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REVIEW ARTICLE

Cocos nucifera Linn.: A Promising Candidate for Drug Development

Bijesh Vatakkeel[1*], R. Mythreyi[1] and E. N. Siju[2]

[1]Chettinad School of Pharmaceutical Sciences, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education, Kelambakkam, Chennai - 603103, Tamil Nadu, India; vadakkeel@gmail.com

[2]Department of Pharmacology, College of Pharmaceutical Science, Government Medical College, Kannur - 670503, Kerala, India

Abstract

Cocos nucifera Linn. (Arecaceae) is a common palm found in different parts of the world and is consumed for various purposes, especially food and oil. It is widely used as a nutraceutical globally. *Cocos nucifera* has a wide range of conventional medical applications in inflammation, protozoal and microbial infection, cancer, hepatic illness, diabetes, mellitus, pain, epilepsy, fungal infection, and depression. Different parts of *C. nucifera* like leaves, flowers, roots, oil, and cotyledon were explored for scientific authentication in various illnesses. The presence of phytochemicals like amino acids (lauric acid, arginine, caprylic acid, linoleic acid and palmitic acid), vitamin C, saponins, phenols, terpenoids, phenolics, and tannins were reported in *C. nucifera* and this knowledge further hint for hidden pharmacological activities. This paper presents a review of the phytopharmacological activities of *C. nucifera* so that it may be used for developing a promising herbal candidate for the drug discovery process.

Keywords: Antidiabetic, Antioxidant, *Cocos nucifera*, DPPH, MTT

1. Introduction

Cocos nucifera Linn. (Arecaceae) is mainly cultivated in tropical areas like India, Africa, and America for edible coconut fruit[1]. The *C. nucifera* is also known as the "tree of life" or "tree of heaven" and nature's greatest gift to man as every part of the plant has value for the community's consumption[2].

The various parts of the *Cocos nucifera* plant like leaves, flowers, oil, endocarp, and roots were used traditionally in folkloric medicine by the diverse communities of the world. In traditional medicine, the fruits of the *C. nucifera* tree have long been used as painkillers, antibacterial, parasiticides, antineoplastic, and cardiotonic[3]. The tender coconut water and coconut kernel have a variety of medicinal characteristics, including antibiotic, fungicidal, antiviral, anthelmintic, antidermatophytic, antioxidant, hypoglycemic, hepatoprotective, and immunomodulatory[4]. Coconut milk is used for the treatment of illnesses like hematemesis, gallstones, and urinary issues. Coconut oil has been used as a burn wound remedy[5]. Additionally, coconut oil supports the immunological system in people. They are found to diminish the proinflammatory cytokines[6,7].

Numerous scientific studies were carried out in the different parts of *Cocos nucifera* to standardize and validate the claims of folkloric knowledge and these documented research outputs are to be compiled in an updated manner so that further studies can be promoted and a promising new chemical entity can be developed.

1.1 Taxonomical Classification

Domain: Eukaryota
Kingdom: Plantae
Phylum: Spermatophyta
Subphylum: Angiospermae
Class: Monocotyledonae
Order: Arecales

*Author for correspondence

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Family: Arecaceae
Genus: *Cocos*
Species: *Cocos nucifera*

1.2 Synonyms

English (Coconut); Hindi (*Nariyal*) Bengali (*Nariel*); French (*Coco, Noix de coco*); German (*kokospalme*); Italian (*cocco*); Malayalam (*keram*); Lao (*Sino-Tibetan*, *Phaawz*); Tamil (*tennai-maram*), Malay (*Kelapa*); Mandinka (*Tubabsibo,coc*); Spanish (*cocotero,coco de agua, coco*); Swahili (*Mnazi*); Thai (*ma phrao*); Trade name (coconut); Manipuri (*Yubi*); Marathi (*Naral*).

1.3 Microscopy

The microscopical analysis of the roots of *C. nucifera* root demonstrated the presence of a large inner and outer cortex, as well as a solid round stele. The surrounding compact parenchymatous zone of the cortex is differentiated. In the center, the stele is arranged in a circular shape. The air chambers, metaxylem component, external cortex, pith, phloem, and partition filaments are characteristic of a thin root. A bundle of xylem elements and fibres with black inclusions, xylem elements with annular thickenings, and xylem components with spiral and scalariform thickening are powder characteristics of the root[8].

