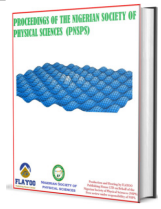
Published by Nigerian Society of Physical Sciences. Hosted by FLAYOO Publishing House LTD

Proceedings of the Nigerian Society of Physical Sciences

Journal Homepage: https://flayoophl.com/journals/index.php/pnspsc



Harnessing the ethnomedicinal potentials of *Citrus aurantiifolia* and *Anacardium occidentale* for local drug development: A strategy to mitigate Nigeria's economic challenges

Anyim Godwin[a,*], Success Chimbuchi Ogbonna[b], Adetoun Elizabeth Morakinyo[b]

[a]*Department of Biochemistry, Federal University of Health Sciences, Ila-Orangun, P.M.B. 204, Osun State, Nigeria*
[b]*Department of Biochemistry, Adeleke University, Ede, P.M.B. 250, Osun State, Nigeria*

ABSTRACT

Nigeria possesses a vast botanical landscape of 7,895 plant species, in which 963 species are medicinal plants while 6,932 serve other purposes. The global medicinal plant sector is shifting from raw exports toward standardised, plant-based active pharmaceutical ingredients (APIs), a market projected to reach $271.14 billion by 2026. Nigeria is currently the fifth largest producer of cashew but earns only a few million dollars compared to other countries from a similar production volume. This comprehensive review synthesises current pharmacological and economic data regarding *C. aurantiifolia* (Lime) and *A. occidentale* (Cashew) as drivers for Nigeria's bio-economy. Literature published between 2009 and 2026 was retrieved from five major academic databases, focusing on phytochemical efficacy, safety profiles, and industrial value chains. *C. aurantiifolia* contains bioactive flavonoids (hesperidin, eriocitrin) with antioxidant and anti-inflammatory properties, while *A. occidentale* demonstrates significant metabolic, antioxidant and antimicrobial potentials. Also, cashew byproducts like cashew nut shell liquid (CNSL) has immense industrial application. The review evaluates the transition from traditional ethnomedicinal use to structured drug discovery pipelines, addressing necessary stages such as bioassay-guided fractionation and toxicity standardisation. The review concludes that, by integrating indigenous botanical knowledge with modern pharmaceutical processing, Nigeria can bridge the gap between ethnomedicine and industrial API production, offering a scientifically-grounded strategy to mitigate national economic challenges.

Keywords: *Anacardium occidentale*, *Citrus aurantiifolia*, Bio-economy, Artificial intelligence, machine learning.

DOI:10.61298/pnspsc.2026.3.261

1. INTRODUCTION

Nigeria is the most populous and fourth-largest economy in Africa, covering an estimated area of 923,768 square km [1]. The land occupies 910,768 square km, while the water bodies account for 13,000 square km [2]. The vast landscape supports a rich biological heritage of approximately 7,895 plant species across 338 families and 2,215 genera [3, 4]. Within this flora, 963 species (spanning 144 families and 611 genera) are recognised as medicinal plants, with the Fabaceae family currently dominating the country's ethnomedicinal pharmacopeia [5].

*Corresponding Author
e-mail: anyim.godwin@fuhsi.edu.ng, anyimgodwin2015@gmail.com (Anyim Godwin)

While early assessments suggested only 0.4% of Nigeria's flora was threatened, recent evaluations indicate a sharp rise in biodiversity loss driven by anthropogenic pressures [6]. This decline underscores the urgent need to document and value the remaining 6,932 species, which are categorised into six functional economic groups [6]. These range from neglected wild edible plants that provide essential micronutrients to species used for structural timber, industrial fibers, and domestic energy for approximately 70% of the rural population [7, 8]. Other groups serve vital roles in traditional rites, bio-pesticides, or livestock forage [9–11].

Despite this extensive functional classification, there is still a critical gap in the high-value industrial transition of many species. Harnessing the ethnomedicinal potentials of *Citrus aurantiifolia* and *Anacardium occidentale* for local drug development offers a transformative strategy to bridge this gap. Both species are traditionally valued for their diverse biological activities, yet they often remain confined to rudimentary use-cases [12–14]. The strategic transition of indigenous flora from basic ethnobotanical categories into high-purity pharmaceutical lead compounds serves as a vital nexus for addressing Nigeria's pressing healthcare needs and economic diversification.

2. MATERIALS AND METHODS

A structured literature search was conducted to ensure a rigorous and comprehensive synthesis of the pharmacological and economic potential of *Citrus aurantiifolia* and *Anacardium occidentale*; linking phytochemical profiles to industrial drug development and national bio-economy strategies.

2.1. SEARCH STRATEGY AND INFORMATION SOURCES

Primary literature searches were performed across five major academic and multidisciplinary databases: PubMed, ScienceDirect, Google Scholar, Scopus, and ResearchGate. The search was restricted to articles, clinical reports, and industrial reviews published between 2009 and 2026 to ensure the inclusion of both foundational data and the most recent advances in API (active pharmaceutical ingredient) processing.

2.2. KEYWORDS AND SELECTION CRITERIA

The search utilised a combination of Boolean operators (AND, OR) and specific keywords, including: "*Anacardium occidentale*," "*Citrus aurantiifolia*," "Cashew nut shell liquid (CNSL)," "Hesperidin/Eriocitrin," "Bioassay-guided fractionation," "Toxicity standardisation," "Antioxidant efficacy," "Antiinflammatory efficacy," "Antimicrobial potential," "Nigeria bio-economy," "API value chain," "Pharmaceutical industrialisation," and "Ethnomedicinal documentation."

2.3. INCLUSION AND EXCLUSION CRITERIA

Only peer-reviewed original research, systematic/comprehensive reviews, and official government or international reports (Nigerian Federal Ministry of Environment, WHO, World Bank, Mordor intelligence) were included to maintain scientific depth. Preference was given to studies that provided quantitative data on bioactive compound potency, standardised extraction methods, or comparative economic analyses of agricultural value chains. Thematic analysis was then used to synthesise these findings into the structured sections of this review.

3. FRAMEWORK FOR ANALYSIS

The literature was analysed to evaluate therapeutic evidence, map the transition from crude extracts to standardised APIs, and assess the scalability of local drug development as an economic mitigation strategy.

4. ETHNOMEDICINAL USES OF *Citrus aurantiifolia*

Despite the recent advances in medical sciences and modern medicines, 80% of the global population, including Nigeria still depend on medicinal plants for their healthcare needs [15]. The industrial worlds engage in the purification of APIs from their medicinal plant species for standardised drug production. Whether consumed raw or purified, medicinal plants have shown proven safety profile, potency, and cultural acceptability. Our findings have shown that the medicinal plant sector is rapidly pivoting from raw material exports toward high-value standardised phytochemicals and plant-based APIs [16–18]. Various parts of *C. aurantiifolia* have been employed in traditional medicine.

4.1. *Citrus aurantiifolia* LEAVES

The leaves have been reported in the treatment of oral thrush, sore throats, and jaundice fever [19]. Patients with insomnia often drink the floral infusion to promote sleep [20]. Pounded leaf decoction is used for eye wash, and a remedy for stomach discomfort [21]. The leaf poultice is used for treatment of foot ulcers, skin conditions, and the abdomenal pain after childbirth [22]. Crushed leaves are placed to the forehead to relieve headaches and inhaled to revive unconscious patients.

4.2. *Citrus aurantiifolia* FRUIT JUICE

A mixture of the fruit juice and honey (or palm oil) is drunk for relief of cough [23]. The fruit juice is consumed as tonic for libido and antidote for poison [24]. It is also used to increase stamina and treat uterine bleeding. It is also used as facial wash to rejuvenate skin and remove stain [25]. The diluted fruit juice is used as mouth wash to treat sore mouth and sore throat [26].

