ISSN 1998 – 409X

REVIEW ARTICLE

Phytochemical Composition, Secondary Metabolites, and Pharmacological Potential of Tall Cultivars of *Cocos nucifera* L.: A Critical Review for Pharmaceutical Applications

N. Asha[1], S. Velmurugan[1], M. Anand[2], K. Vanitha[3], I. Johnson[4]

[1]Department of Spices and Plantation Crops, Horticultural College and Research Institute, Tamil Nadu Agricultural University, Coimbatore, Tamil Nadu, India, [2]Department of Food Process Engineering, Horticultural College and Research Institute, Tamil Nadu Agricultural University, Coimbatore, Tamil Nadu, India, [3]Department of Fruit Science, Horticultural College and Research Institute, Tamil Nadu Agricultural University, Coimbatore, Tamil Nadu, India, [4]Department of Millets, Horticultural College and Research Institute, Tamil Nadu Agricultural University, Coimbatore, Tamil Nadu, India

Abstract

The coconut palm *Cocos nucifera* L. is one of the most economically and medicinally important tropical plants on the globe, with tall cultivars being the most widespread and commercially exploited genetic group of the species. Although ample agronomic literature exists on the growth and productivity of this crop, more focus is needed on the pharmacological and pharmaceutical potential of tall coconut cultivars in the realm of pharmaceutical sciences. This review aims to discuss in detail the phytochemical composition, secondary metabolite profile and the medicinal properties that have been reported for different cultivars of *C. nucifera*, focusing on its importance in pharmaceutical drug discovery and development. A comprehensive literature search was conducted using PubMed, Scopus, Google Scholar, and Web of Science from 2010 to 2026. This review summarizes evidence that key tissue compartments of tall cultivars, including the endosperm, testa, shell, haustorium, inflorescence, and coconut water, are rich in medium-chain fatty acids (especially lauric acid), protocatechuic acid, kaempferol, terpenoids, and novel sesquineolignan compounds. *In vitro* and *in vivo* pharmacological activities substantiate remarkable antioxidant, anti-diabetic, anti-inflammatory, and antimicrobial properties among various tissue compartments. Molecular docking of key bioactive compounds derived from the plant against validated pharmaceutical targets such as α-glucosidase and kinase-associated pathways demonstrates an acceptable computational profile, warranting further preclinical studies. The review highlights key areas requiring standardized extraction protocols, bioavailability data, and further clinical validation, and suggests specific research directions to propel tall coconut cultivar-derived constituents toward well-designed drug discovery pipelines.

Key words: *Cocos nucifera*, drug discovery, medium-chain fatty acids, molecular docking, pharmacological activity, phytochemistry, tall cultivar

INTRODUCTION

The coconut palm, *Cocos nucifera* L. (Arecaceae), one of the most ancient and useful cultivated palms, has been documented for over 4000 years across tropical and subtropical regions.[1] There are two main morphological types, the tall and dwarf palms, and most of the cultivars cultivated in South and Southeast Asia, Pacific Islands, Caribbean, and sub-Saharan Africa belong to

Address for correspondence:
S. Velmurugan, Department of Spices and Plantation Crops, Horticultural College and Research Institute, Tamil Nadu Agricultural University, Coimbatore, Tamil Nadu, India.
E-mail: svelmurugan@tnau.ac.in

Received: 16-08-2026
Revised: 21-09-2026
Accepted: 28-09-2026

© 2026 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY 4.0)

the tall type.[2] Every part of the coconut fruit, including the exocarp, mesocarp, endosperm, testa, coconut water, and shell, contains unique classes of bioactive compounds that have been utilized for generations in African, Asian, and Caribbean traditional medicine systems.[1]

The pharmacognostic value of *C. nucifera* has been appreciated in the fields of Ayurvedic, Unani and African traditional medicine, and various medicinal preparations were used, derived from the coconut, for healing wounds, urinary complaints, intestinal infections, and metabolic diseases in earlier years.[3] Modern phytochemical studies bear out these ethnopharmacological uses, with a biochemical basis in the wide range of secondary metabolites produced by this plant. Subsequent systematic reviews have confirmed this understanding, with the nutritional and bioactive attributes of coconut palm fruit supporting its functional food and therapeutic applications across several disease areas.[4] In the pharmacognostic literature, in particular, tall cultivars have taken a relevant role due to their widespread geographical distribution, long productive period that can reach 80 years and a high accumulation of mass of pharmacologically active tissues during the productive period.[5]

The acquisition of pharmaceutical interest in plant compounds is one example of the worldwide appreciation that plants are, and will continue to be, an invaluable source of drug leads. Approximately 70–80% of the world's population relies on traditional medicines derived from plants for primary healthcare, and approximately 50% of approved anti-tumor drugs are inspired by natural products.[6] Cultivars of tall *C. nucifera* are strategically important in this context, as they contain chemically diverse secondary metabolites from a range of classes, including lipid-based compounds, polyphenolic compounds, and terpenoid compounds, and are also widely available around the world.[3] Nevertheless, even as the evidence of pharmacological activity increases, published literature is still scattered, each study being associated with a specific type of tissue or specific activity, and few reviews critically analyze this evidence in a pharmaceutical sciences context.

This review aims to fill this gap by thoroughly analyzing the phytochemical composition as well as pharmacological activities of tall cultivars of *C. nucifera*, based on original research papers from 2010 to 2026. The specific focus of the review is on the significance of the identified bioactive compounds for pharmaceutical use, the basis of evidence for the most important pharmacological activity, the rising significance of the molecular docking approach in target identification of coconut bioactive derivatives, pharmaceutical applications, and potential drug delivery systems for them. This review summarizes state-of-the-art evidence from various tissue compartments and cultivar types of the tall group and aims to develop concerted pathways to move coconut phytochemical constituents toward the preclinical and clinical research pipelines.

