents, assay conditions, or animal models, and (iii) the position of the underlying study designs on the evidence hierarchy described below (analytical/compositional chemistry and replicated in vitro assays were treated as capable of supporting "high" confidence for descriptive/compositional claims; single-laboratory in vivo pharmacology findings were capped at "moderate"; and any claim requiring extrapolation to human dosing was capped at "limited" regardless of the preclinical evidence volume). This is a transparent, judgement-based classification rather than a validated bias-risk score, and is presented as such in Table 1.

Table 1. Evidence hierarchy and study-type classification of sources included in this scoping review.

Study Type	Approximate Number of Sources	Translational Relevance	Representative Refs.
Analytical/compositional chemistry (GC-MS, HPLC, proximate analysis)	18	High — directly descriptive of composition, subject to sampling/provenance limits	20,40,41,72,73
In vitro bioassay (antioxidant, antimicrobial, enzyme inhibition)	22	Moderate-high for mechanism plausibility; not directly predictive of in vivo effect size	14,17,18,19,75
In vivo animal pharmacology / toxicology (rodent models)	16	Moderate — establishes plausible mechanism and dose-response in rodents; requires caution extrapolating to humans	24-30, 32-39
Agronomy, genetics, and postharvest field studies	12	High for the specific germplasm/locations studied; limited generalizability across all agroecological zones	7,9,10,42-45,47-50
Ethnobotanical / socio-economic survey and qualitative research	8	High for the specific communities studied; qualitative, not intended to be statistically generalizable	9,11,12,13,51-53
Methodological / analytical reference works (non-*Cola*-specific)	6	Foundational — underpins interpretation of assay results, not itself *Cola*-specific evidence	58-71 (selected)
Human clinical studies	0	Not applicable — no human trials identified	—

Approximate Number of Sources" denotes the count of the 82 included sources whose primary study design falls into each category. Categories are mutually exclusive by primary design and sum to exactly 82 (18+22+16+12+8+6+0). A source that also reports a secondary method (e.g., a GC-MS study that additionally runs a DPPH assay) is classified here by its primary design only; Figure 3, by contrast, classifies the same 82 sources by evidence theme rather than by study design, which is why the two counts differ.

RESULTS

Eighty-two sources met the eligibility criteria and form the evidentiary basis of this review (Figure 1), spanning phytochemical and GC-MS profiling studies, pharmacological and toxicological investigations, fatty acid and nutritional composition studies, agronomic and genetic characterization, postharvest handling research, ethnobotanical and socio-economic scholarship, and core methodological reference works. Figure 2 shows the distribution of included sources by publication period, Figure 3 shows their distribution across evidence themes, Figure 4 shows their approximate geographic distribution, and Figure 5 summarizes the conceptual framework linking phytochemical classes to reported activities. Table 2 summarizes representative sources across these themes.

Table 2. Representative characteristics of sources included in this scoping review, organized by evidence theme.

Ref.	Species / Focus	Study Type	Key Contribution
2,14,15,16	*C. nitida* & *C. acuminata*, seed	Qualitative phytochemical screening	Establishes consistent phytochemical class profile across species
17	*C. acuminata*, seed	Anticholinesterase & antioxidant assays	DPPH, OH radical scavenging, Fe2+ chelation; AChE/BChE inhibition
18	*C. acuminata*, nut	Phytochemical profiling & antioxidant potential	DPPH, NO, TBARS, TAC, FRAP IC50 values benchmarked against ascorbic acid/BHT
19	*C. acuminata*, seed	Multi-solvent phytochemical/antibacterial/antioxidant	NO and FRAP scavenging by solvent type
40	*C. gigantea*, seed oil	GC-MS fatty acid & sterol profiling, DPPH/ABTS	Detailed fatty acid and phytosterol GC-MS dataset for a related *Cola* sp.
41	*C. millenii*, leaf	GC-MS, total phenolics/flavonoids, DPPH/FRAP	GC-MS volatile/semi-volatile profile including n-hexadecanoic acid and squalene
42	*C. nitida*	Genetic/bioactive-compound variability	Establishes intraspecific/varietal variability in bioactive compound content
20	*C. nitida*, *C. acuminata*	HPLC polyphenol quantification	Quantifies catechin, epicatechin, procyanidins, caffeine
24-28	*C. nitida*, seed infusion	In vivo antidiabetic/hepatic/cardiometabolic pharmacology	Series of rodent studies on antidiabetic and organ-protective effects
29,30	*C. nitida*, leaf	In vivo antimalarial pharmacology	Antimalarial activity against *Plasmodium berghei*
31-39	*C. nitida*, *C. acuminata*	Toxicology / reproductive & hepatic safety	Dose-dependent adverse effects on hormones, liver, kidney
72,73	*C. nitida*, *C. acuminata*, *G. kola*	Proximate & nutritional/mineral composition	Comparative macronutrient and mineral profiling
9,43,44,45	*Cola* spp.	Genetic diversity / cytogenetics	Chromosome counts, isoenzyme and morpho-agronomic variability
7,10,47-50	*C. nitida*, *C. acuminata*	Agronomy, value chain, postharvest handling	Production constraints, curing/storage practices, weevil management
9,11,12,13,51-53	*C. nitida*, *C. acuminata*	Ethnobotany, socio-economics, cultural anthropology	Ceremonial, symbolic, and livelihood significance
74	*C. nitida*, multi-part extract	Green nanotechnology	Phytosynthesis of TiO2 nanoparticles with antimicrobial/antioxidant activity