1.4 Botanical Description

Cocos nucifera is a slender palm tree distributed in the tropical region. It has a cylindrically shaped trunk with a brown or brownish-grey-coloured surface. The surface of the trunk has circular leaf scars. The leaves of *C. nucifera* are pinnate and feather-shaped with a length of 6-8 meters. The roots are fasciculate, smooth surfaced and capped with a dark brown root cap. The flowers appear as branched clusters located at the base of the leaves. The spadix of the inflorescence is stout and erect, enclosed by the tough spathe. The axis is branched, with the branches bearing sessile flowers, both staminate and pistillate. The fruits are drupe and ovoid shaped. The fruits consist of brown fibrous bark and hard shell. The central cavity consists of coconut water.

1.5 Phytochemistry of *Cocos nucifera* Linn.

The literature review on the phytochemistry (Figure 1) of different parts of *C. nucifera* is given below:

1.5.1 Coconut Cotyledons

The methanolic extract contains carbohydrate and chloroform extract contain lipids as primary metabolites. The secondary metabolites present in cotyledons are cardiac glycosides, phenolics, and tannins[9].

1.5.2 Endosperm

The endosperm of *C. nucifera* contains carotenoids, tannins, flavonoids, alkaloids, steroids, phenols, saponins, and trace amounts of glycosides[10].

1.5.3 Inflorescence

The phytochemical analysis of *C. nucifera* flowers indicated that steroids, alkaloids, flavonoids, phenolic substances, and tannins were present[1].

1.5.4 Coconut Shell

Alkaloids, steroids, flavonoids, glycosides, saponins, tannins, and phenols were discovered in the crude extracts[11].

1.5.5 Coconut Oil

The triglycerides present in coconut oil are exclusively short-chain and medium-chain saturated fatty acids as well as unsaturated fatty acids. The main medium-chain fatty acid in coconut oil is lauric acid. Caprylic acid, capric acid, caproic acid, and myristic acid are additional medium-chain saturated fatty acids that are present. Palmitic acid and stearic acid are two examples of long-chain fatty acids. Linoleic acid, linolenic acid, arachidonic acid, and eicosanoic acid are among the unsaturated fatty acids present[12].

1.5.6 Leaf

The coconut leaf methanolic extract underwent phytochemical analysis, which revealed that it contained considerable amounts of flavonoids, phenols, saponins, terpenoids, and triterpenes. A small amount of tannins, alkaloids, and glycosides are also found[13].

1.5.7 Liquid Albumen

Vitamin C, nicotinic acid, pantothenic acid, biotin, riboflavin, folic acid, and trace amounts of vitamins B1, B6, and C are also present. Other nutrients include amino acids, L-arginine, plant hormones (auxin, 1,3-diphenylurea, and cytokinin), and enzymes

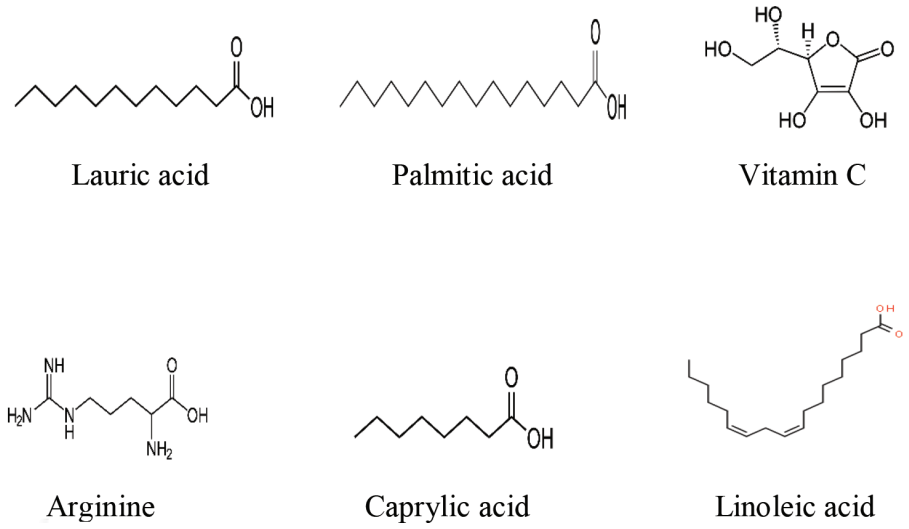

Figure 1. Major phytochemicals of *Cocos nucifera*.