LITERATURE SEARCH STRATEGY

A comprehensive literature search was conducted to identify peer-reviewed publications relevant to the phytochemistry, pharmacology, and pharmaceutical applications of *C. nucifera* tall cultivars. Electronic databases searched included PubMed (MEDLINE), Scopus, Web of Science, and Google Scholar with searches conducted between June 2026 and August 2026. Search terms used included "*Cocos nucifera*," "coconut tall cultivar," "coconut phytochemistry," "coconut pharmacology," "coconut bioactive compounds," "coconut antioxidant," "coconut anti-diabetic," "coconut anti-inflammatory," "coconut antimicrobial," "coconut molecular docking," "coconut drug discovery," "coconut fatty acids," "coconut phenolics," "coconut testa," "coconut shell secondary metabolites" and "coconut pharmaceutical applications," applied individually and in combination. Inclusion criteria comprised original research articles, systematic reviews, and comprehensive review articles published in English between 2010 and 2026. Eligible studies reported phytochemical data, pharmacological activity data, or pharmaceutical applications of *C. nucifera* with specific relevance to tall cultivar tissues, pharmacological characterization or drug discovery contexts. Studies focused exclusively on agronomy, plant breeding, crop improvement, or non-pharmacological agronomic traits were excluded from the study. A total of 34 references meeting these criteria were included in the final synthesis.

BOTANICAL DESCRIPTION AND ETHNOPHARMACOLOGICAL SIGNIFICANCE

C. nucifera tall cultivars are monoecious, allogamous palms that typically reach mature heights of 20–30 m, with a productive lifespan of >60 years. The fruit is botanically a drupe with three anatomical regions, namely, a smooth, thin exocarp; a fibrous, thick mesocarp, or husk; and a hard, lignified endocarp or shell, inside of which an edible endosperm is present, comprising the nutritive coconut water and testa.[2] Tall cultivars have characterized reproductive biology, with the male and female flowers occurring at different times on the same spadix, which leads to protandrous inflorescence and allows outcrossing and genetic diversification within and between populations.[7] This morphological and reproductive complexity is pharmacognostically relevant as it results in tissue-specific secondary metabolite profiles, which vary widely within anatomical compartments, within different developmental stages and between tall accessions from different geographical origins.

The genetic complexity of the diversity within tall cultivars has been verified by genomic characterization, including the sequencing of the Hainan Tall genome, and has resulted in the finding of a molecular basis for the variation in secondary

metabolite profiles observed across different accessions of tall cultivars.[8] Tall cultivars such as West Coast Tall, Sri Lanka Tall, Hainan Tall, and Mexican Pacific Tall have been targets of phytochemical studies and showed significant differences in bioactive compound content for various tissues.[9]

Ethnopharmacologically, coconut is in a central position in the traditional medicine systems of the areas where tall cultivars are located. Coconut oil extracted from the endosperm is used in South Asian traditional medicine as a base for medicinal oils and ointments, and coconut water as a rehydrating agent, a diuretic and an anthelmintic.[1] The shell has been utilized in West African traditional medicine to make charcoal-based medicines for gastrointestinal troubles, while the husk fiber has been used topically for skin troubles.[9] Coconut inflorescence sap is used throughout the Pacific Islands as food for its alleged hypoglycemic and anti-inflammatory properties, whereas the testa has been used in preparations for inflammatory diseases.[5] The overall diversity of ethnopharmacological uses offers a solid justification for systematic pharmacological studies of cultivar-derived bioactives with a view to identifying the tissue-specific bioactive profiles of tall cultivars that may be relevant to the initiation of therapeutic pathways in available disease categories, consistent with the current priorities of the pharmaceutical sector.

PHYTOCHEMICAL COMPOSITION OF TALL COCONUT CULTIVARS

Fatty acid profile and lipid-based constituents

The lipid fraction of coconut endosperm from tall cultivars constitutes the most extensively characterized class of bioactive constituents. The fatty acid profile of tall cultivar endosperm is dominated by medium-chain fatty acids (MCFAs), which collectively account for approximately 85% of total fatty acid content.[10] Lauric acid (C12:0) is the most abundant individual fatty acid, typically representing 47–50% of total fatty acids in mature endosperm of tall cultivars, followed by myristic acid (C14:0) at approximately 17%, capric acid (C10:0) at approximately 6–7%, and caprylic acid (C8:0) at approximately 5–6%.[10] This MCFA-rich composition is of direct pharmaceutical relevance because MCFAs, unlike long-chain fatty acids, are absorbed directly through the portal circulation without requiring chylomicron formation, enabling rapid metabolic utilization and potent antimicrobial activity through disruption of microbial membrane integrity at physiologically relevant concentrations.[11]

The coconut sap collected from tall cultivar inflorescences presents a nutritionally and phytochemically distinct profile from the endosperm, characterized by lower lipid content but significant concentrations of sucrose, glucose, and fructose alongside minerals and amino acids that collectively define its nutraceutical and pharmaceutical utility.[11] Comparative studies of fatty acid profiles across tender and mature coconut tissues have further demonstrated that the ratio of unsaturated to saturated fatty acids shifts with tissue maturity, with mature endosperm accumulating progressively higher proportions of saturated MCFAs, while tender coconut tissues retain relatively higher proportions of unsaturated fatty acids.[12] This maturity-dependent compositional shift carries direct implications for both pharmaceutical formulation, where the degree of saturation influences lipid excipient behavior, and for nutraceutical applications, where specific fatty acid ratios are targeted for therapeutic benefit.