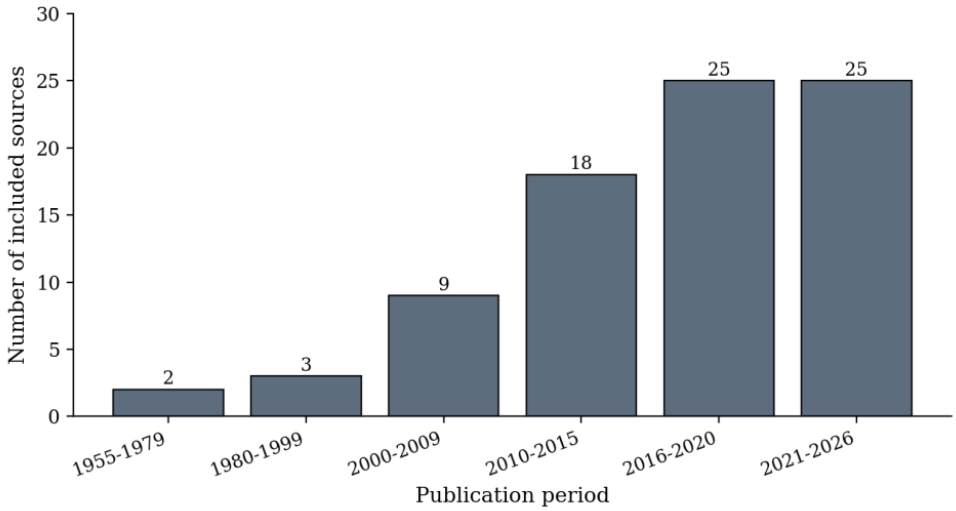


Figure 2. *Distribution of included sources by publication period (n = 82).*

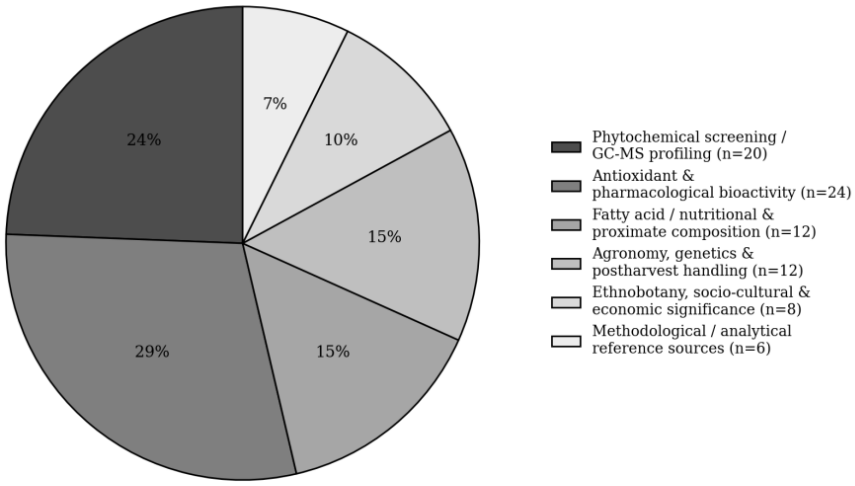


Figure 3*. Distribution of included sources by evidence theme (n = 82).*

Phytochemical classes reported across Cola species

Qualitative phytochemical screening of *C. acuminata* and *C. nitida* seed extracts across independent studies converges on a consistent set of positive classes: alkaloids, flavonoids, tannins, phenols, cardiac glycosides, terpenes (triterpenes), steroids, and saponins, with anthraquinones and phlobatannins consistently reported as absent [2,14,15,16]. Quantitative estimates from ethanolic seed extracts place tannin content around 6.5%, saponins around 8%, and alkaloids around 2%, with *C. acuminata* generally reported to contain higher flavonoid and carbohydrate content than *C. nitida*, while *C. nitida* tends to show higher alkaloid, saponin, phenol, and steroid content [2]. Comparable phytochemical classes — alkaloids, saponins, tannins, and cardenolides — have also been reported across four *Cola* species (*C. nitida*, *C. acuminata*, *C. gigantea*, and *C. millenii*) in a chemotaxonomic comparison, supporting the inference of a genuinely reproducible, genus-level phytochemical signature rather than an artefact of any single laboratory's method [15]. Root, bark, leaf, and pulp extracts of *C. millenii* similarly show alkaloids, tannins, saponins, cardiac glycosides, and terpenes, with distribution varying by plant part and extraction solvent [75,76,77,78,79]. Table 3 summarizes the qualitative phytochemical profile reported for kolanut seed.

Table 3. Phytochemical classes reported in kolanut (Cola spp.) seed across included studies.

Phytochemical Class	Reported Status	Source(s)
Alkaloids	Present	2,15,19,75
Flavonoids	Present	2,15,19,75
Tannins	Present	2,15,19,75
Phenols	Present	2,15,18,19
Cardiac glycosides	Present	2,15,19,75
Terpenes / Triterpenes	Present	2,15,19,75
Steroids	Present	2,15,19
Saponins	Present	2,15,19,75
Anthraquinones	Absent	2,15,19
Phlobatannins	Absent	2

GC-MS-identified compounds

Dedicated GC-MS phytochemical fingerprinting specific to *C. acuminata* seed extracts is limited within the accessible peer-reviewed literature. Where GC-MS has been applied to *Cola* species, the most detailed datasets available are for related species: methanolic leaf extract of *C. millenii* yielded 25 identifiable compounds, with n-hexadecanoic acid, 6-octadecenoic acid, octadecanoic acid, squalene, and vitamin E among the higher-concentration hits,[41] while GC-MS of *C. gigantea* seed oil identified nine fatty acids alongside four phytosterols (cholesterol, campesterol, stigmasterol, and β-sitosterol), with β-sitosterol the most abundant non-fatty-acid constituent [40]. Complementary HPLC-based work directly on *C. acuminata* (alongside two *C. nitida* varieties) quantified appreciable levels of (+)-catechin (27-37 g/kg), caffeine (18-24 g/kg), (−)-epicatechin (20-21 g/kg), and procyanidins B1 and B2 (7-19 g/kg) across the three kola varieties analyzed, with caffeine identified as the most potent antioxidant contributor among the metabolites tested [20]. A broader review of the *Cola* genus additionally lists theobromine, theophylline, quinic acid, chlorogenic acid, sterols, flavonoid glycosides, cardenolides, rostratanic acid, bauerenol, lupeol, betulinic acid, and stigmasterol among reported constituents across species [3]. Together, these findings indicate that kolanut's polyphenolic and purine-alkaloid content is comparatively well characterized, even where full-scan GC-MS fingerprinting of the seed oil itself remains sparse for *C. acuminata* specifically. Representative GC-MS- and HPLC-identified compounds are listed in Table 4.

Table 4. Representative GC-MS- and HPLC-identified compounds in Cola species (C. acuminata data supplemented with closely related species where indicated).

Compound	Species / Part	Approx. Abundance	Source
n-Hexadecanoic acid (palmitic acid)	*C. millenii*, leaf	32.5%	41
6-Octadecenoic acid	*C. millenii*, leaf	32.9%	41
Squalene	*C. millenii*, leaf	7.7%	41
Vitamin E (α-tocopherol)	*C. millenii*, leaf	7.9%	41
β-Sitosterol	*C. gigantea*, seed oil	49.7% (of sterol fraction)	40
Stigmasterol	*C. gigantea*, seed oil	34.1% (of sterol fraction)	40
Caffeine	*C. nitida* / *C. acuminata*, seed	18-24 g/kg	20
(+)-Catechin	*C. nitida* / *C. acuminata*, seed	27-37 g/kg	20
(−)-Epicatechin	*C. nitida* / *C. acuminata*, seed	20-21 g/kg	20
Procyanidins B1/B2	*C. nitida* / *C. acuminata*, seed	7-19 g/kg	20

This gap — the paucity of GC-MS data specific to Nigerian-grown *C. acuminata* seed oil, as opposed to leaf material or related species — is one of the clearest evidence gaps identified by this review and is discussed further below.