4.3. OTHER PARTS OF *C. aurantifolia*

Root decoction is drunk for treatment of fever, diarrhea, colic, dysentery, and gonorrhea. Rind is burned as a mosquito pesticide [27]. The mesocarp is utilised for facial cleansing to prevent acne. The rind essential oil is for treatment of colds, sore throats, bronchitis, asthma, arthritis. It is applied as a toner and astringent to treat wounds and acne on oily skin. Stem bark decoction has been shown to relief flatulence and promotes digestion.

4.4. GLOBAL TOP 5 PRODUCERS OF LIME/LEMON *Citrus aurantiifolia*

The lime fruit juice is a widely consumed cuisine in many cultures; with India and Mexico as the world's largest producers [25]. Table 1 presents the global top 5 producers of lime/lemon.

Table 1. Global top 5 producers of lime/lemon (2025).

Country/ Continent	Production (metric tons)	Export Revenue (Est.)	Reference
India (Asia)	3,787,000	$4.65 Billion	[25]
Mexico (N. America)	3,500,000	$2.99 Billion	[25]
China (Asia)	2,700,000	$2.6 Billion	[25]
Turkey (Asia/Europe)	1,500,000	$1.47 Billion	[25]
Argentina (S. America)	1,600,000	$1.73 Billion	[25]

Table 2. Taxonomical classification of *C. aurantiifolia*.

Rank	Classification
Kingdom	Plantae
Phylum	Tracheophyta
Class	Magnoliopsida
Order	Sapindales
Family	Rutaceae
Genus	*Citrus*
Species	*aurantiifolia*

Figure 1. Photograph of *C. aurantiifolia* showing the fruits, leaves, and flowers.

4.5. TAXONOMICAL CLASSIFICATION OF *C. aurantiifolia (christm.)* SWINGLE

Common names for *C. aurantiifolia* in Nigeria include Lime (English), Lemun Tsami (Hausa), Osan wewe (Yoruba), Afunfanta (Igbo) [26].

4.6. PHYTOCHEMICAL PROFILE OF *Citrus aurantifolia*

Every part of *C. aurantiifolia* (including fruits, stems, leaves, flowers, seeds, and roots) contains varying concentrations of bioactive components; including flavonoids, terpenoids, phenolics, limonoids, and alkaloids [27]. Transitioning from raw material exportation to standardised APIs requires precise analytical frameworks [28]. Validated methods such as the HPLC analysis of flavonoids on Ascentis® Express C18, demonstrate that the primary bioactive constituents in lime fruit juice (specifically Eriocitrin, Hesperidin, and Naringin), can be effectively isolated, quantified, and used as APIs in drug development. Hesperidin is the major component of *C. aurantiifolia* responsible for its potency [28].

4.6.1. Flavonoids

Hesperidin and eriocitrin are major flavonoids found in *C. aurantiifolia* with established antioxidant property [29]. Apigenin, rutin, kaempferol, quercetin, and nobiletin have also been reported in *C. aurantiifolia* extract [34]. The *C. aurantiifolia* fruit peel has more flavonoids than seeds, juice, and fruit [30]. HPLC analysis of flavonoids in hand-squeezed lime fruit juice on Ascentis® Express C18 identified five flavonoids: Apigenin 6,8-di-C-glucoside, diosmetin 6,8-di-C-glucoside, eriocitrin, narirutin, hesperidin (major component). Phucharoenrak *et al.* [35] carried out a metabolomic analysis of the ethanolic seed extract using LC-qTOF/MS and GC-HRMS and identified 84 compounds with Hesperidin, Limonin, Neohesperidin, 5,7-Dimethoxycoumarin, 7-Methoxy-coumarin, Bergaptol, Bergamottin, 5-Geranoxy-7-methoxy-coumarin as predominant constituents. Flavonoids are rich in biological activities: acting as antioxidants, regulating enzyme activity, preventing cancer cell growth, antibacterial, hypoallergenic, antidiarrheal, and anti-inflammatory properties.

4.6.2. Terpenoids

Terpenoids are volatile low-molecular-weight substances often present in essential oils [36]. Al-Aamri *et al.* [37] identified 33 compounds with *D*-Limonene (63.35%) and Dimethyl-2,6-octadien-1-ol (7.07%) as predominant constituents in the leaf's essential oil. Similarly, 34.81% β-pinene and 20.15% d-limonene were found to be among the terpenoid content in the ethanolic leaf extract. Monoterpenes, alcoholic terpenes, aldehyde terpenes, ketone terpenes, and ester terpenes are the several types of terpenoids found in *C. aurantiifolia* [36]. Patil *et al.* [38] reported limonin, limonexic acid, isolimonexic acid, β-sitosterol glucoside, limonin glucoside as seed extract constituents responsible for pro-apoptotic and pancreatic cancer inhibition. Terpenoids possess potent antibacterial, antioxidant, and anti-inflammatory properties.

4.6.3. Phenolics

The *C. aurantiifolia* fruit maturity stage is known to affect its phenolic content; immature fruits demonstrated higher phenolic content than mature fruits. The phenolic content is also influenced by the extraction process, and solvent concentration. The ethanolic extract showed higher total phenolic content than aqueous and methanol crude extracts [30]. The total phenolic content of the leaf, extracted with 96% ethanol

was higher than the same leaf sample extracted with 70% alcohol. Thus, the higher the solvent concentration, the higher the phenolic content and some other constituents. Four phenolic acids identified in *C. aurantiifolia* pulp include tannic acid, gallic acid, ferulic acid, and coumaric acid in their order of abundance. Phucharoenrak *et al.* [31] reported presence of 5,7-dimethoxycoumarin, 7-methoxy-coumarin, bergaptol, bergamottin, 5-geranoxy-7-methoxy-coumarin in *C. aurantiifolia* ethanolic seed extract.

4.6.4. Alkaloids

The three primary alkaloids in *Citrus* genus include synephrine, tyramine, and octopamine [32]. The *C. aurantiifolia* peel showed higher alkaloid content than the pulp. The *C. aurantiifolia* alkaloids and glycosides could be employed as dietary supplements considering their biological properties including anticancer activity.

4.6.5. Limonoids

Limonoids are major phytochemical constituents found in citrus fruits. Two types of limonoids in citrus have been shown to be glycosides and aglycones. The aglycones include the dicarboxylic acids, acidic mono-lactones, and neutral dilactones. The aglycones are insoluble in water and exhibit characteristic bitter taste. The bitter taste of *C. aurantiifolia* is likely caused by presence of limonoid aglycones. Glycosides (sugar component) known as limonin and nomilin are the most significant components [33]. The limonoids fall within the class of oxygenated tetracyclic triterpenoids and their biological properties include antitumor, anti-obesity, and antihyperglycemic, antioxidant, antibacterial, larvicidal, antimalarial, and antiviral, hypoallergenic, anti-inflammatory, antiproliferative, antimutagenic.

4.7. PHARMACOLOGICAL ACTIVITIES OF *Citrus aurantiifolia*

4.7.1. Antioxidant activity

The antioxidant activity of *C. aurantiifolia* is attributed to the hydrogen-donating property of its flavonoid, carotene, and vitamin C content [29]. The lime juice used as a solvent to extract cashew bark (LJECB) was reported to elicit antioxidant activity (*in vitro*), raised the HDL-c level, and showed no significant effect on liver-kidney function at the doses tested [34]. Similarly, the methanol extracts of the peel and leaves demonstrated strongest antioxidant activity [35]. Furthermore, LJECB also promoted gastric ulcer healing and attenuated pepsin activity in indomethacin-induced gastric ulceration in Wistar rats [36]. The *C. aurantiifolia*, rich in vitamin C antioxidant, shields low-density lipoprotein (LDL) and plasma lipids from peroxidative damage caused by oxidative stress.