Coconut water from tall cultivars represents a phytochemically distinct fraction. Studies conducted across multiple maturity stages demonstrate that coconut water composition changes significantly during fruit development, with total soluble solids, sugar concentrations, and amino acid profiles peaking at intermediate maturity stages and declining in over-mature fruits.[13] The physicochemical properties of coconut water, including pH, electrical conductivity, and osmolarity, also vary with cultivar type and environmental conditions, parameters of direct relevance to its application as a natural electrolyte base in pharmaceutical and nutraceutical formulations.[14]

Phenolic compounds, flavonoids, and terpenoids

The polyphenolic fraction of tall coconut cultivars, distributed across testa, shell, haustorium, and inflorescence tissues, encompasses a structurally diverse array of pharmacologically active compounds. Phenolic profiling of coconut haustorium tissue has identified protocatechuic acid, gallic acid, caffeic acid, quercetin, kaempferol, and various terpenoid compounds, with concentrations varying significantly by tissue maturity and extraction method.[15] The testa of tall cultivar coconuts has been identified as particularly rich in phenolic compounds, with reported values of protocatechuic acid reaching up to 34,015 µg/g dry weight and kaempferol reaching up to 9,271 µg/g in certain tall accessions, values that place coconut testa among the most phenolic-rich byproducts of the coconut processing industry globally.[16] This remarkable phenolic concentration in a tissue that is routinely discarded during coconut processing represents both an opportunity for pharmaceutical raw material valorization and a critical argument for the systematic bioactivity-guided fractionation of coconut testa extracts.

The shell of tall cultivar coconuts, similarly discarded as an agricultural waste product at industrial scale, has been demonstrated to harbor a range of bioactive secondary metabolites including tannins, lignins, flavonoids, and phenolic acids with documented antioxidant and antimicrobial properties.[17] The pharmacological characterization of coconut shell constituents carries significant implications for the pharmaceutical valorization of coconut processing

waste streams, identifying a high-volume byproduct as a potential source of standardizable bioactive raw materials suitable for extraction and incorporation into pharmaceutical preparations.

Table 1 summarizes the major phytochemical constituents identified across key tissue compartments of tall *C. nucifera* cultivars, along with their primary pharmacological activities as documented in the current literature.

Novel bioactive compounds

Beyond the well-characterized phenolic and lipid fractions, recent investigations have identified structurally novel secondary metabolites in tall coconut cultivars that meaningfully expand the pharmacological relevance of the species. Elsbaey *et al*. isolated and characterized *nuciferol C*, a novel sesquineolignan dimer from *C. nucifera*, and demonstrated its bioactivity through *in vitro* assays alongside theoretical investigation using computational chemistry methods.[20] This discovery is particularly significant because sesquineolignans represent a structurally distinct class of plant metabolites with documented bioactivity across cytotoxic, antioxidant and anti-inflammatory endpoints in other plant sources, and their identification in coconut opens previously unexplored avenues for the pharmacognostic investigation of tall cultivar tissues using advanced isolation and dereplication techniques.

SECONDARY METABOLITES AND THEIR PHARMACOLOGICAL BASIS

The secondary metabolite diversity of tall *C. nucifera* cultivars extends beyond individual compound classes to encompass complex interactions between lipid-based, polyphenolic, and terpenoid fractions that collectively underpin the documented pharmacological activities of the plant. Transcriptomic investigations of coconut tissues using RNA sequencing approaches have identified the genetic regulatory networks controlling secondary metabolite biosynthesis, including genes encoding enzymes in the phenylpropanoid and fatty acid biosynthesis pathways, providing a mechanistic basis for understanding how phytochemical composition varies across tissue types, maturity stages, and cultivar accessions.[21] This genomic evidence is critical for pharmaceutical purposes because it demonstrates that the observed variation in secondary metabolite profiles across tall cultivar accessions is genetically regulated rather than purely environmentally driven, implying that cultivar selection can be used as a tool for optimizing the pharmaceutical-grade phytochemical yield of raw material collections.

Proteomic profiling of coconut endosperm has further elucidated the enzyme complement involved in lipid and secondary metabolite accumulation, demonstrating that tall cultivar endosperm expresses a distinct proteome compared to dwarf cultivars that reflect its specific metabolic priorities in fatty acid synthesis and storage protein accumulation.[22] Metabolomic studies of aromatic coconut varieties, which represent a subset of the tall group characterized by their distinctive fragrance profile, have identified a range of volatile and non-volatile secondary metabolites including specific phenolic glycosides and terpenoid compounds not detected in standard tall accessions, suggesting that aromatic tall cultivars may represent a pharmacognostically valuable subgroup warranting dedicated phytochemical investigation.[23] Critically, the chemical distinctiveness of aromatic tall cultivars from standard tall accessions implies that metabolomic profiling of diverse tall accessions is necessary before any representative phytochemical characterization of the group can be considered complete.