Fatty acid composition

As with GC-MS profiling, granular GC-FID/GC-MS fatty acid composition data specific to *C. acuminata* seed oil are not well represented in the readily accessible literature; comparative data instead come chiefly from *C. gigantea* seed oil. In *C. gigantea*, GC-MS analysis of trans-esterified seed oil identified nine fatty acids, with linoleic acid (40.7%), palmitic acid (20.3%), 9,12-hexadecadienoic acid (13.5%),

stearolic acid (11.7%), and stearic acid (9.3%) as the dominant components, yielding an overall unsaturated fatty acid content of 89.4% against 10.6% saturated [40]. Linoleic and palmitic acids emerge as the recurring dominant unsaturated and saturated fatty acids, respectively, across the *Cola* genus fatty-acid literature located in this review, a pattern broadly consistent with other tropical seed oils rich in linoleic acid, and comparable in overall unsaturation to bitter kola (*Garcinia kola*) seed lipids, which also show linoleic and oleic acids as dominant unsaturated components [80]. Proximate analyses of *C. nitida* additionally report crude fat contents in the range of 0.2-5.7%, depending on nut type and processing stage, with *C. acuminata* generally reported to contain higher fat content than *C. nitida* [72,73]. The fatty acid profile of *C. gigantea* seed oil is shown in Table 5.

Table 5. Fatty acid composition reported for Cola gigantea seed oil,[40] used here as the closest available compositional reference for the genus in the absence of dedicated C. acuminata GC-FID data.

Fatty Acid	Composition (%)	Notes
Linoleic acid (C18:2)	40.7	Dominant unsaturated fatty acid
Palmitic acid (C16:0)	20.3	Dominant saturated fatty acid
9,12-Hexadecadienoic acid (C16:2)	13.5	—
Stearolic acid (C18:2, acetylenic)	11.7	Uncommon acetylenic fatty acid; first reported in this genus
Stearic acid (C18:0)	9.3	—
10-Nonadecenoic acid (C19:1)	3.3	Odd-chain fatty acid, minor
Lauric, myristic, tricosanoic acids	<1.0 each	Minor constituents
Total saturated fatty acids	10.6	—
Total unsaturated fatty acids	89.4	—

No comparably detailed GC-FID fatty acid dataset specific to *C. acuminata* seed oil from Nigerian sources was identified in the course of this review.

Antioxidant potential

The antioxidant activity of kolanut extracts is comparatively well documented. Aqueous extract of *C. acuminata* nuts exhibited concentration-dependent DPPH radical scavenging with an IC50 of 6.01 µg/mL, closely comparable to ascorbic acid (6.31 µg/mL); the same extract showed strong nitric oxide scavenging (IC50 5.56 µg/mL, more potent than ascorbic acid's 10.02 µg/mL) and TBARS inhibition (IC50 29.16 µg/mL, more potent than BHT's 60.27 µg/mL), alongside a total antioxidant capacity IC50 of 4.89 µg/mL and FRAP IC50 of 32.44 µg/mL [18]. In a separate study, aqueous extract of *C. acuminata* seed demonstrated DPPH, hydroxyl radical scavenging, and Fe2+-chelating ability alongside anticholinesterase activity (AChE IC50 14.6 µg/mL; BChE IC50 96.2 µg/mL), supporting proposed neuroprotective and antioxidant mechanisms [17]. A third comparative study across chloroform, n-hexane, and ethanol extracts found the ethanol extract most effective at nitric oxide scavenging and ferric reducing power relative to the other solvents [19]. Seed extracts of *C. acuminata* from Benin similarly showed IC50 values below 10 µg/mL in ABTS assays and below 100 µg/mL in DPPH assays, with seeds richer in polyphenols than leaves [14]. Caffeine-rich *C. nitida* infusions have separately demonstrated potent in vitro antioxidant activity linked to abatement of redox imbalance in hepatic and cerebellar tissue in diabetic rodent models [24,27].

Quantitative synthesis of reported antioxidant and fatty acid values

The antioxidant and fatty-acid endpoints reported with sufficient numeric detail across the included sources are compiled in Table 6. Because only a small number of studies report directly comparable IC50 values for *C. acuminata* using the same assay, and only one detailed GC-MS fatty-acid dataset was located for the genus, most endpoints below rest on a single reported value rather than a range across independent studies; these are therefore listed as reported values rather than summarized with minimum/maximum/mean/median statistics, which would be identical to the single value by construction and could otherwise be misread as evidence of a real range. No formal meta-analysis was attempted given the heterogeneity of extraction solvents and assay conditions discussed later in this section.

Table 6. Reported antioxidant IC50 and fatty acid values for kolanut extracts and oil compiled in this review.

Endpoint	Reported Value	Basis
DPPH IC50 (µg/mL), aqueous *C. acuminata*	6.01	Single reported value (n=1)
Nitric oxide IC50 (µg/mL)	5.56	Single reported value (n=1)
TBARS IC50 (µg/mL)	29.16	Single reported value (n=1)
FRAP IC50 (µg/mL)	32.44	Single reported value (n=1)
AChE inhibition IC50 (µg/mL)	14.6	Single reported value (n=1)
Saturated fatty acids, *C. gigantea* oil (%)	10.6 total (5 SFAs, range <1.0-20.3)	One dataset [40]
Unsaturated fatty acids, *C. gigantea* oil (%)	89.4 total (4 UFAs, range 3.3-40.7)	One dataset [40]

Pharmacological and bioactivity profile

A substantial pharmacological literature, concentrated on hot-water or ethanolic *C. nitida* seed infusions, documents antidiabetic activity in type 2 diabetic rat models, including depletion of blood glucose, serum triglycerides, and LDL-cholesterol alongside elevation of serum insulin and HDL-cholesterol [25]. Related studies from the same research programme report cardioprotective effects against diabetic cardiomyopathy,[26] hepatoprotective effects against diabetic hepatic injury via improved antioxidant and cholinergic function,[28] and neuroprotective effects against hyperglycaemia-induced cerebellar oxidative injury with upregulation of Nrf2 expression [27]. Caffeine-rich *C. nitida* infusions additionally inhibit carbohydrate-catabolic enzymes and abate redox imbalance in models of Fe2+-induced hepatic toxicity [24]. It is worth flagging explicitly that this entire cluster of antidiabetic/cardioprotective/hepatoprotective/neuroprotective findings originates predominantly from a single South Africa-based research programme using a common hot-water infusion protocol; this strengthens internal consistency but means the findings are not yet independently replicated by unrelated laboratories, a distinction developed further below.