4.7.2. Antibacterial activity

The antibacterial activity of *C. aurantiifolia* was found to be mediated by phenolics and derivatives which work by denaturing bacterial cell proteins. Studies have shown that *C. aurantiifolia* root inhibits the growth of *Staphylococcus aureus, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Betahaemolytic streptococci, Escherichia coli* and *Neisseria gonorrhoeae* [37].

4.7.3. Anti-inflammatory properties

The anti-inflammatory activities of *C. aurantiifolia* peel essential oil are attributed to the presence of limonene, α-terpinene, and geranial components [38]. The anti-inflammatory activity was found to include the inhibitory effect of the essential oil on protein extravasation, cytokine synthesis, and neutrophil infiltration. Due to the high concentration of citral in *C. aurantiifolia* essential oil, high dose could lead to myelotoxicity [39]. Also, Kasim *et al.* [40] demonstrated that the ethanolic extract of *C. aurantiifolia* stem bark influenced the growth of *S. typhi* in *Balb/c* mice, often driven by raised interleukin-6 (IL-6) level. Following the injection of *S. typhi* on Day 5, the IL-6 cytokine level was found to be significantly high. Administration of 750 mg/kg lime peel extract on the 10th day was associated with a significant decrease in IL-6 level and *S. typhi* growth. This indicates that *C. aurantiifolia* peel extract elicited both antibacterial and anti-inflammatory properties by lowering the blood level of IL-6 which in turn, inhibited *S. typhi* proliferation.

4.7.4. Anti-cancer activity

Citrus aurantiifolia inhibited the growth of liver cancer, colon cancer, neuroblastoma, pancreatic cancer, and prostate cancer [41]. Hesperidin, limonin, neohesperidin, 5,7-dimethoxycoumarin, 7-methoxy-coumarin, bergaptol, bergamottin, 5-Geranoxy-7-methoxy-coumarin, limonin, limonexic acid, isolimonexic acid, β-sitosterol glucoside, limonin glucoside were phytoconstituents responsible for its anticancer properties.

4.7.5. Immuno-modulatory activity

The *C. aurantiifolia* fruit juice was reported to elicit potent immuno-modulatory activity [42]. The study observed a significant reduction in body weight and feed intake in rats administered with *C. aurantiifolia* juice. The juice elevated the red blood cell count and haemoglobin level.

5. *Anacardium occidentale* AND PHYTOCHEMICAL PROFILE

Anacardium occidentale has rich phytochemical profile, nutritional composition (vitamins, minerals, amino acids, lipids, carbs) and biological properties (antioxidant, anti-inflammatory, anti-ulcerogenic, cardio-protective, etc.) [43].

The phytochemical profile of *A. occidentale* is dominated by anacardic acids, cardol, and cardanol within the cashew nut shell liquid (CNSL). The pseudofruit and leaves are rich sources of quercetin, catechins, and carotenoids which are polyphenols responsible for their antioxidant and glucose-regulating activities. The presence of these phytoconstituents facilitates a broad range of pharmacological applications, from industrial polymer synthesis to the development of standardised antimicrobial APIs [44].

5.1. NUTRITIONAL COMPOSITION OF CASHEW

The nutritional composition includes water-soluble vitamins (vitamin C, B1, B2, B3, B6) and fat-soluble vitamins (K, E, A), calcium, potassium, and magnesium in cashew apple juice. The cashew nut is highly rich in oil, essential amino acids (lysine, tryptophan, phenylalanine, methionine, threonine, isoleucine, leucine, valine, histidine) and eight non-essential amino acids

Table 3. Major nutrients or bioactive components in cashew and implications.

Parts	Major bioactive components	Key data and implications
Kernel (nut)	High lipid content; stable edible oil, essential amino acids	Oil yield 47–56% (raw to roasted); unsaturated fatty acids predominate; oleic 34.75–65.60% and linoleic present, supporting edible-oil and snack value [45]
Cashew apple (pseudofruit)	High moisture, sugars, polyphenols, carotenoids	Moisture >80% w/w, sugars ≈10% w/w, high polyphenols/flavonoids/tannins supporting antioxidant and functional-food use [49]
Testa (skin)	Concentrated polyphenols	Testa rich in polyphenols and contributes antioxidant capacity of kernel products [49]
Cashew nutshell and CNSL	Long-chain phenolic compounds	Cashew nutshell liquid contains aliphatic long-chain phenols usable in coatings and industrial formulations [49]

(cystine, tyrosine, alanine, aspartic acid, glutamic acid, glycine, proline, serine) [45–47]. The pseudofruit (apple) is rich in water and polyphenols; testa and nutshell are rich in phenolics and industrial lipids [46]. Cashew nut's physicochemical indices (acid value, peroxide, saponification and iodine values) indicate an edible, non-drying oil with good oxidative stability, and roasting does not alter the fatty-acid profile or antioxidant activity [46]. Defatted cashew kernel cake has nutrient properties comparable to groundnut cake and can be used as an alternative protein source in poultry, with feed-cost reductions of 9.1% and acceptable performance when replacing groundnut cake [47].

Several popular drinks in north America are made from fresh cashew apple juice and include cashew apple wine, probiotic beverages [48]. One cup serving of cashew provides 5 g of protein, 1 g of fiber and 16 g of fat, 750 mg of copper, 167 mg of phosphorus, 89 mg of magnesium, 27 mg of manganese, 23 mg of folate, 11 mg of iron, and 9 mg of zinc [45]. Cashews are considered safe and beneficial for managing blood sugar levels in diabetic patients due to their low glycemic index of 22 [45]. Major bioactive nutrients in cashew and implications are presented in Table 3.

5.2. GLOBAL TOP 5 PRODUCERS OF CASHEW NUTS

Ivory Coast (Africa) is the world's largest producer of cashew averaging 1,044,449.95 metric tons per year [25]. Table 4 presents the global top 5 producers of cashew nuts. The 2026 estimated bioeconomy from cashew is $10.57 billion. Although, Ivory Coast is the global largest producer of cashew, they are not making the most revenue as Vietnam, which mostly engages in cashew processing. This observation suggests that the true wealth is not in the export of the raw material but in the processing to finished products. Nigeria is currently the fifth largest producer of cashew but earns only a few million dollars compared to other countries from a similar production volume (Table 4). Major cashew-producing states include Kogi, Oyo, Kwara, Enugu, and Niger states.

The local names of cashew in Nigeria include cashew (English), Kaju (Yoruba), Kashu (Igbo) and Fisa (Hausa).

Table 4. Global top 5 producers of cashew nuts.

Country	Production (metric tons)	Export Revenue	Role in market
Ivory Coast (Africa)	1,044,449.95	$1.17 Billion	Largest grower/ exporter
India (Asia)	800,000	$2.35 Billion	Huge producer & largest consumer
Cambodia (Asia)	800,000	$1.5 Billion	Major supplier to Vietnam
Vietnam (Asia)	350,000	$5.2 Billion	#1 in processing/ export
Nigeria (Africa)	340,000	$400 million	Raw cashew nut exporter

Table 5. Taxonomical classification of *A. occidentale*.

Rank	Classification
Kingdom	Plantae
Phylum	Magnoliophyta
Class	Magnoliopsida
Family	Anacardiaceae
Genus	*Anacardium*
Species	*occidentale*

Figure 2. Photograph of *A. occidentale* showing fruits, leaves, nuts and flowers.

5.3. TAXONOMICAL CLASSIFICATION OF *A. occidentale* (LINNAEUS)

5.4. ETHNOMEDICINAL USES OF CASHEW

The stem bark or leaf decoction is drunk for treatment of fever, skin rashes, sore throat, cough, rheumatoid arthritis, gastric ulcer, hemorrhoids, severe diarrhea, diabetes, worm, teeth bleeding, hypertension. The roots are utilised in the treatment of cough, stomach pain, tooth decay, hypertension, malaria, and diarrhea. The apple is used for scorpion or bee sting, syphilis, cholera, kidney disease, as well as diuretic [44, 48]. The nut oil is used to treat cracked heels, hypertension, purgative, cholera, hookworms, and warts. The cashew gum has been used in the treatment of inflammatory disorders, analgesic, asthma, T2D, diarrhea, warts, coughs [49].