Proteomic analysis of zygotic embryos from *C. nucifera* has additionally identified stress-response proteins and enzyme systems with potential biotechnological applications, demonstrating that embryo tissue, rarely considered in

Table 1: Major phytochemical constituents of tall *Cocos nucifera* cultivars by tissue compartment and their documented pharmacological activities

Tissue	Major phytochemical constituents	Primary pharmacological activity	References
Endosperm (oil)	Lauric acid, myristic acid, capric acid, and caprylic acid	Antimicrobial, anti-inflammatory, and antioxidant	[10,12]
Coconut water	Sugars, amino acids, cytokinins, phenolics, and minerals	Antioxidant, anti-diabetic, and antilipidemic	[13,14]
Testa	Protocatechuic acid, kaempferol, epicatechin, and gallic acid	Antioxidant, anti-inflammatory, and anti-diabetic	[16]
Shell	Tannins, lignins, phenolic acids, and flavonoids	Antioxidant and antimicrobial	[17]
Haustorium	Quercetin, protocatechuic acid, and terpenoids	Antioxidant and anti-inflammatory	[15]
Inflorescence sap	Sucrose, glucose, flavonoids, and phenolics	Anti-diabetic and anti-inflammatory	[11,18]
Flower	Phenolics, flavonoids, and cytotoxic compounds	Antioxidant, anthelmintic, and anti-diabetic	[19]

conventional phytochemical surveys, may contribute bioactive proteins with pharmaceutical relevance that have thus far been overlooked in the literature.[24] Metabolomic and transcriptomic analysis of female flower development in coconut has identified stage-specific accumulation of flavonoids and phenolic precursors that peak at early developmental stages, a finding with practical implications for optimizing harvest timing in pharmaceutical raw material collection and for identifying the developmental windows of maximum secondary metabolite accumulation in floral tissues.[25]

PHARMACOLOGICAL ACTIVITIES

Antioxidant activity

The antioxidant activity of tall *C. nucifera* cultivar-derived materials has been documented across multiple tissue types and extraction systems, with results demonstrating both direct radical scavenging capacity and indirect antioxidant mechanisms operating through enzyme modulation pathways. Protein fractions extracted from coconut endosperm have demonstrated significant antioxidant activity in 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) and ferric reducing antioxidant power assays, with hydrolyzate fractions showing particularly high activity attributable to the release of bioactive peptides with intrinsic radical-scavenging capacity during enzymatic hydrolysis.[26] This finding is pharmacologically important because it identifies coconut endosperm protein hydrolysates as a category of bioactives distinct from the better-characterized lipid and phenolic fractions, and one with structural properties amenable to further characterization and potential incorporation into peptide-based nutraceutical formulations.

The antioxidant potential of coconut water from tall cultivars has been investigated using metabolomic profiling of Thai coconut varieties representing both traditional and breeding accessions, with DPPH radical scavenging activity ranging from 51% to 55% across all tested varieties and 27 distinct metabolites, including gallic acid, caffeic acid, and quercetin, identified as contributors to this antioxidant capacity.[27] Critically, the study demonstrated that breeding-variety coconut water preparations contained higher concentrations of antioxidant metabolites compared to traditional varieties, an important discriminating observation for pharmaceutical raw material sourcing that suggests breeding-program accessions may be preferable for consistent high-yield antioxidant raw material production. At the mechanistic level, coconut water from tall cultivar accessions has been shown to promote glucose uptake and modulate antioxidative enzyme activities in muscle and hepatic tissue models, with effects attributed to the synergistic action of phenolic constituents on reactive oxygen species generation and catabolic enzyme inhibition.[28] This dual action combining direct radical scavenging with indirect antioxidant enzyme modulation characterizes coconut water as a pharmacologically complex antioxidant matrix rather than a simple radical scavenger, and supports its investigation as a dietary supplement adjunct in oxidative stress-related conditions.

Anti-diabetic and antilipidemic activity

The anti-diabetic pharmacological profile of tall coconut cultivar extracts has been investigated across several tissue types including endocarp, inflorescence, and coconut water, with results demonstrating multiple mechanisms of glycemic modulation that collectively define a multi-target anti-diabetic pharmacological profile. Extracts of *C. nucifera* endocarp demonstrated significant anti-diabetic and antilipidemic effects in a streptozotocin-induced diabetic rat model, with treated animals showing improvements in fasting blood glucose, serum triglycerides, total cholesterol and low-density lipoprotein cholesterol levels, and histopathological examination revealing partial restoration of pancreatic beta-cell architecture in treated groups compared to diabetic controls.[29] These findings are particularly noteworthy because the concurrent improvement in both glycemic and lipidemic parameters suggests that coconut endocarp extracts may address multiple components of the metabolic syndrome, a multi-factorial condition for which single-target pharmacological approaches have frequently shown limited clinical efficacy.

Pharmacological investigation of *C. nucifera* flower material identified significant α-glucosidase inhibitory activity alongside antioxidant and anthelmintic activities, with the reported inhibitory activity at a level warranting direct comparison with reference standard inhibitors in validated assay systems.[19] α-glucosidase inhibition is a validated anti-diabetic therapeutic mechanism, and the identification of this activity in coconut flower material expands the tissue-specific pharmacological profile of tall cultivars beyond the more commonly investigated endosperm and water fractions into floral tissues not previously associated with anti-diabetic applications.

Anti-diabetic and anti-inflammatory activities have also been documented in parallel for *C. nucifera* inflorescence extracts. Vinod and Rani demonstrated that ethanolic and aqueous fractions of coconut inflorescence exhibited significant inhibition of carrageenan-induced paw edema in rat models alongside meaningful reductions in blood glucose in alloxan-induced diabetic rats, with the ethanolic fraction demonstrating superior activity in both assay systems attributable to its higher phenolic and flavonoid content as quantified by spectrophotometric analysis.[18] This parallel anti-diabetic and anti-inflammatory activity in the same tissue fraction is particularly relevant from a pharmaceutical standpoint because type 2 diabetes is characterized by chronic

low-grade systemic inflammation, and compounds that address both pathways simultaneously may offer therapeutic advantages over single-target agents in the management of this condition.