Antimicrobial and antifungal activity has been demonstrated across multiple *Cola* species and plant parts: *C. acuminata* seed and leaf extracts inhibit reference and clinical *Staphylococcus* strains,[14,81] *C. millenii* bark, leaf, root, and seed/pulp extracts show broad-spectrum antibacterial and antifungal activity,[75,76,77,78,79,82] and a four-species chemotaxonomic comparison (*C. nitida*, *C. acuminata*, *C. gigantea*, *C. millenii*) found consistent antimicrobial activity linked to shared alkaloid, saponin, and tannin content [15]. Antifungal activity against phytopathogenic fungi has additionally been reported for multiple *Cola* nut extracts [16]. *C. nitida* leaf extracts have shown dose-dependent antimalarial activity against *Plasmodium berghei* in mice, with improvement of malaria-associated haematological derangements,[29] although kolanut consumption at high concentrations has also been proposed to mimic malaria-like morbidity through combined caffeine and cyanide effects, with implications for antimalarial drug-resistance pressure[30] — a genuinely contradictory pair of findings discussed further below. In nanotechnology applications, phytosynthesis of titanium dioxide nanoparticles using leaf, pod, seed, and seed-shell extracts of *C. nitida* has yielded nanoparticles with antimicrobial, dye-degradation, antioxidant, and anticoagulant activity, illustrating an emerging industrial application of kolanut phytochemicals [74].

Set against this pharmacological promise, a distinct toxicological literature raises safety considerations relevant to habitual and high-dose kolanut consumption. Aqueous *C. nitida* seed extracts have been associated with reduced serum reproductive hormone concentrations and sperm count in male rats,[32,33] and dose-dependent supplementation of *C. acuminata*, *C. nitida*, and *Garcinia kola* seeds altered serum testosterone, gonadotropins, lipid profiles, and liver enzyme activities in a 12-week feeding study [36]. Diuretic activity with altered renal electrolyte handling has been reported for aqueous *C. nitida* seed extract,[34] while GC-MS-guided toxicity studies of ethanolic *C. nitida* extracts and isolated caffeine have documented dose-dependent changes in body weight, haematology, and serum biochemistry in rats [35,39]. Early foundational toxicology work similarly reported histopathological changes in liver,

kidney, brain, and testis following kola-nut extract administration,[38] while a formal food-ingredient safety assessment concluded that kola nut extract's pharmacological/toxicological profile parallels that of an equivalent caffeine dose at typical consumption levels [31].

Nutritional, proximate, and mineral composition

Comparative proximate analysis of *C. nitida*, *Garcinia kola* (bitter kola), and *Aframomum melegueta* (alligator pepper) found *C. nitida* to have the highest moisture, crude fat, and crude fibre contents (66.4%, 5.71%, and 7.13% respectively) among the three traditional snack nuts, alongside the highest potassium (3484.67 mg/kg) and phosphorus (411.43 mg/kg) content [72]. A separate nutritional and anti-nutrient analysis of three Beninese kola nuts found protein content ranging from 4.95% (*Garcinia kola*) to 10.64% (*C. acuminata*), with *C. acuminata* showing the highest total phenolic content among the three species analyzed [73]. These findings are broadly consistent with the qualitative phytochemical profile described above, reinforcing *C. acuminata*'s characterization as comparatively rich in phenolics and flavonoids relative to *C. nitida*.

Toxicological and safety considerations

This theme is closely linked to the pharmacological bioactivity findings above; in brief, the toxicological evidence base spans reproductive endocrinology,[32,33,36] renal and hepatic function,[34,37,38] and formal food-safety assessment,[31] with a consistent signal that adverse effects emerge primarily at high or chronic dosing rather than at levels typical of habitual social kolanut chewing.

Agronomy, genetic diversity, and postharvest handling

Cytogenetic studies establish a mitotic chromosome count of 2n = 40 across *Cola* species, with no physiological or structural barriers to interspecific pollination between *C. nitida* and *C. acuminata*, consistent with the close phytochemical similarity observed between the two species [44]. Isoenzyme and morpho-agronomic studies document substantial genetic variability within and between *Cola* germplasm collections in Cameroon and Nigeria, with direct relevance to selection for nutraceutical quality [9,43,45]. In Ghana, genetic variability studies of kola bioactive-compound content have identified opportunities for breeding programmes targeting nutraceutical quality, though such variability has not yet been systematically examined for *C. acuminata* across Nigeria's diverse agroecological zones [42]. Kola production and marketing constraints — including reproductive barriers, undesirable agronomic traits, low yield, and pest/disease pressure — have been documented across Niger State, Ogun State, and other production zones in Nigeria, as well as in Ghana's kola value chain [7,10,47]. The classic agronomic literature on tropical tree-crop cultivation situates these constraints within the broader management challenges of perennial West African tree crops [8].

Postharvest handling has an outsized influence on kolanut quality reaching the market. Traditional curing methods (soaking, wrapping in leaves such as *Mitragyna stipulosa*, and storage in baskets or polyethylene-lined containers) aim to reduce fungal spoilage and weevil (*Balanogastris kolae*) infestation, with reported nut losses of up to 98% infestation in untreated controls under experimental storage conditions [48]. Comparative studies of rural processing methods and postharvest storage treatments confirm substantial effects on nut quality characteristics,[48,49] while trader-level surveys document continued reliance on chemical preservatives such as phostoxin alongside indigenous curing knowledge [50].

Ethnobotanical, socio-cultural, and economic significance

Kolanut's societal role in Nigeria and West Africa extends well beyond its pharmacological profile. Ethnobotanical and anthropological scholarship documents kolanut's centrality to Igbo, Yoruba, Hausa, and other Nigerian cultural contexts, where it functions as a symbol of hospitality, unity, and identity, and is indispensable to marriage, chieftaincy installation, funeral, and reconciliation ceremonies [9,11,12,13]. Socio-economic surveys across Ogun, Niger, and South-Eastern Nigerian states, as well as Ghana's kola value chain, document kolanut's role as a major income source for farmers, processors, and traders, with Nigeria historically producing the majority of the world's *C. nitida* crop [7,10,47,51]. Comparative ethnobotanical work in Benin and Cameroon similarly documents substantial market variation in kola prices and use patterns across *Cola* species [43,51]. Figure 4 summarizes the approximate geographic distribution of the included sources by country of study or corresponding-author affiliation; the concentration of sources in Nigeria, alongside a distinct cluster of South Africa-based pharmacology studies, is itself informative about which parts of the evidence base are geographically

embedded in kolanut-producing communities versus generated in international laboratories using imported or unspecified-provenance material.