Notably, each documented ethnomedicinal application represents a high-priority pharmacological lead or the foundation for bioprospecting. Transitioning from ethnomedicine to clinical application requires the isolation of active principles followed by rigorous *in vitro* and *in vivo* validation to establish dose-response relationships and safety profiles [50].

5.5. BIOLOGICAL ACTIVITIES OF *A. occidentale (Linnaeus)*

5.5.1. Antioxidant activity

Kernel testa and pseudofruit are rich in polyphenols and flavonoids that contribute significant antioxidant capacity; and studies show that non-thermal processing method was the best method of preserving these activities in the pseudofruit [51]. The antioxidant activity of various parts of *Anacardium occidentale* is primarily driven by high concentrations of vitamin C, phenolics, tannins, and anacardic acids. Cashew stem-bark extracted with lime fruit juice enhanced antioxidant status in indomethacin-induced ulcer in Wistar rats; which was associated with ulcer healing.

5.5.2. Metabolic and enzyme inhibition

The cashew stem-bark extracted with lime fruit juice significantly inhibited aggressive pepsin activity in indomethacin-induced ulcer in Wistar rats; which promoted ulcer healing [36].

5.5.3. Anti-inflammatory and tissue effects

Silva *et al.* [52] reported the antinociceptive and anti-inflammatory activities of cashew gum in complete Freund's adjuvant-induced arthritis. The cashew gum reduced prostration, joint edema, and polymorphonuclear migration without altering the body weight. The histomorphological analysis showed that the cashew gum promoted gastroprotective and hepatoprotective effects against the adjuvant-induced damage.

5.5.4. Cardiometabolic and other pharmacology

Biological properties attributed to cashew bioactive constituents include anti-tumor, neuroprotective, cardiovascular protection, anti-diabetic and gastroprotective effects [49, 52].

5.5.5. Processing and activity retention

Roasting and conventional heat treatments produce only minor changes in fatty-acid composition and generally preserve antioxidant activity in kernels under the tested conditions [47].

6. DRUG DEVELOPMENT POTENTIAL: PIPELINES FROM TRADITION TO API PRODUCTION

Transitioning ethnomedicinal knowledge to industrialised APIs requires a structured, multi-stage pipeline: ethnobotanical selection, extraction, bioassay-guided isolation, structural identification, standardisation, safety profiling, and scalable synthesis [53]. This ensures that the therapeutic effects of *C. aurantiifolia* and *A. occidentale* are not only validated but also standardised for safety and global regulatory compliance. This process is increasingly integrating AI and machine learning (ML) for virtual screening and pharmacokinetic prediction, bridging traditional medicine with modern, compliant pharmaceutical manufacturing [54].

6.1. ETHNOBOTANICAL SELECTION AND DOCUMENTATION

The initial phase in drug discovery pipeline involves gathering of the indigenous knowledge, ensuring ethical compliance, and validating the pharmacological potential of plant extracts, such as anti-inflammatory, antioxidant or anti-tumor properties [50]. The crude extracts of the selected herbal materials are obtained using solvents of varying polarities such as ethanol, methanol, or aqueous solution.

6.2. BIOASSAY-GUIDED FRACTIONATION

Bioassay-guided fractionation is another critical stage in drug discovery pipeline [55]. It streamlines the purification of crude extracts by isolating active compounds based on their biological activity. Sophisticated techniques like high-resolution chromatography (HPLC, VLC, LC-MS) are used to separate the crude extract into smaller fractions to isolate specific bioactive compounds [56]. The fractionation is followed by bioassay screening, in which each fraction is tested in a biological assay (e.g., DPPH scavenging for antioxidant activity, cyclooxygenase II for anti-inflammatory activity or MIC determination for antimicrobial efficacy) [57]. Only the active fractions are selected for further sub-fractionation and this is considered as iterative refinement. This process continues until pure, bioactive compounds (such as hesperidin and eriocitrin in *C. aurantiifolia*) are isolated. Adeniyi-Akee [24] reported the bioassay-guided isolation, characterisation and cytotoxicity of mosquito-repellent compounds from selected medicinal plants (*Citrus paradisi*, *Citrus sinensis*, and *Citrus limon*).

6.3. IDENTIFICATION OF BIOCHEMICAL TARGETS AND VALIDATION

Following isolation, crucial steps include structural elucidation using advanced methods (NMR, MS, IR) and identifying biological pathways the compound affect [58]. Bioactivity is then assessed via *in silico* modeling or AI-enhanced validation to aid lead optimisation [59]. Studies have identified limonin, luteolin, and myricetin from *C. aurantiifolia* fruit peels as having potential anti-plasmodial, anti-hyperglycemic, and antioxidant activities, often interacting with crucial target proteins *in silico* [60, 61].

6.4. LEAD OPTIMISATION AND AI-ENHANCED VALIDATION (2025 TREND)

Lead optimisation involves the use of structural approach to determine if the lead compound can be modified to increase po-

tency or decrease toxicity [62]. Artificial intelligence (AI) and machine learning (ML) have been used to predict molecular interactions, optimise pharmacological profiles, and reduce drug discovery time by up to 70% [63]. Recent advancements in computational methodologies have integrated machine learning to streamline the screening of bioactive constituents within *Citrus* essential oils, facilitating more efficient process optimisation, authenticity verification, and the discovery of novel therapeutic compounds [64].

6.5. STANDARDISATION AND PHARMACOKINETIC PROFILING

Standardisation is a crucial transition step in the development of botanical APIs to ensure consistency of the pharmaceutical product. It ensures that every dose contains a consistent concentration of bioactive markers [65] such as hesperidin in *C. aurantiifolia*. It also involves establishing quality control metrics for raw materials (such as soil quality and harvest timing), to ensure reproducibility in extract potency. The standardised lead can then be evaluated for pharmacokinetic properties (absorption, distribution, metabolism, excretion ADME) to determine how the lead compound behave within a biological system [66]. The information from the pharmacokinetic profiling is essential for determining dosage intervals and predicting potential drug-herb interactions.

6.6. SAFETY AND TOXICITY STANDARDISATION

This involves determining the median lethal dose (LD_{50}) and assessing sub-chronic toxicity in animal models to ensure the lead compound (API) does not damage vital organs like the liver, kidneys, heart, GIT, Blood cells [67]. High concentration of citral in *C. aurantiifolia* essential oil was reported to elicit myelotoxicity [39]. High doses of lime essential oil leads to mild hepatotoxicity and nephrotoxicity [68]. Normal, dietary consumption of *C. aurantifolia* fruit juice does not cause toxicity. Lime peel oils are known to contain furanocoumarins, which can cause photosensitisation, a form of skin reaction upon exposure to ultraviolet light. The key phytochemicals in the essential oil include germacrene isomers, pinene, citral, and limonene.

6.7. PRE-CLINICAL AND CLINICAL TRIALS

Clinical trials represent the definitive translational bridge between fundamental laboratory discovery and therapeutic application, functioning as the rigorous benchmark for evaluating the safety and efficacy of novel drug candidates. The laboratory testing is moved from *in vitro* and *in vivo* models to human trials to establish efficacy and dosage. AI has been employed in various stages of drug discovery, from hit identification to lead optimisation, and possible impact on clinical outcomes [69]. While there is significant *in vitro* and animal study research on *C. aurantiifolia*, search results showed that much of the studies is in the pre-clinical stage rather than human clinical trials [70].