Anti-inflammatory activity

The anti-inflammatory activity of tall coconut cultivar extracts is mechanistically linked to their polyphenolic constituent profile, particularly the documented capacity of phenolic acids, flavonoids, and terpenoids identified in testa, shell, and inflorescence tissues to inhibit pro-inflammatory mediators and modulate inflammatory signaling cascades.[18] The MCFA fraction of coconut oil has also been implicated in anti-inflammatory mechanisms through modulation of eicosanoid biosynthesis and reduction of lipopolysaccharide-induced inflammatory signaling, pathways with well-established relevance to both acute and chronic inflammatory conditions.[5] The multifactorial nature of coconut-derived anti-inflammatory activity, combining lipid-based and polyphenolic mechanisms operating through distinct molecular targets, positions tall cultivar extracts as complex anti-inflammatory matrices amenable to bioactivity-guided fractionation approaches aimed at isolating the most potent and pharmacologically selective anti-inflammatory constituents for further development.

Antimicrobial activity

Antimicrobial activity has been documented for coconut water from tall cultivars against both Gram-positive and Gram-negative bacterial pathogens and against fungal organisms. Phytochemical screening of coconut water confirmed the presence of flavonoids, tannins, saponins, and alkaloids as constituents contributing to antimicrobial activity, and zone of inhibition measurements against *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae,* and *Candida albicans* confirmed significant inhibitory activity across all tested organisms.[30] The antimicrobial activity of coconut-derived constituents is mechanistically supported by the well-established membrane-disrupting properties of lauric acid and its monoglyceride derivative monolaurin, which have demonstrated potent *in vitro* activity against enveloped viruses, Gram-positive bacteria and certain Gram-negative organisms by disrupting lipid bilayer integrity at the microbial cell membrane, a mechanism that is concentration-dependent and structurally specific to medium-chain saturated fatty acids.[10] The convergence of phenolic-based and MCFA-based antimicrobial mechanisms in the same plant material provides a strong rationale for investigating synergistic antimicrobial formulations incorporating standardized coconut-derived fractions as components of novel antimicrobial preparations.

MOLECULAR DOCKING STUDIES AND TARGET IDENTIFICATION

Molecular docking studies of phytochemicals derived from *C. nucifera* against validated pharmaceutical targets have provided quantitative computational evidence supporting the pharmacological activities documented in experimental assays. Natural product-based drug discovery programs have increasingly employed molecular docking as a primary *in silico* screening tool, with validated docking platforms including AutoDock Vina, GOLD, Glide, and Discovery Studio providing reliable binding energy predictions for phytochemical interactions with protein targets across therapeutic areas.[31] As shown in Table 2, computational analyses of coconut-derived bioactives against relevant pharmaceutical targets have generated preliminary evidence supporting the identification of priority compound-target pairs for further validation.

Nutraceutical phytochemicals with structural profiles comparable to those identified in coconut tissues have been

Table 2: Summary of molecular docking and computational studies on *Cocos nucifera* tall cultivar bioactives

Bioactive compound or study	Computational approach	Target or endpoint	Key outcome	References
Nuciferol C and structural analogues	Theoretical *in silico* investigation	Multiple bioactivity targets	Novel bioactivity confirmed computationally	[20]
Nutraceutical phenolics including coconut-derived	AutoDock and related platforms	Disease-relevant protein targets	Binding affinity data generated for nutraceutical leads	[32]
Natural product phytochemicals	AutoDock Vina, GOLD, Glide, Discovery Studio	Multiple pharmaceutical targets	Docking frameworks validated for natural product leads	[31]
Coconut endosperm regulators	ATAC-seq[a] chromatin accessibility	Transcription factor targets	Regulatory networks governing secondary metabolite accumulation mapped	[33]
Broad phytochemical drug discovery	Multiple *in silico* platforms	Validated drug targets across disease areas	Phytochemical-to-drug translation pathway established	[6]

[a]ATAC-seq: Assay for transposase-accessible chromatin with sequencing

comprehensively assessed through large-scale molecular docking exercises against disease-relevant targets including kinases, glucosidases, and inflammatory pathway proteins, establishing a methodological framework that is directly applicable to the systematic *in silico* screening of coconut bioactive libraries.[32] The discovery of nuciferol C, a structurally novel sesquineolignan from *C. nucifera*, was accompanied by theoretical computational investigation demonstrating bioactivity potential for this compound class, representing the first application of molecular docking specifically to a newly identified coconut-derived compound and establishing a precedent for computational-guided investigation of coconut secondary metabolites.[20] Transcriptomic and chromatin accessibility analyses of coconut endosperm tissue have simultaneously identified the transcription factor networks governing secondary metabolite accumulation, providing a genomic basis for understanding which cultivar accessions may be most productive for pharmaceutical raw material yields and for targeting biosynthetic engineering approaches to enhance the accumulation of pharmaceutically desirable compounds.[33] The broader significance of molecular docking for phytochemical drug discovery has been comprehensively reviewed in recent literature, documenting that natural product-derived and natural product-inspired compounds continue to contribute meaningfully to approved drug pipelines, with six of 53 US Food and Drug Administration-approved drugs in 2023 inspired by natural product structures.[6] This continued contribution underscores the pharmaceutical relevance of systematic *in silico* investigation of the *C. nucifera* bioactive library through molecular docking and identifies it as an essential component of any structured drug discovery program targeting tall cultivar-derived constituents.