(acid phosphatase, catalase, dehydrogenase, diastase, peroxidase[1].

1.5.8 Coconut Shell

Aqueous distillate from the shell powder of *C. nucifera* Linn. was examined, and several compounds were found, including dodecanoic acid, tetradecanoic acid, pentadecanoic acid, hexadecanoic acid, and squalene.

2. Pharmacological Studies of *Cocos nucifera* Linn.

The researchers subjected various parts of the *C. nucifera* to confirm the traditional medicinal uses. They can be summarized as below.

2.1 Antioxidant and Antimicrobial Activity

The antioxidant activity of the ethanolic extract, dry distilled extract, and aqueous extracts of the *C. nucifera* endocarp was investigated by Rajeev KS *et al*., using a DPPH radical scavenging assay. They used the Agar disc diffusion method to examine the antibacterial and antifungal properties of extracts. The research revealed *C. nucifera*'s promising anti-inflammatory, anti-bacterial, and antifungal properties. All of the *Trichophyton* species - *Trichophyton mentagrophytes*, *Trichophyton tonsurans*, *Trichophyton rubrum*, and Microsporum species like *Microsporum canis*, *M. audouinii* and *T. violaceum* are susceptible to the antifungal properties of the alcohol extract[14]. Jose M *et al*., evaluated the antimicrobial properties of *C. nucifera* (coconut) husk against common oral pathogens. The antibacterial activity of the alcohol-based *C. nucifera* extract was significantly concentration-dependent. The inhibitory effect was more severe with Candida and the majority of cariogenic organisms, with a zone of inhibition spanning from 4.6mm to 16.3mm[15].

In 2021, Uche Chidiebere evaluated the antibacterial activity of the ethanolic extract of *C. nucifera* (coconut) husk ash against a variety of harmful bacteria, including *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Escherichia coli*, as well as their capacity to treat wounds in experimental rats. On albino rats, an excision wound model was used to assess the healing capacity of the ointment made from ethanolic extract of *C. nucifera* husk. The antibacterial study was performed using the agar well diffusion method. The findings demonstrated that topical route administration of extract made from coconut husk ash blended into an ointment base accelerated wound healing, specifically increasing epithelialization in treatment groups[16]. The antioxidant activity of protein fractions was assessed by Li Y *et al*[17]. The protein fractions of coconut cake were examined for their characterisation, nutritional value, and antioxidant activity. Prolamin, glutelin-1, and glutelin-2 all possessed significant reducing power and good radical scavenging activity, and globulin and prolamin both exhibited significant ion chelating properties. Additionally, every fraction except glutelin-2 could successfully shield DNA from oxidative damage[17].

Udaya Prakash Nyayiru Kannaian *et al.,* studied the antioxidant activities of *C. nucifera* using DPPH, FRAP, FTC, TBA, and Nitric oxide radical scavenging assays. High content of secondary metabolites was extracted by methanolic extraction using cold percolation, and there was also noticeable antioxidant activity[18]. The antibacterial activity of the mesocarp of *C. nucifera* was assessed by Indira Bairy KS *et al*[26]. The fresh mesocarp of an unripe coconut was processed by filtration and mixing to get the crude aqueous extract. Gram-positive and gram-negative bacteria were used. When tested, it had an antibacterial impact on all gram-positive cocci[26].

2.2 Hepatoprotective Activity

Manikantan *et al.*, looked at the anti-hepatotoxic activities of the acetone extract from the inflorescence of coconut. The study's findings showed that the groups pre-treated with the extract exhibited a significant decrease in liver superoxide dismutase levels, reduced glutathione, glutathione-S-transferase, and glutathione peroxidase levels, and also inhibited the rise in serum transferase and alkaline phosphatase levels. Additionally, the extract reduced the increased level of malondialdehyde[19]. The preventive effects of alcoholic and aqueous extracts of endocarp against hepatotoxicity induced by paracetamol in rats were investigated by Nishant Singh Katiyar *et al*[20]. Both extracts considerably decreased the raised blood levels of liver enzymes caused by paracetamol. Animals given the two extracts were partially or completely protected against histological alterations (steatosis, necrosis, etc.)[20].