6.8. SCALABLE INDUSTRIAL PRODUCTION

This involves shifting from lab-scale extraction to industrial production, utilising green chemistry to ensure, for example, sustainable synthesis and reduced environmental impact [71]. Large scale valorisation of approximately 15 million tons of annual citrus waste (peels, seeds, pulp) has been reported [72]. Major industrial products include essential oils (mainly *D*-limonene), pectin, flavonoids, and citrus peels for biofuel.

6.9. REGULATORY APPROVAL AND INTELLECTUAL PROPERTY (IP) DOCUMENTATION

The drug approval process is an indispensable regulatory mandate designed to safeguard the integrity of the pharmaceutical market by verifying the pharmacological viability and manufacturing consistency of new drug candidates [73]. This involves strict adherence to regulatory standards to ensure that the API is safe, effective and pure. It involves documenting all the extraction protocols, tested therapeutic markers, pharmacokinetic profile, safety and toxicity profile, standardised chemical process development that confirms that the API is safe and effective. The detailed information is compiled and forwarded to the international regulatory bodies like NAFDAC, FDA, or EMA. These regulatory bodies are the final gatekeeper for local drug development.

7. INDUSTRIAL AND ECONOMIC IMPLICATIONS

Cashew and lime fruits possess unique nutritional and pharmacological properties that drive high-value opportunities in global food and industrial markets. The opportunities include cashew kernel processing and oil, pseudofruit preservation and functional foods, animal feed from byproduct cakes, industrial use of CNSL, and utilisation of pomace and other wastes for added-value products [74]. Also, large scale valorisation of citrus waste (peels, seeds, pulp) has been reported for biofuel [72]. High-value products and industrial applications derived from *Anacardium occidentale* components is presented in Table 6.

8. CHALLENGES AND FUTURE DIRECTIONS

Transitioning from crude botanical extracts to standardised APIs in Nigeria faces significant hurdles, including inconsistent phytochemical profiles, high infrastructural costs for high-purity isolation, and a complex global regulatory landscape. Furthermore, the rapid loss of biodiversity due to anthropogenic pressures threatens the very genetic resources required for long-term drug discovery. Future directions must prioritise the integration of Artificial Intelligence and Machine Learning to accelerate hit-to-lead optimisation and toxicity prediction [75]. Leveraging green chemistry innovations and biotechnological approaches to valorise citrus and cashew processing waste, Nigeria can establish a sustainable, circular bio-economy that ensures both healthcare sovereignty and international economic competitiveness.

9. CONCLUSION

In conclusion, the review shows that the medicinal plant sector is rapidly pivoting from raw material exports toward high-value standardised phytochemicals and plant-based active pharmaceutical ingredients (APIs). By transitioning indigenous flora from basic ethnobotanical categories into high-purity pharmaceutical lead compounds, Nigeria can concurrently safeguard its domestic healthcare infrastructure and build long-term economic resilience. The strategic integration of *Citrus aurantiifolia* and *Anacardium occidentale* into the local drug development pipeline

Table 6. High-value products and industrial applications derived from *Anacardium occidentale* components.

Product/ Application	Description
Kernel processing and oil	The high oil yield and stable high-oleic profile support edible oil production, roasted-nut snacks, and high-value kernel exports [47].
Cashew apple products	High moisture, sugar and polyphenol contents of cashew apple enable juicing, fermented beverages and development of functional foods [47].
Animal feed from byproducts	Defatted cashew kernel cake serves as a protein-rich replacement for groundnut cake in poultry diets, improving feed efficiency, lowering feed costs, and strengthens local livestock value chains [46].
Industrial applications of CNSL	The long-chain phenolic compounds are suitable for surface coatings, insulating formulations and other industrial uses, offering a high-value non-food revenue stream [49].
Pomace and residues	Techniques for drying and stabilising cashew pomace enable its use in ingredient development or fermentation feedstocks, reducing postharvest losses and opening industrial feedstock opportunities [74].
Employment generation	Expansion of small and medium-scale cashew processing will create more jobs across women-led processing groups and youth in collection, sorting, processing and marketing nodes [75].
Foreign exchange and export value addition	Moving beyond raw nut export to processed kernels, edible oil, apple-derived products and CNSL-based industrial products will significantly increase unit value and export earnings potential [75].
Food security and affordability	Use of defatted cashew kernel cake as an alternative protein feed reduces poultry feed costs ($\sim$ 9.1% reduction reported in one feeding trial), potentially lowering animal-protein prices and improving food affordability [47].
Industrial development and substitution	CNSL and pomace provide feedstocks for coatings, insulators, and ingredient industries, creating upstream-downstream linkages and reducing import dependence for specialty chemicals and feed ingredients [75].

offers a transformative pathway to mitigate national economic challenges. Ultimately, leveraging these bio-resources through modern biotechnological and computational frameworks serves as a vital nexus for achieving pharmaceutical sovereignty and long-term economic diversification.

9.1. RECOMMENDATIONS

1. Strategic phytochemical standardisation - Stakeholders must begin to prioritise the transition from crude extract preparation to the isolation of high-purity pharmaceutical lead compounds. Establishing standardised fingerprints for bioactive metabolites in *C. aurantiifolia* and *A. occidentale* is essential to meet international regulatory benchmarks and ensure therapeutic consistency.
2. Integration of advanced computational tools - To accelerate drug discovery timelines, researchers should adopt an "*in silico*-first" approach. Utilising machine learning and LSTM-based models for predicting pharmacokinetic profiles and toxicity can significantly reduce the cost and time associated with traditional bench-to-bedside transitions.
3. Valorisation of agricultural waste - Nigeria should implement a circular bio-economy model by focusing on the extraction of APIs from citrus and cashew processing by-products. Utilising fruit rinds and pomace as a source of high-value bioflavonoids not only reduces environmental impact through green chemistry but also provides a low-cost raw material stream for local manufacturing.
4. Policy alignment for pharmaceutical sovereignty - The Nigerian Federal Ministry of Environment and health regulatory bodies should provide incentives for the local development of plant-based APIs. This can mitigate economic challenges, reduce the fiscal burden of drug imports, and safeguard national healthcare infrastructure.

DATA AVAILABILITY

The data will be available on request from the corresponding author.

ACKNOWLEDGMENT

The authors specially thank the TETFUND for the sponsorship to attend the 4th International Conference of the Nigerian Society of Physical Sciences (NSPS), Zazzau held at Ahmadu Bello University, Zaria, Nigeria.

References

[1] International Monetary Fund, "World economic outlook database: Nigeria", IMF **2025** 1. https://www.imf.org/external/datamapper/profile/NGA.
[2] Worldometer, "Nigeria population (live)", Worldometer **2026** 1. https://www.worldometers.info/world-population/nigeria-population/.
[3] K. S. Aina, E. Iyiola, O. R. Oyewumi & O. O. Edward, "Biodiversity as a tool for sustainable socio-economic development in Nigeria", Russian Journal of Agricultural and Socio-Economic Sciences **5** (2022) 125. https://doi.org/10.18551/rjoas.2022-05.23.
[4] Federal Ministry of Environment, "Fourth national biodiversity report", Federal Government of Nigeria (2010). https://www.cbd.int/doc/world/ng/ng-nr-04-en.pdf.
[5] B. O. Rafiu, A. O. Omotayo, I. O. Lawal & A. O. Aremu, "Ethnobotanical uses of plants in Nigeria: An analysis of current research trends and patterns", Journal of Ethnobiology and Ethnomedicine **21** (2025) 57. https://doi.org/10.1186/s13002-025-00788-y.
[6] Federal Ministry of Environment, "National strategy for combating wildlife and forest crime in Nigeria (2022-2026)", Federal Government of Nigeria **2022** 1.
[7] J. Clemente-Villalba, F. Burló, F. Hernández & Á. A. Carbonell-Barrachina, "Valorisation of wild edible plants as food ingredients and their economic value", Foods **12** (2023) 1012. https://doi.org/10.3390/foods12051012.
[8] C. K. Khoury, S. Sotelo, D. Amariles & G. Hawtin, "The plants that feed the world", FAO Report (2023). https://www.fao.org/newsroom/story/The-plants-that-feed-the-world/en.
[9] S. R. Mathura, R. Maharaj & N. Ratkovich, "Emerging trends in biopolymer edible coatings for enhancing the shelf life of neglected and underutilised crops", Frontier in Food Science Technology **5** (2025) 1641117. https://doi.org/10.3389/frfst.2025.1641117.