PHARMACEUTICAL APPLICATIONS AND DRUG DELIVERY PROSPECTS

The diverse phytochemical profile of tall *C. nucifera* cultivars supports multiple potential pharmaceutical applications spanning drug formulation, nutraceutical development, and cosmeceutical applications. Coconut water has been explored beyond its traditional beverage applications as a pharmaceutical excipient, an isotonic carrier for oral drug delivery and a potential component of wound care formulations due to its unique combination of electrolytes, cytokinins, and antimicrobial phenolics.[34] The comprehensive documentation of coconut water's versatility across health applications, including its rehydration efficacy, cytokinin-driven potential in cell proliferation contexts and antioxidant capacity, establishes a multi-functional profile that supports its investigation as a multi-component pharmaceutical matrix rather than a single-ingredient nutraceutical.[34]

The MCFA fraction of coconut oil from tall cultivars has attracted particular attention in pharmaceutical formulation science as a penetration enhancer, a lipid-based drug delivery vehicle, and an antimicrobial excipient. Lauric acid and its derivatives are recognized pharmaceutical excipients that enhance the transdermal and mucosal permeation of co-administered drugs by fluidizing lipid bilayer membranes, a property of direct relevance to topical and transmucosal formulation development for drugs with limited skin penetration.[5] The potential of coconut-derived lipid fractions as vehicles in self-emulsifying drug delivery systems, solid lipid nanoparticles, and phytosome complexes represents an underexplored but pharmacologically rational research frontier that merits systematic investigation through pharmaceutical preformulation studies.

The documented activity of coconut water in modulating longevity-associated molecular pathways provides an additional and clinically relevant dimension to its pharmaceutical application profile. Na Nakorn *et al*. demonstrated that coconut water decreased mechanistic target of rapamycin and protein kinase B protein expression while increasing AMP-activated protein kinase, forkhead box O3, and sirtuin 6 activity in human dermal fibroblast models, a pattern of molecular changes associated with cellular longevity and resistance to oxidative senescence.[27] This pharmacological profile, intersecting antioxidant, anti-inflammatory, and longevity-pathway modulation at the molecular level, positions tall cultivar coconut water as a scientifically substantiated candidate for cosmeceutical and nutraceutical formulations targeting skin ageing and cellular senescence, applications where the demand for evidence-based plant-derived actives is currently high and the regulatory pathway is well established.

TOXICOLOGICAL PROFILE AND SAFETY ASSESSMENT

A critical evaluation of the pharmacological potential of tall *C. nucifera* cultivar-derived materials requires parallel consideration of their toxicological profile and safety margins, without which pharmacological promise cannot be translated into pharmaceutical development. The long history of dietary and traditional medicinal use of coconut across tropical populations provides an empirical basis for assessing the general safety of coconut-derived preparations in commonly consumed forms, though formal preclinical toxicological characterization of specific fractions and isolated compounds remains incomplete for many tissue compartments.[1]

Coconut oil and its MCFA constituents have been the subject of safety assessments in both animal models and clinical settings, with studies generally demonstrating acceptable safety profiles at dietary and supplemental intake levels in healthy human populations. Cytotoxicity assessments of *C. nucifera* flower extracts demonstrated selective cytotoxicity against cancer cell lines with comparatively lower toxicity toward normal cell models, a selectivity index suggestive of a potentially useful therapeutic window for

further investigation of the cytotoxic fraction in oncological contexts.[19] For coconut water, the anti-diabetic rat model studies by Akter *et al*. demonstrated that endocarp extract administration at tested doses did not produce significant hepatotoxic or nephrotoxic markers in treated animals, supporting the safety of this fraction at pharmacologically active doses within the tested animal model parameters.[29]

However, it must be critically acknowledged that the current toxicological evidence base for specific isolated phytochemical constituents of tall coconut cultivars is largely confined to *in vitro* cell viability assays and short-duration rodent model studies with limited dose-range investigation. Clinical safety data for standardized coconut-derived pharmaceutical preparations are essentially absent, and the translation of ethnopharmacological safety assumptions into pharmaceutical product development requires rigorous formal toxicological characterization encompassing genotoxicity, reproductive toxicity and chronic systemic toxicity studies conducted according to current regulatory guidelines. The heterogeneity of extraction methods, solvent systems, and test organisms reported across the reviewed literature also substantially limits direct comparability of safety assessments between studies, a methodological gap that itself represents a research priority requiring the establishment of standardized assay conditions.

RESEARCH GAPS AND FUTURE DIRECTIONS

A critical synthesis of the available evidence reveals several significant and interrelated research gaps that currently limit the advancement of tall *C. nucifera* cultivar-derived constituents toward pharmaceutical development. First, the absence of standardized extraction and phytochemical characterization protocols across published studies creates substantial methodological heterogeneity in reported bioactive values, making it difficult to establish reliable reference ranges for quality-controlled pharmaceutical raw material production. The development of validated analytical methods based on high-performance liquid chromatography coupled with mass spectrometry for key tall cultivar bioactive constituents, including protocatechuic acid, kaempferol, and lauric acid, is an essential and immediate research priority before pharmaceutical-grade specifications can be established.

Second, the bioavailability and pharmacokinetic profiles of key isolated constituents from tall coconut cultivars remain largely uninvestigated in physiologically relevant models. While *in vitro* pharmacological data are accumulating for phenolics, flavonoids, and MCFAs, the oral bioavailability, systemic distribution, metabolic fate, and excretion profiles of these compounds in human subjects are essentially unknown, a critical deficit that must be systematically addressed before clinical development can progress. Phytosome complexation and nanoparticle-based delivery systems offer potential solutions to the well-documented bioavailability limitations of polyphenolic compounds, and their application to coconut testa phenolics in particular warrants systematic investigation through *in vitro* permeation models and *in vivo* pharmacokinetic studies.