2.3 Anticancer Activity

Cocos nucifera Linn.'s anticancer efficacy was evaluated by Nicole M Tayler *et al*[21]. This study involved extracting and testing *C. nucifera* against a line of breast cancer cells[21]. The anti-cancer properties of the ethanolic extract of *C. nucifera* flowers were assessed by VM Berlin Grace and Monisha M *et al*[22]. The MTT test was used to determine the extract's anti-cancer impact on a human lung cancer cell line, and an *in vitro* assay for the degradation of egg albumin was used to determine the extract's anti-inflammatory efficacy. Tannins and phytosterols are present, according to the biochemical assays. The gas chromatography-mass spectrometry examination identified a total of 152 phytochemicals, which also included a few fatty acids, polyphenols, and terpenes as well as various phytosterols. The extract had a 96.15% dose-dependent growth inhibitory effect on the cell line. The discovered secondary metabolites, including eugenol, catechol, stigmasterol, campesterol, and t-butyl hydroquinone, might have exerted these medicinal effects[22]. The proanthocyanidins soluble in ethyl acetate from the immature inflorescence of *C. nucifera*. were tested for their anticancer property. Compared to tamoxifen, EASPA also had higher cytotoxic action against Hela cells, but PC3 cells showed less cytotoxicity[23].

A brief communication on the anti-neoplastic properties of *C. nucifera* was written by PR Koscheket *et al*[24]. He evaluated the aqueous husk fibre fractions from the different varieties of *C. nucifera* husks for their *in vitro* anti-tumour properties. Cytotoxicity against cancer cells was determined by the MTT assay[24]. The anticancer properties of the ethanolic extract of *C. nucifera*'s tender fruits were investigated by Shrabanti Dev *et al*[25]. According to this study, tender fruit ethanolic extract has a significant amount of antioxidant activity. When compared to a carcinogenic control, the extract dramatically reduced the number, size, yield, and burden of the tumours in skin cancer model mice produced by DMBA and Croton oil. Natural antioxidants including GSH, SOD, and catalase were boosted by the extract[25].

2.4 Antiparasitic, Anti-malarial Activity

The effectiveness of the fruit of *C. nucifera* against intestinal parasites in sheep was examined by Oliveira LM *et al*[27]. The studies were performed on the ethyl acetate extract that was produced from the liquid of green coconut husk fibre. The *in vitro* assay was done using Haemonchuscontortus for larval development and egg hatching test. At the highest studied concentrations, extract efficacy was 100% for egg hatching and 99.77% for larval development[27]. Adebayo JO *et al.*, assessed the antimalarial and toxicological potentials of husk fibre extracts of five Nigerian species of *C. nucifera*. The results demonstrated that alkaloids, tannins, and flavonoids are present in WAT (West African Tall) ethyl acetate extract fraction (WATEAEF), and were effective against *Plasmodium falciparum* and *Plasmodium berghei*[28].

The use of *Cocos nucifera* as an antimalarial treatment in Malaysian indigenous medicine was examined by Al Adhroey AH *et al*[29]. The findings showed that the extract had some phytochemical components and was safe to take orally from a toxicological perspective. In all three *in vivo* assessment experiments, the extract considerably decreased the parasitemia. However, the extract did not substantially prolong the period of survival of the infected mice[29]. The antiplasmodial efficacy of *C. nucifera* leaves was examined by Tayler N.M. *et al*., in mice infected with *Plasmodium berghei*. Comparing intramuscular administration of a *C. nucifera* leaf decoction to intraperitoneal, subcutaneous, and intragastric approaches, the results demonstrated that intramuscular administration to mice produced the best effects. The extract has a 48% inhibitory preventive impact, but no curative benefit, according to their findings. Finally, in a 4-day suppressive trial, they discovered that when delivered intramuscularly, the extract can limit the growth of the parasite by up to 54% at sub-toxic levels[30]. Nicole M Tayler *et al*., analysed the antiparasitic activity of the *C. nucifera* L. The effectiveness of *C. nucifera* husk, leaves, pulp, and milk against *Trypanosoma cruzi*, *Leishmania donovani*, and *Plasmodium falciparum* parasites was examined in this study. The aqueous decoctions of leaves only showed antiplasmodial activity[21].