[10] A. Mayere & A. L. Shekarau, ''Evaluation of briquettes produced from four selected sawdusts combination at quaternary levels'', Physics Access **2** (2022) 56.

[11] J. Kumar, A. Ramlal, D. Mallick & V. Mishra, ''An overview of some biopesticides and their importance in plant protection for commercial acceptance'', Plants **10** (2021) 1185. https://doi.org/10.3390/plants10061185.

[12] N. Karki, H. Achhami, B. B. Pachhai, S. Bhattarai, D. K. Shahi, L. R. Bhatt & M. K. Joshi, ''Evaluating citrus juice: A comparative study of physicochemical, nutraceutical, antioxidant, and antimicrobial properties of citrus juices from Nepal'', Heliyon **10** (2024) e40773. https://doi.org/10.1016/j.heliyon.2024.e40773.

[13] World Health Organization, ''WHO global report on traditional, complementary and integrative medicine 2024'', WHO **2024** 1. https://www.who.int/publications/i/item/9789240111387.

[14] F. Boylan & D. Silveira, ''Medicinal plants: global market trends and the transition to high-value phytochemical exports (2023–2030)'', Manuscript in preparation (2026).

[15] M. R. Modibbo, H. Ibrahim, M. Y. Sulaiman & B. Zakir, ''Maganin Gargajiya: Assessing the benefits, challenges, and evidence of traditional medicine in Nigeria'', Cureus **16** (2024) e71425. https://doi.org/10.7759/cureus.71425.

[16] I. Umar & G. S. Okeh, ''Determination of antimicrobial activities of crude extract (juice) of Citrus aurantifolia on some selected bacteria'', Sokoto Journal of Medical Laboratory Science **9** (2024) 301. https://sokjmls.com.ng/index.php/SJMLS/article/view/619.

[17] Z. Abbaspoor, A. Siahposh, N. Javadifar, S. Faal Siahkal, Z. Mohaghegh & F. Sharifipour, ''The effect of Citrus aurantium aroma on the sleep quality in postmenopausal women: A randomized controlled trial'', International Journal of Community Based Nursing and Midwifery **10** (2022) 86. https://doi.org/10.30476/IJCBNM.2021.90322.1693.

[18] F. S. Ouattara-Soro, P. Acray-Zengbe, K. Y. J. Febry & G. Abizi, ''Study of the analgesic effect of the aqueous extract of the leaves of Citrus aurantifolia (Rutaceae) in mice'', GSC Biological and Pharmaceutical Sciences **14** (2021) 207. https://doi.org/10.30574/gscbps.2021.14.3.0072.

[19] M. Falana, Q. Nurudeen, S. S. Salimon & I. B. Abubakar, ''Ethnopharmacological survey of medicinal plants used in the management of skin-related conditions in Ilorin, North-central, Nigeria'', Traditional and Integrative Medicine **8** (2023) 56. https://doi.org/10.18502/tim.v8i1.12404.

[20] H. A. Bankole, M. I. Kazeem, A. A. Fatai, R. A. Lawal, S. O. Lawanson, R. T. Ogunyemi, T. O. Ajiboye & R. O. Olayemi, ''Citrus aurantifolia (Christm.) Swingle extract ameliorates oxidative stress, dyslipidemia, and inflammation in galactose-induced aging in female rats'', South African Journal of Botany **168** (2024) 221. https://doi.org/10.1016/j.sajb.2024.03.027.

[21] D. A. E. Zialé, D. A. Adou, K. C. C. N'gaman-Kouassi, J. Deschamp, N. Bouchemal, T. L. Palama, M. Lecouvey, J. A. Mamyrbeková-Békro & Y. A. Békro, ''Characterization, antioxidant and anticholinesterase activity of compounds isolated from alkaloid extracts of Citrus aurantifolia root bark'', Journal of the Turkish Chemical Society Section A: Chemistry **11** (2024) 1227. https://doi.org/10.18596/jotcsa.1395690.

[22] E. A. Miles & P. C. Calder, ''Effects of citrus fruit juices and their bioactive components on inflammation and immunity: A narrative review'', Frontiers in Immunology **12** (2021) 712608. https://doi.org/10.3389/fimmu.2021.712608.

[23] M. Nawaz, B. Ullah, M. G. Abbas, M. Binyameen, V. Apšegaitė, R. Mozūraitis & M. Azeem, ''Antibacterial and mosquito repellent potential of eight citrus cultivars and their chemical composition'', Molecules **27** (2022) 7488. https://doi.org/10.3390/horticulturae11010009.

[24] M. A. Adeniyi-Akee, ''Bioassay-guided isolation, characterisation and cytotoxicity of mosquito repellent compounds from selected medicinal plants'', Ph.D. dissertation (2023).

[25] Mordor Intelligence, ''Lime market size & share analysis - growth trends & forecasts (2025-2030)'', Industry Report (2025). https://www.mordorintelligence.com/industry-reports/lime-market.

[26] U. A. Imam & G. S. Susan, ''Determination of antimicrobial activities of crude extract (juice) of Citrus aurantifolia (Lemun Tsami) on some selected bacteria'', Sokoto Journal of Medical Laboratory Science **9** (2024) 118. https://sokjmls.com.ng/index.php/SJMLS/article/view/619.

[27] N. N. Indriyani, J. A. Anshori, N. Permadi, S. Nurjanah & E. Julaeha, ''Bioactive components and their activities from different parts of Citrus aurantifolia (Christm.) Swingle for food development'', Foods **12** (2023) 2036. https://doi.org/10.3390/foods12102036.

[28] N. N. Indriyani, J. A. Anshori, N. Permadi, S. Nurjanah & E. Julaeha, ''Bioactive components and their activities from different parts of Citrus aurantifolia (Christm.) Swingle for food development'', Foods **12** (2023) 2036. https://doi.org/10.3390/foods12102036.

[29] J. Fernández-Cabal, K. A. Avilés-Betanzos, J. V. Cauich-Rodríguez, M. O. Ramírez-Sucre & I. M. Rodríguez-Buenfil, ''Recent developments in Citrus aurantium L.: An overview of bioactive compounds, extraction techniques, and technological applications'', Processes **13** (2025) 120. https://doi.org/10.3390/pr13010120.

[30] Y. Xu, P. He, B. He & Z. Chen, ''Bioactive flavonoids metabolites in citrus species: Their potential health benefits and medical potentials'', Frontier in Pharmacology **16** (2025) 1552171. https://doi.org/10.3389/fphar.2025.1552171.

[31] P. Phucharoenrak, C. Muangnoi & D. Trachootham, ''Metabolomic analysis of phytochemical compounds from ethanolic extract of lime (Citrus aurantifolia) peel and its anti-cancer effects'', Molecules **28** (2023) 2965. https://doi.org/10.3390/molecules28072965.

[32] A. Koh, R. Chess-Williams & A. E. Lohning, ''HPLC-UV-QDa analysis of Citrus aurantium-labelled pre-workout supplements suggest only a minority contain the plant extract'', Journal of Pharmaceutical and Biomedical Analysis **193** (2020) 113746. https://doi.org/10.1016/j.jpba.2020.113746.