Third, the remarkable secondary metabolite diversity across tall cultivar accessions, as evidenced by differential metabolomic profiles reported across Hainan Tall, West Coast Tall, and aromatic tall varieties, strongly suggests that cultivar-specific phytochemical profiling should become a standard component of pharmacognostic investigations rather than an optional supplement to generalized "coconut" phytochemical studies.[8,23] Cultivar selection for pharmaceutical raw material production should be guided by systematic comparative phytochemical data derived from well-curated germplasm collections rather than by agronomy-driven material availability.

Fourth, the molecular docking evidence reviewed in this paper identifies α-glucosidase, kinase-associated pathways, and inflammatory mediator targets for coconut-derived bioactives, but formal target validation through enzymatic assays, cellular target engagement studies, and receptor binding experiments remains to be completed for most identified candidate compounds. The novel sesquiterpene lignan nuciferol C and the MCFA monolaurin represent particularly underinvestigated candidates that merit targeted pharmacological characterization through structure-activity relationship studies and advanced *in silico* modeling, including molecular dynamics simulation and absorption, distribution, metabolism, excretion, and toxicity property prediction.[20]

Finally, there is a complete absence of clinical trial data investigating any standardized *C. nucifera* tall cultivar-derived preparation for any pharmacological endpoint in human subjects. The translation of promising preclinical data into structured phase I and phase II clinical investigations, particularly for the anti-diabetic and antioxidant applications most robustly supported by the current evidence base, represents the single most critical research gap in the field and the step most necessary for establishing scientific credibility for tall coconut cultivar-derived pharmaceuticals within the regulatory and clinical communities.

CONCLUSION

The review has critically synthesized the available evidence on the phytochemical composition, secondary metabolite profile, and pharmacological potential of tall *C. nucifera* cultivars, demonstrating that these palms represent a pharmacognostically rich and pharmacologically versatile source of bioactive compounds with clear relevance to pharmaceutical drug

discovery and development. The unique MCFA-rich lipid fraction centered on lauric acid, the diverse polyphenolic profile concentrated in testa, shell, and haustorium tissues and the novel sesquineolignan compounds identified in recent investigations collectively define a chemically complex matrix with documented antioxidant, anti-diabetic, anti-inflammatory, and antimicrobial activities supported by *in vitro*, *in vivo,* and computational evidence. Computational investigation of coconut-derived phenolics against relevant pharmaceutical targets reveals promising *in silico* profiles that support the prioritization of specific compound-target combinations in future drug discovery programs.

The review also highlights the substantial limitations of the current evidence base, particularly the fragmented and methodologically heterogeneous phytochemical literature, the near-complete absence of clinical data, and the lack of systematic bioavailability characterization for key isolated constituents. Addressing these gaps through standardized phytochemical profiling across tall cultivar accessions, rigorous pharmacokinetic characterization of priority compounds, advanced drug delivery system development for polyphenolic constituents, and well-designed clinical investigations represents the research agenda necessary to realize the full pharmaceutical potential of tall *C. nucifera* cultivars. The convergence of traditional ethnopharmacological evidence, contemporary phytochemical data, and emerging computational pharmacology approaches provides a strong and scientifically grounded foundation on which this research agenda can be comprehensively built and advanced.

REFERENCES

1. Nampoothiri KU, Naik M, Lal MT, editors. The Coconut Palm (*Cocos nucifera* L.) - Research and Development Perspectives. Singapore: Springer; 2018.
2. Beveridge FC, Kalaipandian S, Yang C, Adkins SW. Fruit biology of coconut (*Cocos nucifera L.*). Plants (Basel) 2022;11:3293.
3. Roopan SM. An overview on biological and medicinal importance of *Cocos nucifera*. Appl Biochem Biotechnol 2016;179:1309-24.
4. Yuktha SK, Hegde K. The science of *Cocos nucifera*: Insights into its nutritional and medicinal applications. Int J Pharm Sci 2025;3:261-70.
5. Vatakkeel B, Mythreyi R, Siju EN. *Cocos nucifera* Linn.: A promising candidate for drug development. J Nat Remedies 2024;24:28-35.
6. Chihomvu P, Ganesan A, Gibbons S, Woollard K, Hayes MA. Phytochemicals in drug discovery-a confluence of tradition and innovation. Int J Mol Sci 2024;25:8792.
7. Perera PI, Perera L, Hocher V, Verdeil JL, Yakandawala DM. Inflorescence development in coconut (*Cocos nucifera* L.). S Afr J Bot 2010;76:482-92.
8. Xiao Y, Xu P, Fan H, Baudouin L, Xia W, Wu Y, *et al*. The genome draft of coconut (*Cocos nucifera*). GigaScience 2017;6:1-11.
9. Ajibola OO. Nutritional composition and bioactive properties of tropical coconut palm fruit with functional food applications. Discov Food 2026;6:21.
10. Reynolds KB, Cullerne DP, El Tahchy A, Rolland V, Blanchard CL, Wood CC, *et al*. Identification of genes involved in lipid biosynthesis through de novo transcriptome assembly from *Cocos nucifera* developing endosperm. Plant Cell Physiol 2019;60:945-60.
11. Asghar MT, Yusof YA, Mokhtar MN, Ya'acob ME, Mohd Ghazali H, Chang LS, *et al*. Coconut (*Cocos nucifera* L.) sap as a potential source of sugar: Antioxidant and nutritional properties. Food Sci Nutr 2020;8:1777-87.
12. Jiang R, Xue D, Chen Y, Lv X, Ni L, Liu Z. Comparative study of the fatty acid and phenolic profiles of tender and mature coconut for coconut milk production. Foods 2025;14:4023.
13. Zhang Y, Li X, Liu X, Kan J, Song F, Zhu K, *et al*. Chemical components, nutritional value, volatile organic compounds and biological activities in vitro of coconut (*Cocos nucifera* L.) water with different maturities. Foods 2024;13:863.
14. Hamilton PD, Charles KT, Loh AM, Loïc NN, Germain K, Elie F. Physicochemical, nutritional, antioxidant properties and stability monitoring of coconut (*Cocos nucifera* L.) water from two localities in Cameroon. Heliyon 2024;10:e40712.
15. Kim RH, Lee SJ, Lee K, Hwang KT, Kim J. Profiling of phenolic acids, flavonoids, terpenoids, and steroid derivatives in coconut (*Cocos nucifera* L.) haustorium. Food Sci Biotechnol 2023;32:1841-50.
16. Ramesh SV, Pandiselvam R, Shameena Beegum PP, Saravana Kumar RM, Manikantan MR, Hebbar KB. Review of *Cocos nucifera* L. testa-derived phytonutrients with special reference to phenolics and its potential for encapsulation. J Food Sci Technol 2023;60:1-10.
17. Sreekala V, Kumar SS, Parvathy S, Arun KB. Bioactive secondary metabolites from coconut (*Cocos nucifera* L.) shell. Anc Sci Life 2024;38:93-100.
18. Vinod NP, Rani DJ. Anti inflammatory and anti diabetic activity of *Cocos nucifera* inflorescence. Int J Clin Exp Med Sci 2024;10:11-6.
19. Aktar MJ, Hossain N, Akter J, Siddiq MM, Kuddus MR, Rashid MA, *et al*. Pharmacological potential of *Cocos nucifera* L. Flowers: Phytochemical, cytotoxic, antioxidant, anthelmintic and anti-diabetic insights. Asian J Biol Sci 2026;19:40-50.
20. Elsbaey M, Igarashi Y, Alnajjar R, Darwish KM, Miyamoto T. Nuciferol C, a new sesquineolignan dimer from *Cocos nucifera* L.: Bioactivity and theoretical investigation. RSC Adv 2024;14:25900-7.
21. Fan H, Xiao Y, Yang Y, Xia W, Mason AS, Xia Z, *et al*. RNA-Seq analysis of *Cocos nucifera*: Transcriptome sequencing and *de novo* assembly for subsequent functional genomics approaches. PLoS One 2013;8:e59997.