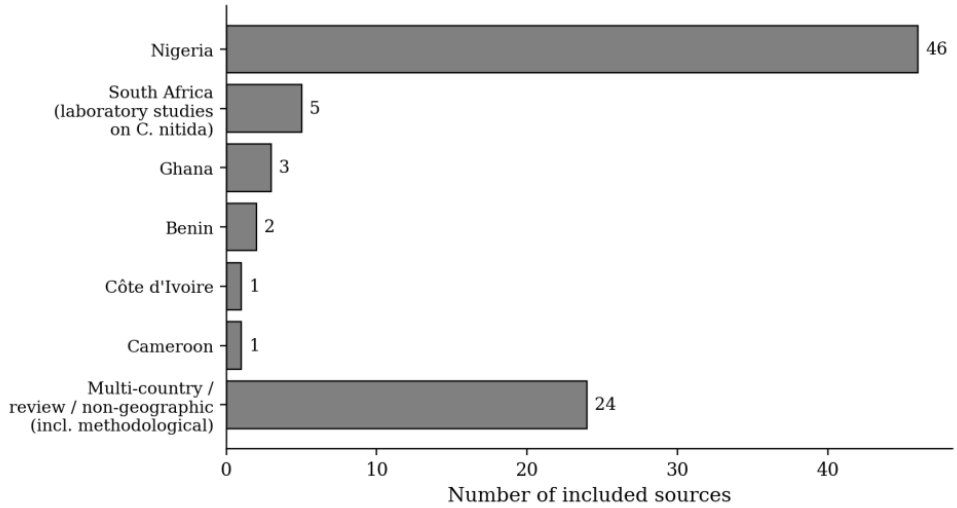


Figure 4. *Approximate geographic distribution of included sources, by country of study or corresponding-author affiliation (n = 82).*

Confidence ratings by evidence theme

Table 7 presents narrative confidence ratings for each major evidence theme, following the approach described above. Readers should treat "high" confidence as indicating consistent, replicated, descriptive findings, not as a certification of methodological quality equivalent to a formal risk-of-bias assessment.

Table 7. Narrative confidence ratings by evidence theme. These are transparent, judgement-based classifications and not validated risk-of-bias scores.

Evidence Theme	Confidence Rating	Justification
Qualitative phytochemical class profile (alkaloids, tannins, flavonoids, etc.)	High	Replicated across ≥6 independent research groups and 4 species with consistent direction of findings
Antioxidant assay potency (DPPH, NO, FRAP, TBARS)	Moderate-high	Consistent direction of effect across studies, but few directly comparable IC50 values and assay conditions vary
GC-MS/GC-FID fatty acid composition specific to *C. acuminata*	Limited	No dedicated *C. acuminata* dataset identified; reliant on extrapolation from *C. gigantea*
In vivo antidiabetic/hepatoprotective/cardioprotective pharmacology	Moderate	Internally consistent, but concentrated in one research programme; not yet independently replicated; preclinical only
Antimicrobial and antimalarial activity	Moderate	Replicated across several species and laboratories, but assay conditions vary and mechanisms are inferred rather than confirmed
Reproductive/hepatic/renal toxicity at high or chronic dose	Moderate	Consistent direction of effect across independent studies; dose-response thresholds not harmonized
Human clinical efficacy or safety at any endpoint	Limited	No human clinical trials identified; all pharmacological/toxicological evidence is preclinical
Agronomic/genetic variability in bioactive-compound content	Moderate-high	Well documented within specific germplasm collections; not yet systematically linked to compositional/bioactivity endpoints
Ethnobotanical, cultural, and socio-economic significance	High	Convergent qualitative evidence across multiple ethnic, national, and disciplinary sources

Synthesis across evidence: convergence, divergence, and sources of heterogeneity

Several patterns of both convergence and divergence emerge when the included sources are compared directly rather than summarized sequentially. First, on phytochemical class presence/absence, there is strong convergence: every included qualitative screening study, regardless of species, solvent, or country of origin, reports the same core set of positive classes (alkaloids, flavonoids, tannins, phenols, cardiac glycosides, terpenes, steroids, saponins) and the same two consistent absences (anthraquinones, phlobatannins) [2,14,15,16,19,75]. This is the single most reproducible finding in the entire evidence base and supports the high-confidence rating above (Table 7).

Second, on antioxidant potency, extraction solvent is the dominant source of heterogeneity rather than species identity: ethanol extracts consistently outperform chloroform and n-hexane extracts on nitric-oxide-scavenging and ferric-reducing assays within the same study,[19] and aqueous extracts dominate the most potent IC50 values reported [17,18]. Because different studies report IC50 values for different solvents, different assay conditions, and sometimes different reference standards (Table 6, Table 8), the apparent "superiority" of kolanut over ascorbic acid or BHT in some assays should be read as solvent-and-assay-specific rather than as an intrinsic species-level property.

Table 8. Antioxidant IC50 values reported for Cola acuminata extracts across assays. Sources: aqueous nut extract IC50 values;[18] cholinesterase inhibition values.[17]

Assay	Extract	Sample IC50 (µg/mL)	Reference Standard	Standard IC50 (µg/mL)
DPPH	Aqueous nut extract	6.01	Ascorbic acid	6.31
Nitric oxide (NO)	Aqueous nut extract	5.56	Ascorbic acid	10.02
TBARS (lipid peroxidation)	Aqueous nut extract	29.16	BHT	60.27
Total antioxidant capacity	Aqueous nut extract	4.89	—	Not reported
FRAP	Aqueous nut extract	32.44	—	Not reported
AChE inhibition	Aqueous seed extract	14.6	—	Not reported
BChE inhibition	Aqueous seed extract	96.2	—	Not reported

Third, the pharmacological literature on antidiabetic, cardioprotective, hepatoprotective, and neuroprotective effects of *C. nitida* infusion is highly internally consistent — but this consistency partly reflects the fact that a large share of it originates from one research programme using a shared hot-water infusion protocol and a shared diabetic-rat model [24,25,26,27,28]. Convergent findings from a single, methodologically related cluster of studies constitute weaker independent evidence than the same number of findings from unrelated laboratories, even though the studies numerically outnumber the toxicology literature.

Fourth, there is a genuine and unresolved contradiction between the antimalarial-activity literature, which reports that *C. nitida* leaf extract reduces parasitaemia and improves haematological indices in *Plasmodium berghei*-infected mice,[29] and the malaria-morbidity literature, which proposes that habitual high-dose kolanut consumption can produce malaria-like symptoms via combined caffeine and cyanide effects and may create drug-resistance pressure [30]. These two literatures address different exposure routes (isolated leaf extract at controlled experimental doses versus habitual whole-nut consumption at socially typical, higher, and less controlled doses) and are not directly comparable, but the review found no study that reconciles them within a single dose-response framework — itself a notable evidence gap discussed further below.

Fifth, geographic and varietal variation is documented at the genetic and agronomic level[42,43,45] but has not been linked forward to the phytochemical and pharmacological endpoints reviewed above; conversely, the phytochemical and pharmacological literature rarely specifies the genotype, growing region, or postharvest handling of the nuts used. This disconnect between the agronomic-genetic and the phytochemical-pharmacological literatures is arguably the single largest structural gap identified by this review, because it means that an apparently well-replicated finding (e.g., the core phytochemical class profile) cannot currently be attributed to species identity, genotype, growing region, or postharvest handling individually.