[33] M. S. Al-Aamri, N. M. Al-Abousi, S. S. Al-Jabri, T. Alam & S. A. Khan, ''Chemical composition and in-vitro antioxidant and antimicrobial activity of the essential oil of Citrus aurantifolia L. leaves grown in Eastern Oman'', Journal of Taibah University Medical Sciences **13** (2018) 108. https://doi.org/10.1016/j.jtumed.2017.12.002.

[34] A. E. Morakinyo, S. O. Babarinde & A. Godwin, ''Effect of lime juice extract of cashew bark on lipid biomarkers in indomethacin-induced gastric ulcerated Wistar rats'', Journal of Phytomedicine and Therapeutics **23** (2024) 1472. https://doi.org/10.4314/jopat.v23i2.7.

[35] M. R. Loizzo, R. Tundis, M. Bonesi, F. Menichini, D. De Luca, C. Colica & F. Menichini, ''Evaluation of Citrus aurantifolia peel and leaves extracts for their chemical composition, antioxidant and anti-cholinesterase activities'', Journal of the Science of Food and Agriculture **92** (2012) 2960. https://doi.org/10.1002/jsfa.5708.

[36] A. E. Morakinyo, A. Godwin, S. O. Babarinde, C. Okeke, R. Dangana & T. A. Oyedepo, ''Anti-ulcer activity of lime juice extract of cashew bark (LJECB) in indomethacin-induced wistar rats and ulcerogenic potential in healthy gastric mucosa'', Next Research **2026** (2026) 101492. https://doi.org/10.1016/j.nexres.2026.101492.

[37] B. B. Ajayi, T. T. Adebolu, M. K. Oladunmoye & B. O. Oladejo, ''Evaluation of antibacterial activity of Citrus aurantium L. leaf extracts on bacteria isolated from blood of hepatitis B positive individuals in Ondo State, Nigeria'', Microbes and Infectious Diseases **4** (2023) 304. https://doi.org/10.21608/mid.2021.103642.1206.

[38] J. Yang, S.-Y. Lee, S.-K. Jang, K.-J. Kim & M.-J. Park, ''Anti-inflammatory effects of essential oils from the peels of citrus cultivars'', Pharmaceutics **15** (2023) 1595. https://doi.org/10.3390/pharmaceutics15061595.

[39] J. L. Amorim, D. L. R. Simas, M. M. G. Pinheiro, D. S. A. Moreno, C. S. Alviano, A. J. R. da Silva & P. D. Fernandes, ''Anti-inflammatory properties and chemical characterization of the essential oils of four Citrus species'', PLOS ONE **11** (2016) e0153643. https://doi.org/10.1371/journal.pone.0153643.

[40] V. N. Kasim, M. Hatta, R. Natzir, V. Hadju, Y. Hala, Budu, G. Alam, S. As'ad, A. Febriza & H. H. Idrus, ''Antibacterial and anti-inflammatory effects of lime (Citrus aurantifolia) peel extract in Balb/c mice infected by Salmonella typhi'', Journal of Biological Research **93** (2020) 2. https://doi.org/10.4081/jbr.2020.8951.

[41] Y.-S. Shi, Y. Zhang, H.-T. Li, C.-H. Wu, A. F. El-Baba, J.-H. Pan, Z.-L. Li, J. Pang, Q.-X. Chen & G.-Y. Kai, ''Limonoids from Citrus: Chemistry, anti-tumor potential, and other bioactivities'', Journal of Functional Foods **75** (2020) 104213. https://doi.org/10.1016/j.jff.2020.104213.

[42] O. C. Ezeigwe, C. O. Okpala, M. O. Enemali, M. C. Okafor, E. L. Iloanya, C. B. Okeke, C. U. Ilo & J. J. Charles, ''Effect of Citrus aurantifolia juice on bodyweight and haematological indices of Wistar rats'', African Journal of Food Science **16** (2022) 151. https://doi.org/10.5897/ajfs2022.2175.

[43] B. Salehi, M. Gültekin-Özgüven, C. Kirkin, B. Özçelik, M. F. B. Morais-Braga, J. N. P. Carneiro & N. Martins, ''Antioxidant, antimicrobial, and anticancer effects of Anacardium plants: An ethnopharmacological perspective'', Frontier in Endocrinology **11** (2020) 295. https://doi.org/10.3389/fendo.2020.00295.

[44] L. A. Mtashobya, S. T. Mgeni & J. K. Emmanuel, ''Potential contributions of cashew apple juice to nutrition, medicine and bioethanol generation: An outlook'', Natural Product Communications **20** (2025) 1. https://doi.org/10.

1177/1934578X251357414.

[45] B. P. B. Rai, ''Nutritional value and health benefits of cashew nuts'', Journal of Food Science and Nutrition **11** (2025) 226. https://doi.org/10.24966/FSN-1076/100226.

[46] B. Gonçalves, T. Pinto, A. Aires, M. C. Morais, E. Bacelar, R. Anjos, J. Ferreira-Cardoso, I. Oliveira, A. Vilela & F. Cosme, ''Composition of nuts and their potential health benefits - An overview'', Foods **12** (2023) 942. https://doi.org/10.3390/foods12050942.

[47] O. P. Olatidoye, O. Akinlua & O. J. Folayan, ''Influence of roasting conditions on physicochemical and fatty acid profile of raw and roasted cashew kernel grown in Nigeria'', Journal of Culinary Science & Technology **18** (2020) 5. https://doi.org/10.31895/hcptbn.15.1-2.7.

[48] F. S. Codjia, D. S. Dabadé, P. Agbobatinkpo, I. Collombel, N. Achir, P. Azokpota & J. Dossou, ''Fermented cashew apple beverages: Current state of knowledge and prospects'', Beverages **11** (2025) 49. https://doi.org/10.3390/beverages11020049.

[49] Y. Y. Chen, N. Y. Li, X. Guo, H. J. Huang, P. Garcia-Oliveira, M. M. Zhao & L. R. Wen, ''The nutritional and bio-active constituents, functional activities, and industrial applications of cashew (Anacardium occidentale): A review'', Frontiers in Food Science and Technology **4** (2023) 1606. https://doi.org/10.1002/fft2.250.

[50] I. Ullah, S. Akhtar, M. Adnan, J. Nawab, S. Ullah & M. Abdullah-Al-Wadud, ''Ethnobotanical knowledge and ethnomedicinal uses of plant resources by urban communities of Khyber Pakhtunkhwa, Pakistan: a novel urban ethnobotanical approach'', Journal of Ethnobiology and Ethnomedicine **21** (2025) 13. https://doi.org/10.1186/s13002-025-00766-4.

[51] S. Soumahoro, M. L. Kouame, W. K. Yao, A. Toure & Y. R. Soro, ''Cashew apples: Physico-chemical analysis and occurrence of yeasts for processing into bioethanol'', World Journal of Biological Pharmaceutical and Health Sciences **17** (2024) 160. https://doi.org/10.30574/gscbps.2024.29.1.0362.

[52] D. P. B. Silva, I. F. Florentino, L. K. S. Moreira, P. M. Galdino, A. M. Menegocci, M. L. Rocha, B. G. Vaz, J. R. Sabino, L. M. Lião, H. D. Ferreira, T. F. S. Pavoni, J. R. de Paula, F. A. Vanderlinde & E. A. Costa, ''Anti-arthritic and safety pharmacological effects of gum extract from Anacardium occidentale in rats'', Revista Brasileira de Farmacognosia **31** (2021) 74. https://doi.org/10.1007/s43450-021-00135-8.

[53] N. Chaachouay & L. Zidane, ''Plant-derived natural products: a source for drug discovery and development'', Drugs Drug Candidates **3** (2024) 184. https://doi.org/10.3390/ddc3010011.