22. Félix JW, Granados-Alegría MI, Gómez-Tah R, Tzec-Simá M, Ruíz-May E, Canto-Canché B, *et al*. Proteome landscape during ripening of solid endosperm from two different coconut cultivars reveals contrasting carbohydrate and fatty acid metabolic pathway modulation. Int J Mol Sci 2023;24:10431.
23. Zhou L, Sun X, Yarra R, Iqbal A, Wu Q, Li J, *et al*. Combined transcriptome and metabolome analysis of sugar and fatty acid of aromatic coconut and non-aromatic coconut in China. Food Chem Mol Sci 2024;8:100190.
24. Granados-Alegría MI, Canto-Canché B, Gómez-Tah R, Félix JW, Tzec-Simá M, Ruiz-May E, *et al*. Proteomic profiling of *Cocos nucifera* L. Zygotic embryos during maturation of dwarf and tall cultivars: The dynamics of carbohydrate and fatty acid metabolism. Int J Mol Sci 2024;25:8507.
25. Lu L, Zhang Y, Dong Z, Yang W, Yu R. Integrated metabolomic and transcriptomic profiles provide insights into the molecular mechanisms in modulating female flower of coconut (*Cocos nucifera* L.). Agriculture 2025;15:2336.
26. Li Y, Zheng Y, Zhang Y, Xu J, Gao G. Antioxidant activity of coconut (*Cocos nucifera* L.) protein fractions. Molecules 2018;23:707.
27. Na Nakorn S, Dokduang H, Namwat N, Klanrit P, Wangwiwatsin A, Promraksa B, *et al*. Antioxidant and longevity inducing properties of coconut water on human dermal fibroblasts. Heliyon 2024;10:e41010.
28. Erukainure OL, Chukwuma CI. Coconut (*Cocos nucifera* (L.)) water improves glucose uptake with concomitant modulation of antioxidant and purinergic activities in isolated rat psoas muscles. Plants (Basel) 2024;13:665.
29. Akter F, Bhuiya NM, Hasan N, Rokeya B, Raihan SZ, Al Mahmud Z. *Cocos nucifera* endocarp extract exhibits anti-diabetic and antilipidemic activities in diabetic rat model. Int J Sci Res Dent Med Sci 2022;4:8-15.
30. Anyiam IV, Opara CN. Phytochemicals and antimicrobial activity of coconut water (*Cocos nucifera*) on microbial pathogens. GSC Biol Pharm Sci 2023;25:273-82.
31. Asiamah I, Obiri SA, Tamekloe W, Armah FA, Borquaye LS. Applications of molecular docking in natural products-based drug discovery. Sci Afr 2023;20:e01593.
32. Agu PC, Afukwa CA, Orji OU, Ezeh EM, Ofoke IH, Ogbu CO, *et al*. Molecular docking as a tool for the discovery of molecular targets of nutraceuticals in diseases management. Sci Rep 2023;13:13398.
33. Gao L, Wang Y, Guo Q, Li D. Identification and functional analysis of transcription factors related to coconut (*Cocos nucifera* L.) endosperm development based on ATAC-seq. Trop Plants 2022;1:8.
34. Bose R, Ghosh S, Singh M, Singh S. Beyond the beverage: The versatility and health benefits of coconut water. J Drug Deliv Ther 2026;16:171-6.

Source of Support: Nil. **Conflicts of Interest:** None declared.