DISCUSSION

Phytochemical diversity and bioactivity

The consistent presence of alkaloids, flavonoids, tannins, phenols, cardiac glycosides, terpenes, steroids, and saponins across independent studies of *C. acuminata*, *C. nitida*, *C. gigantea*, and *C. millenii*, and the equally consistent absence of anthraquinones and phlobatannins, suggests a genuinely reproducible phytochemical signature for the genus rather than an artefact of any single laboratory's method [2,15,75]. These compound classes have well-documented pharmacological associations — tannins and phenols with antioxidant and antimicrobial activity, saponins with membrane-active and hypocholesterolaemic effects, and alkaloids (most notably caffeine, present at 18-24 g/kg in kola nuts) with central nervous system stimulant activity — which collectively provide a plausible phytochemical basis for kolanut's traditional stimulant and medicinal uses [1,3,20].

Fatty acid profile: nutritional and industrial implications

Although dedicated fatty acid data for *C. acuminata* seed oil specifically are sparse, the genus-level pattern — linoleic acid and palmitic acid as the dominant unsaturated and saturated fatty acids respectively, with unsaturated fatty acids substantially exceeding saturated fatty acids in *C. gigantea* (89.4% versus 10.6%) — is consistent with the broader push in the plant-oil literature toward unconventional oilseed sources with more favourable fatty acid ratios than palm oil [40]. If this pattern holds for *C. acuminata*, as the phytochemical and antioxidant similarities across the genus suggest it plausibly might, kolanut oil could represent an underutilized candidate for edible-oil diversification and, given its saponin content, secondary applications in soap and cosmetic manufacture, paralleling conclusions drawn for *Garcinia kola* oil in comparable West African contexts [80].

Antioxidant potency in context

The DPPH IC50 of 6.01 µg/mL and nitric oxide IC50 of 5.56 µg/mL reported for aqueous *C. acuminata* nut extract[18] are notably potent relative to many plant-oil and plant-extract antioxidant benchmarks in the wider literature, where IC50 values in the tens or low hundreds of µg/mL are more typical [62,63,64]. As discussed above, this potency is extract- and assay-specific rather than a fixed species-level constant: antioxidant potency varies meaningfully with extraction solvent, as shown by the differential nitric oxide and ferric-reducing performance of ethanol versus chloroform and n-hexane extracts [19]. Reported IC50 values should therefore be read as characterizing a specific extract-assay combination rather than “kolanut” as an undifferentiated whole.

Mechanistic pathways linking phytochemicals to bioactivity

Figure 5 summarizes a conceptual framework, synthesized from the compositional and pharmacological literature reviewed here, linking kolanut's major phytochemical classes to plausible mechanisms and reported biological activities. Caffeine and theobromine are purine alkaloids classically associated with adenosine-receptor antagonism and phosphodiesterase inhibition, mechanisms consistent with kolanut's traditional stimulant use and, at the biochemical level, with the carbohydrate-catabolic-enzyme inhibition reported for caffeine-rich *C. nitida* infusions [24]. The polyphenolic fraction (catechin, epicatechin, procyanidins, tannins) is the most plausible driver of the antioxidant and redox-pathway effects reported across DPPH, FRAP, and TBARS assays and in the Nrf2-upregulation findings observed in diabetic rodent brain tissue,[20,27] consistent with the well-established radical-scavenging chemistry of flavan-3-ols more generally. Saponins are membrane-active compounds whose reported hypocholesterolaemic and antimicrobial effects are mechanistically consistent with their capacity to interact with cell-membrane sterols and bacterial/fungal membrane components [2,15]. Sterols and fatty acids (β-sitosterol, stigmasterol, linoleic and palmitic acid) plausibly underlie the nutritional and industrial-oil relevance discussed above [40]. It is important to note that this framework is a synthesis of plausible mechanism drawn from the general pharmacology of these compound classes, not a set of mechanisms directly demonstrated within *Cola*-specific studies; few of the included pharmacological studies performed the receptor-binding, enzyme-kinetic, or knockout/knockdown experiments that would be needed to confirm mechanism rather than infer it from compound identity.

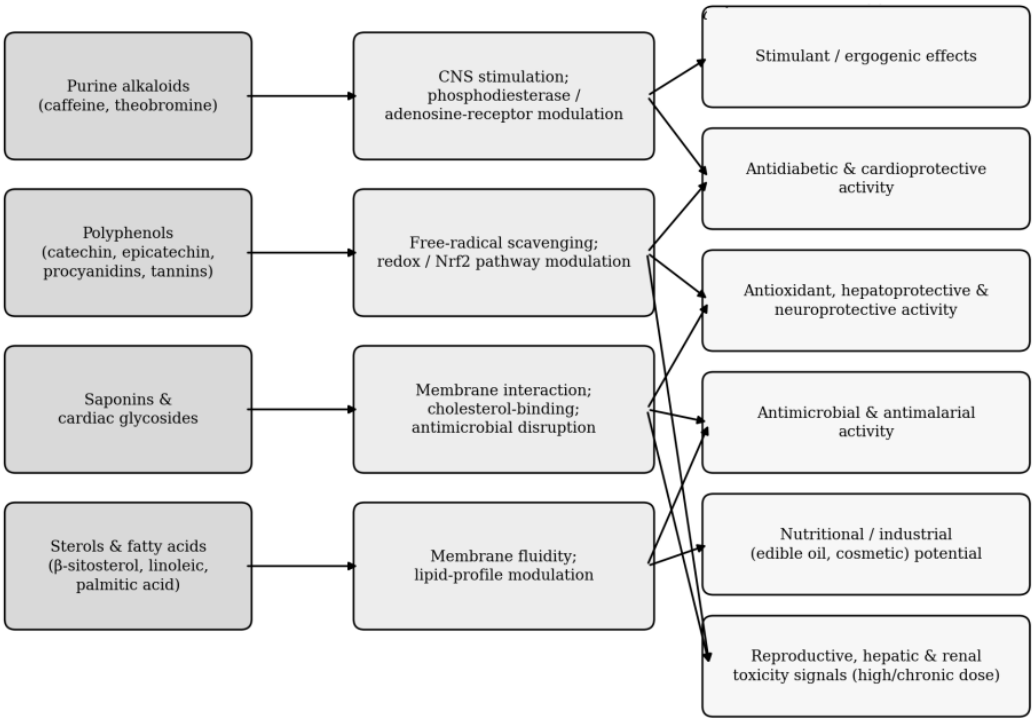


***Figure 5**. Conceptual framework linking phytochemical classes in kolanut (Cola spp.) to proposed mechanisms and reported biological activities.*

Pharmacological promise versus safety signals

A central tension in the kolanut literature is the coexistence of substantial pharmacological promise — antidiabetic, cardioprotective, hepatoprotective, neuroprotective, and antimicrobial activity demonstrated largely at controlled experimental doses in rodent models [24,25,26,27,28,29] — with a parallel toxicological literature documenting adverse reproductive, hepatic, and renal effects at higher or more chronic dosing [31,32,33,34,35,36,37,38,39]. This is not necessarily contradictory: many phytochemicals exhibit hormetic, dose-dependent profiles in which beneficial and adverse effects occupy different regions of the same dose-response curve. However, the current literature rarely bridges these two bodies of work within a single study design, meaning that the therapeutic window relevant to habitual human kolanut consumption — as distinct from either single-dose pharmacological testing or chronic high-dose toxicological testing — remains poorly characterized. This represents a substantive translational gap for any effort to position kolanut-derived compounds as functional-food or nutraceutical ingredients.