[54] L. K. Vora, A. D. Gholap, K. Jetha, R. R. S. Thakur, H. K. Solanki & V. P. Chavda, ''Artificial intelligence in pharmaceutical technology and drug delivery design'', Pharmaceutics **15** (2023) 1916. https://doi.org/10.3390/pharmaceutics15071916.

[55] M. Y. Putra, N. D. Yuliana, R. Firdaus, T. Murniasih, A. Evendi, I. R. Kartika, D. Ramadhani, U. M. Zuhri, J. T. Wibowo & B. Elya, ''Bridging bioassay-guided isolation and metabolomics: toward hybrid strategies in natural product drug discovery'', ChemRxiv (2025). https://doi.org/10.26434/chemrxiv-2025-h1pp9/v3.

[56] G. D'Urso, A. Capuano, F. Fantasma, M. G. Chini, V. De Felice, G. Saviano, G. Lauro, A. Casapullo, G. Bifulco & M. Iorizzi, ''The role of LC-MS in profiling bioactive compounds from plant waste for cosmetic applications: a general overview'', Plants (Basel) **14** (2025) 2284. https://doi.org/10.3390/plants14152284.

[57] B. Y. Vigbedor, J. Osei-Owusu, R. Kwakye & D. Neglo, ''Bioassay-guided fractionation, ESI-MS scan, phytochemical screening, and antiplasmodial activity of Afzelia Africana'', Biochemistry Research International (2022) 6895560. https://doi.org/10.1155/2022/6895560.

[58] S. Sun, Y. Yu, Y. Jo, J. H. Han, Y. Xue, M. Cho, S. J. Bae, D. Ryu, W. Park, K. T. Ha & S. Zhuang, ''Impact of extraction techniques on phytochemical composition and bioactivity of natural product mixtures'', Frontier in Pharmacology **16** (2025) 1615338. https://doi.org/10.3389/fphar.2025.1615338.

[59] A. Bender & I. Cortés-Ciriano, ''Artificial intelligence in drug discovery: what is realistic, what are illusions? Part 2: a discussion of chemical and biological data'', Drug Discovery Today **26** (2021) 1040. https://doi.org/10.1016/j.drudis.2020.11.037.

[60] A. H. Elmaidomy, U. R. Abdelmohsen, A. M. Sayed, F. H. Altemani, N. A. Algehainy, D. Soost, T. Paululat, G. Bringmann & E. M. Mohamed, ''Antiplasmodial potential of phytochemicals from Citrus aurantifolia peels: a comprehensive in vitro and in silico study'', BMC Chemistry **18** (2024) 60. https://doi.org/10.1186/s13065-024-01162-x.

[61] S. Ekambaram, P. Selvan & A. Arshad, ''Analysis of in vitro and in silico anti-hyperglycaemic action of bioflavonoids isolated from different Citrus peels'', Current Science **115** (2018) 1928. https://doi.org/10.18520/cs/v115/i10/1928-1937.

[62] S. Verma & R. Pathak, ''Discovery and optimisation of lead molecules in drug designing'', in *Drug discovery and development*, Elsevier, 2021, pp. 61–84. https://doi.org/10.1016/B978-0-323-89775-4.00004-3.

[63] D. R. Serrano, F. C. Luciano, B. J. Anaya, B. Ongoren, A. Kara, G. Molina, B. I. Ramirez, S. A. Sánchez-Guirales, J. A. Simon, G. Tomietto, C. Rapti, H. K. Ruiz, S. Rawat, D. Kumar & A. Lalatsa, ''Artificial intelligence (AI) applications in drug discovery and drug delivery: revolutionising personalised medicine'', Pharmaceutics **16** (2024) 1328. https://doi.org/10.3390/pharmaceutics16101328.

[64] R. Mai, Y. Li, J. Ren, G. Fan & J. Yang, ''Machine learning in the citrus essential oil industry: a comprehensive review on process optimisation, authentication, and flavor and bioactive compound development'', Trends in Food Science & Technology **165** (2025) 105347. https://doi.org/10.1016/j.tifs.2025.105347.

[65] R. Imran, M. A. U. Haq, Z. S. Amin, S. Sharma, S. Peerzeda, E. Mateev, H. M. Bilal, S. Bashir, K. S. Almaary, A. Irfan, M. Dauelbait & M. Bourhia, ''Standardisation of pharmacognostic characters and phytochemical study of Limeum obovatum vicary'', Scientific Reports **15** (2025) 1. https://doi.org/10.1038/s41598-025-94674-y.

[66] H. Nomura, R. Watanabe & K. Mizuguchi, ''The trends and future prospective of in silico models from the viewpoint of ADME evaluation in drug discovery'', Pharmaceutics **15** (2023) 2619. https://doi.org/10.3390/pharmaceutics15112619.

[67] R. Zhang, H. Wen, Z. Lin, B. Li & X. Zhou, ''Artificial intelligence-driven drug toxicity prediction: advances, challenges, and future directions'', Toxics **13** (2025) 525. https://doi.org/10.3390/toxics13070525.

[68] C. K. Adokoh, D. B. Asante, D. O. Acheampong, Y. Kotsuchibashi, F. A. Armah, I. H. Sirikyi, K. Kimura, E. Gmakame & S. Abdul-Rauf, ''Chemical profile and in vivo toxicity evaluation of unripe Citrus aurantifolia essential oil'', Toxicology Reports **6** (2019) 692. https://doi.org/10.1016/j.toxrep.2019.06.020.

[69] U. Shareef, A. Altaf, M. Ahmed, N. Akhtar, M. S. Almuhayawi, S. K. Al Jaouni, S. Selim, M. A. Abdelgawad & M. K. Nagshabandi, ''A comprehensive review of discovery and development of drugs discovered from 2020-2022'', Saudi Pharmaceutical Journal **32** (2024) 101913. https://doi.org/10.1016/j.jsps.2023.101913.

[70] Y. Choi, S. Kim, D. Kim, K. Park, M. Y. Lee & S. Cho, ''Regulatory safety evaluation of key lime (Citrus aurantiifolia) peel ethanol extract: Acute, 90-day repeated-dose, and genotoxicity studies'', Regulatory Toxicology and Pharmacology **165** (2025) 106005. https://doi.org/10.1016/j.yrtph.2025.106005.

[71] F. Idoko, G. Ezeamii & O. Ojochogwu, ''Green chemistry in manufacturing: Innovations in reducing environmental impact'', World Journal of Advanced Research and Reviews **23** (2024) 2826. https://doi.org/10.30574/wjarr.2024.23.3.2938.

[72] N. N. N. Kham, S. Phovisay, K. Unban, A. Kanpiengjai, C. Saenjum, S. Lumyong, K. Shetty & C. Khanongnuch, ''Valorisation of cashew apple waste into a low-alcohol, healthy drink using a co-culture'', Foods **13** (2024) 1469. https://doi.org/10.3390/foods13101469.

[73] T. G. Bas, ''Innovative formulation strategies for biosimilars: trends focused on buffer-free systems, safety, regulatory alignment, and intellectual property challenges'', Pharmaceuticals (Basel) **18** (2025) 908. https://doi.org/10.3390/ph18060908.

[74] E. D. Osei, A. Amotoe-Bondzie, A. Ataa Pokuah, W. S. Laar, N. A. Afoakwah & E. Ivanišová, ''Cashew apple pomace: Chemical composition and applications in functional food product development - a review'', Food Science & Nutrition **13** (2025) e70185. https://doi.org/10.1002/fsn3.70185.

[75] D. Dermawan & N. Alotaiq, ''From lab to clinic: How artificial intelligence (AI) is reshaping drug discovery timelines and industry outcomes'', Pharmaceuticals (Basel, Switzerland) **18** (2025) 981. https://doi.org/10.3390/ph18070981.