2.5 Hypoglycemic Activity

The alpha-amylase inhibitory effects of *Cocos nucifera* husk were studied by Hamdalat Folake *et al*[31]. The pancreatic-amylase and lipid peroxidation inhibitory effects of methanolic extract and ethyl acetate fraction were identified. The total phenolic content and antioxidant capacity of the ethanolic fraction were significantly larger than those of the methanolic extract. The ethanolic fraction also demonstrated higher inhibitory effects on alpha-amylase activity and lipid peroxidation following intraperitoneal treatment of the *C. nucifera* extract to alloxan-induced hyperglycemic rats, decreasing blood glucose levels within 5 days[31]. A 2012 study by Victor Emojevwe examined the anti-diabetic properties of a coconut husk extract. On 21 diabetic rats induced with alloxan, the *C. nucifera* (coconut) husk was investigated. Blood glucose levels were dramatically lowered after extract consumption in diabetic rats under treatment. The rats that received the extracts (coconut husk tea) and those that received Daonil and Metformin both had the same regeneration, according to histopathological research. Therefore, it was determined that there were considerable hypoglycemic and anti-diabetic benefits of *C. nucifera* (coconut) husk tea in alloxan-induced diabetes. This result is similar to what is produced when Daonil and Metformin are combined, and it may be used as a useful adjunct in the treatment of type 2 diabetes[32].

The anti-diabetic and antilipidemic effects of *Cocos* nut endocarp extract were assessed in a diabetic rat model by Farjana Akter *et al*[33]. The endocarp of the *C. nucifera* was extracted using methanol and h-hexane, chloroform, and ethyl acetate fractions were prepared. Thirty diabetic rats induced by streptozotocin were employed in total, divided into six experimental groups. For a total of 14 days, all the animals received treatment. Acute hypoglycemia effects, lipid profiles, changes in body weight, and fasting blood sugar levels were all monitored. Additionally, phytochemical screening and anti-oxidant tests were carried out. The group given ethyl acetate fraction treatment saw a strong hypoglycemic impact[33]. On streptozotocin (STZ)-induced diabetic rats, Naskar S *et al.,* looked at the impact of the antidiabetic activity on lipid profiles and the cardioprotective effect of hydro-methanol extract of *Cocos nucifera* (HECN). In comparison to the diabetic control group, fasting blood glucose levels were significantly lower in the animals treated with HECN. Serum enzyme levels, lipid peroxidation, and antioxidant enzyme levels, as well as cholesterol and triglyceride levels in treated groups, were restored toward normal levels in comparison to diabetic control groups, and the values were significant and comparable with the standard group[34].

Saranya *et al*., studied the biochemical changes in the antidiabetic activity of coconut flowers in diabetic rats. When given orally for 30 days, a *C. nucifera* flower extract reduced blood sugar, glycosylated haemoglobin, uric acid, and creatinine levels in diabetic rats. The abnormally high levels of serum aminotransferases and alkaline phosphatase returned to normal. The extract administration restored the plasma protein levels in the diabetic rats to levels that were close to normal. The extract increased the amount of glycogen present and improved glycogen synthase and glycogen

phosphorylase activity.[35]. Pinto IF *et al.,* evaluated the hypoglycemic activity of *C. nucifera* water in alloxan-induced diabetic rats. The findings demonstrated that rats in the coconut water and diabetic group had increased body weight and maintained blood glucose levels in comparison to the control group, as well as decreased HbA1c levels[36].

2.6 Anthelmintic Activity

The liquid extracted from the green coconut's bark (Liquid from Bark of Green Coconut (LBGC)) and its butanol extract were tested for their anthelmintic effects on mouse intestinal nematodes by Costa CT *et al*[37]. Phytochemical analyses were used to ascertain the chemical makeup of the LBGC and its butanol extract. The effectiveness of a 1000 mg/kg dosage of butanol extract in lowering the mouse worm load was 90.7%. Triterpenes, saponins and condensed tannins were detected by phytochemical testing in the LBGC and butanol extracts[37].