Human versus animal evidence: translational caution

As Table 1 makes explicit, no human clinical trial of any *Cola* species was identified in the course of this review. Every antidiabetic, cardioprotective, hepatoprotective, neuroprotective, antimicrobial, and antimalarial finding summarized above derives from in vitro assays or rodent models. Rodent-to-human translation in pharmacology is well known to fail for reasons including species differences in drug metabolism, allometric dose scaling, and the artificiality of induced-disease models (e.g., streptozotocin-induced diabetes) relative to the human metabolic conditions the findings are implicitly meant to inform. This review's central recommendation on this point is not that the preclinical findings are unimportant, but that any communication of kolanut's pharmacological potential — whether to farmers, consumers, policymakers, or nutraceutical developers — should explicitly state that clinical efficacy and safety in humans remain unestablished, and that recommendations for therapeutic use should be considered hypothesis-generating rather than clinically actionable pending human trials.

Genetic and agroecological variation

Genetic variability studies demonstrate that bioactive-compound content in kola germplasm varies meaningfully within and between populations in Ghana, Cameroon, and Nigeria,[42,43,45] yet this variability has not been systematically linked to the phytochemical, antioxidant, or fatty acid endpoints reviewed above. Given the well-established influence of soil, altitude, and climate on phytochemical and fatty acid composition in

other tropical oilseeds, and given that Nigeria's kola-producing states span multiple distinct agroecological zones, integrating germplasm/genotype data with compositional analysis represents a natural and currently unrealized extension of the existing agronomic and phytochemical literatures.

Socioeconomic and cultural embeddedness

Kolanut's phytochemical and pharmacological research agenda cannot be separated from its socio-economic and cultural context. The crop supports rural livelihoods across multiple West African countries[7,10,47,51] while carrying ceremonial and symbolic significance that shapes which species, nut colours, and preparation methods are locally preferred, and therefore which nuts predominate in the compositional literature [9,11,12,13,52,53]. Future compositional and pharmacological research would benefit from closer integration with this socio-economic literature — for instance, by sampling nuts across the specific varieties and agroecological zones that dominate actual market supply, rather than convenience samples of unspecified provenance.

Comparison with other stimulant and nutraceutical crops

Kolanut's caffeine and theobromine content invites direct comparison with coffee, cocoa, and tea, the three other major caffeine-containing crops with which it shares both chemistry and, in commercial contexts, formulation (kola-flavoured soft drinks are among the clearest examples). Coffee and tea have accumulated a substantial human clinical evidence base on caffeine pharmacokinetics, safe daily intake thresholds, and drug interactions (e.g., with adenosine-receptor-acting medications and certain antibiotics), whereas kolanut's caffeine-related pharmacology, as noted above, remains entirely preclinical. Where general caffeine safety thresholds are concerned — commonly cited as up to 400 mg/day for healthy adults — these are derived predominantly from coffee-based pharmacokinetic studies and have not been separately validated for kolanut's specific alkaloid-polyphenol matrix, which may plausibly alter caffeine absorption or metabolism relative to coffee. This is a reasonable extrapolation for public-health messaging in the absence of kolanut-specific data, but it is an extrapolation, and should be presented as such rather than as an established kolanut-specific finding. Potential food-drug interactions relevant to concomitant caffeine and tannin/polyphenol intake (e.g., reduced non-haem iron absorption, a well-documented effect of tannin-rich beverages such as tea) are plausible by analogy for kolanut but have not, to this review's knowledge, been directly studied in kolanut-specific human or animal models.

Regulatory status and commercialization prospects

Kola nut extract has an established history as a food-flavouring ingredient, and a formal food-ingredient safety assessment has concluded that its pharmacological/toxicological profile parallels that of an equivalent caffeine dose at typical consumption levels [31] — a finding relevant to its continued acceptability as a flavouring agent in soft drinks and confectionery. However, the regulatory pathway for kolanut-derived extracts positioned as nutraceuticals or functional-food ingredients (as opposed to flavouring agents) is considerably more demanding, typically requiring standardized extract characterization, dose-ranging safety data, and, for any therapeutic claim, human clinical evidence — none of which currently exist for kolanut, as discussed above. Commercialization prospects appear strongest, in the near term, for applications that do not require therapeutic claims: functional-food positioning as an antioxidant-rich natural ingredient, cosmetic/soap applications exploiting saponin and fatty-acid content,[80] and the nanotechnology applications already demonstrated for antimicrobial and dye-degradation purposes [74]. Nutraceutical positioning requiring health claims would require the human trial and standardization work identified as priorities below.

Climate change and sustainability considerations

Kola production is concentrated in humid tropical forest zones of West and Central Africa with specific rainfall and temperature requirements documented in the agronomic literature;[6,8] shifts in rainfall patterns and increased climate variability projected for West Africa plausibly threaten the ecological conditions underpinning current kola cultivation zones, in a manner directly analogous to well-documented climate risks facing cocoa cultivation in the same region. None of the sources identified in this review directly modelled climate-change impacts on kola yield, geographic range, or bioactive-compound content, representing a further evidence gap with direct relevance to the crop's long-term economic sustainability and to breeding priorities. Given kola's perennial tree-crop structure and multi-decade productive lifespan, the absence of forward-looking climate-suitability modelling is a notable omission relative to the equivalent literature for cocoa and coffee.

Implications for policymakers and agricultural stakeholders

For agricultural extension services and policymakers in Nigeria's kola-producing states, three implications follow from this synthesis. First, postharvest loss reduction offers a more immediate, evidence-supported livelihood intervention than pharmacological development, since curing and storage improvements already have demonstrated effectiveness against weevil infestation and fungal spoilage[48,49,50] and require no new clinical evidence to justify extension investment. Second, any public communication about kolanut's health effects — whether from extension officers, nutraceutical marketers, or health authorities — should reflect the preclinical-only status of the pharmacological evidence rather than presenting rodent findings as established human health benefits. Third, genetic conservation and characterization of kola germplasm has dual value for breeding programmes and for enabling the genotype-to-bioactivity research identified as a priority below; this argues for coordinating agronomic germplasm collections (already under way in Ghana and Nigeria) with compositional/phytochemical sampling of the same accessions, rather than treating these as separate research agendas.