2.7 Antiepileptic Activity

The antiepileptic effectiveness of *Cocos nucifera* flowers against experimentally induced convulsions in rats was assessed by Archana B *et al*[38]. Pentylene Tetrazole (PTZ) and Maximal Electroshocks (MES) induced models were used for the investigation. Pretreatment of animals with *C. nucifera* flower extract against MES and Pentylenetetrazol-induced convulsion models showed considerable anticonvulsant efficacy[38].

2.8 Antidepressant Activity

Lima EBC *et al.*, studied the antidepressant activity of *Cocos nucifera*. One hour following the final dose of medicine, the mice underwent the Forced Swimming Test (FST), Tail Suspension Test (TST) and Open Field Test (OFT). Immediately following the behavioural tests, the brains of the animals were taken for neurochemical analysis. The findings revealed that hydroalcoholic extract had an antidepressant-like effect by reducing the immobility duration during the FST and TST examinations. The extract treatment caused levels of malondialdehyde to drop. Additionally, nitrite levels in all doses were reduced by the administration[39].

2.9 Analgesic Activity

Alviano *et al.*, showed that *Cocos nucifera* aqueous husk fibre extract had analgesic properties. The acetic acid-induced writhing response in mice was prevented when *C. nucifera* aqueous extract was taken orally. Treatment of rats with this plant extract (dose of 200 mg/kg) caused attenuation in response to the heat stimulation, as shown by tail flick and hot plate assays[40].

2.10 Peptic Ulcer

Nneli *et al.*, examined the antiulcerogenic properties of coconut extract in rats. The outcomes demonstrated that via macroscopic inspection, coconut milk exhibited protective effects on the inflamed stomach mucosa comparable to those of conventional sucralfate[41].

2.11 Anti-inflammatory Activity

The anti-inflammatory and antinociceptive properties of *Cocos nucifera* Linn. were examined by Sebastian Rinaldi *et al.*, utilising the acetic acid-induced abdominal writhing, Eddy's hot plate, and Rat paw oedema. The findings supported the widespread use of *C. nucifera* in treating several inflammatory illnesses by showing that both the plant and its fractions possess antinociceptive and anti-inflammatory properties[42]. The anti-inflammatory ethanolic extract of *C. nucifera* flowers was assessed by VM Berlin Grace and Monisha M *et al*[22]. An *in vitro* egg albumin degradation assay was used to assess the extract's anti-inflammatory effect. The extract at 1000g/ml and the 4000g/ml treatment exhibited an effective inhibition of protein breakdown (>50%) as a sign of anti-inflammatory activity[22].

2.12 Anti-hypertensive Activity

The anti-hypertensive potential of coconut (*Cocos nucifera* L.) water was assessed by AI Airaodion *et al.*, in Wistar rats. When comparing animals fed a diet without coconut water treatment to those who were fed a diet and treated with coconut water, or to the control group, respectively, in response to heat stimulation, a substantial rise in blood pressure was seen[43].

2.13 Nephroprotective Activity

Famurewa *et al.*, investigated the nephroprotective activity of virgin coconut oil on nephrotoxicity produced by diclofenac in rats. In the study, diclofenac elevated serum urea and creatinine, renal tumour necrosis factor-α and malondialdehyde levels markedly increased and decreased the renal glutathione peroxidase, catalase, and superoxide

dismutase. Histopathological alterations were also seen. Virgin coconut oil pretreatment attenuated histological changes of renal damage and restored antioxidant enzyme activity and TNF-α levels in the kidney[44].

3. Conclusion

It is concluded that researchers from around the world conducted scientific pharmacological evaluations of *Cocos nucifera* to confirm the traditional medicinal uses such as anti-oxidant, anti-inflammatory, anti-protozoal, anti-microbial, anti-cancer, hepatoprotective, anti-diabetic, analgesic, anti-epileptic, anti-fungal, and anti-depressant, and others. These documented scientific studies may aid in the development of safer herbal chemical moiety in drug discovery.

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