Gaps in the literature

Six gaps stand out. First, GC-MS phytochemical fingerprinting conducted directly on *C. acuminata* seed or seed oil — as opposed to leaf material from the related species *C. millenii*, or seed oil from *C. gigantea* — is largely absent from the accessible literature, leaving the specific volatile/semi-volatile compound profile of Nigerian kolanut oil unconfirmed. Second, and relatedly, GC-FID or GC-MS-based fatty acid composition specific to *C. acuminata* seed oil has not been located in this review; existing fatty acid data for the genus derive from *C. gigantea*. Third, ecological and varietal variation — already demonstrated for bioactive compound content in *C. nitida*[42] — has not been systematically examined for *C. acuminata* across Nigeria's different agroecological zones, and more broadly the agronomic-genetic and phytochemical-pharmacological literatures remain disconnected, as discussed above. Fourth, the pharmacological and toxicological literatures remain largely disconnected, with no identified study directly modelling the dose-response relationship between habitual human kolanut consumption levels and either therapeutic or adverse endpoints. Fifth, no human clinical trial of any *Cola* species was identified, leaving every pharmacological claim in a preclinical, hypothesis-generating state. Sixth, socio-economic and ethnobotanical data on kolanut, while rich, have not been systematically cross-referenced with the compositional and pharmacological literature to identify which locally dominant varieties and preparation methods are actually represented in laboratory studies.

Limitations of this review

This synthesis, being a scoping review, prioritized mapping breadth over formal methodological quality appraisal of individual studies, and did not perform meta-analytic pooling of IC50 values, which vary by extraction method, solvent, and assay protocol and are therefore not strictly comparable across studies without such caveats. Screening and selection were conducted by a single reviewer rather than two independent reviewers with a documented disagreement-resolution process, and exact per-database search yields were not separately logged; both are limitations relative to a fully auditable systematic or scoping review and should be remedied by dual independent screening and a logged, database-by-database search if this work is adapted for further submission. The search prioritized English-language, peer-reviewed sources accessible through the databases searched, supplemented by identifiable grey literature; additional Nigerian and West African institutional research not indexed in the databases consulted, or published only in French or other regional languages, may not be fully captured — a particularly relevant limitation given the Francophone West African literature on kola (e.g., from Benin and Côte d'Ivoire) that surfaced even in an English-prioritized search. Where *C. acuminata*-specific data were unavailable, this review drew on closely related *Cola* species for context; while defensible for tentative genus-level inference, this substitution is not a substitute for species-specific confirmatory data. Finally, the confidence ratings in Table 7 are transparent, judgement-based classifications rather than validated risk-of-bias scores, and the ethnobotanical and socio-economic literature charted here is illustrative rather than exhaustive.

Research Priorities

Based on the gaps identified above, the following research priorities are recommended, in approximate order of tractability:

i. Conduct dedicated GC-FID and full-scan GC-MS fatty acid and phytochemical profiling of Nigerian-grown *C. acuminata*

seed oil, sampled across multiple agroecological zones and known varieties.

ii. Link existing and future germplasm/genotype characterization directly to compositional and bioactivity endpoints, by phytochemically profiling the same accessions used in agronomic/genetic studies.

iii. Design dose-ranging pharmacological and toxicological studies that span the full range from single experimental doses to habitual chronic human consumption levels, to characterize kolanut's therapeutic window rather than treating efficacy and toxicity as separate literatures.

iv. Conduct the first human clinical studies of standardized kolanut extracts, beginning with pharmacokinetic and safety (Phase I-equivalent) characterization before any efficacy claims are tested.

v. Apply metabolomic and, where relevant, transcriptomic profiling to characterize genotype-by-environment effects on kolanut phytochemistry, extending beyond the single-compound-class approach of most existing GC-MS studies.

vi. Use molecular docking and enzyme-kinetic studies to test, rather than infer, the mechanistic hypotheses summarized in Figure 5, particularly for the antidiabetic and anticholinesterase activities already reported at the whole-extract level.

vii. Model climate-change impacts on kola cultivation suitability and bioactive-compound content, paralleling existing climate-suitability modelling for cocoa and coffee in the same production zones.

viii. Integrate socio-economic and ethnobotanical sampling frames into compositional research design, so that laboratory studies analyze the specific varieties and preparation methods that dominate actual West African kolanut consumption and trade.

ix. Any future systematic or scoping review building on this work should employ dual independent screening, a logged and database-audited search strategy, and a validated risk-of-bias instrument appropriate to the included study designs, to address the methodological limitations noted above.

CONCLUSION

Kolanut (*Cola* spp.), and Nigerian *C. acuminata* and *C. nitida* in particular, present a phytochemically rich, pharmacologically active, and socio-economically indispensable profile, with a reproducible qualitative phytochemical signature (alkaloids, flavonoids, tannins, phenols, cardiac glycosides, terpenes, steroids, saponins present; anthraquinones and phlobatannins absent) and antioxidant IC50 values that are frequently comparable to, or exceed, standard reference antioxidants in DPPH, nitric oxide, and lipid-peroxidation assays. A substantial pharmacological literature documents antidiabetic, hepatoprotective, cardioprotective, neuroprotective, antimicrobial, and antimalarial activity, counterbalanced by a toxicological literature indicating that adverse reproductive, hepatic, and renal effects emerge at high or chronic dosing; critically, this entire pharmacological and toxicological literature remains preclinical, with no human clinical trials identified. The fatty acid and GC-MS phytochemical evidence base remains comparatively underdeveloped for *C. acuminata* specifically, with the most detailed compositional data currently available drawn from the related species *C. gigantea* and *C. millenii*. Agronomic, genetic, and postharvest research demonstrates substantial variability in kola quality and composition, while ethnobotanical and socio-economic scholarship confirms kolanut's deep cultural and livelihood significance across Nigeria and West Africa — yet these agronomic and socio-economic literatures remain largely disconnected from the phytochemical and pharmacological ones. Future primary research applying GC-FID and GC-MS analysis directly to Nigerian-grown *C. acuminata* seed oil across multiple agroecological zones, human clinical studies bridging the pharmacological and toxicological literatures, and integrated genotype-to-bioactivity studies is recommended, per the numbered priorities above, to close these gaps and to substantiate kolanut's potential as a functional food, nutraceutical, and industrial oil source.

ACKNOWLEDGMENT

The authors have no acknowledgments to declare.

AUTHORS' CONTRIBUTION

OI, EOO, BOO, JOD, BM, HMA and ABA contributed equally to this work. All authors read and approved the final manuscript.

CONFLICT OF INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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